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Article

Palladium-Catalyzed C−H Arylation and Azetidination of Pentacyclic Triterpenoids

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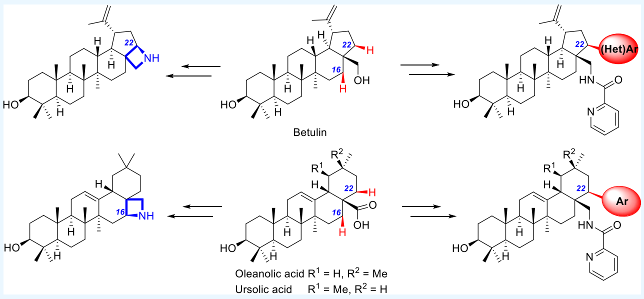
ABSTRACT: Synthetic protocols for site-selective palladium-catalyzed C−H arylation and azetidination of pentacyclic triterpenoids have been developed. Betulin, oleanolic, and ursolic acids were converted into primary amines C(28)-NH_2 that were further transformed into the corresponding picolinamides. The latter was found to be a suitable directing group for triterpenoid C(sp^3)-H (het)arylation with iodo(het)arenes in the presence of $Pd(OAc)_2/CuBr_2/CsOAc$ system. C(sp^3)-H (het)arylation provided yields from 29 to 83%, and the C(22)/C(16) selectivity from 9:1 in the lupane (betulin) series to 19:1 in the oleane and ursane series. The highest isolated yields of C(sp^3)-H arylated products were achieved with iodoarenes bearing electron-donating groups, but the use of electron-deficient iodoarenes gave a significant proportion of *N*-picolinoyl azetidine side product. The latter were obtained with good selectivity as major products when 1-iodo-4-nitrobenzene was used as an additive. C(sp^3)-H arylation revealed C(22)-selectivity in all tested triterpenoid series; however, the azetidination occurred at C(22) in lupane (betulin) series and at C(16) in oleane series. C(sp^3)-H (het)arylation and azetidination is a new entry in the derivatization of natural triterpenoids and can be regarded as a useful tool for further exploration in terms of medicinal chemistry.



INTRODUCTION

Naturally abundant pentacyclic triterpenoids (PCT) are plant secondary metabolites, which have aroused significant interest due to a wide range of their biological activities such as antitumor[1,2] antidiabetic,[3−5] anti-inflammatory,[6−8] and antiviral properties.[9,10] Betulin and oleanolic, ursolic, and betulinic acids are the most naturally abundant and therefore most notorious compounds of this type.[11−13] Development of semisynthetic derivatives of PCTs by chemical modifications is known to ameliorate certain designed properties, among others: cytotoxic selectivity toward cancer cells, enhanced aqueous solubility,[14] and bioavailability.[15]

The vast majority of synthetic methods for the decoration of PCT core involve the use of C(3) and C(28) C−O functionalities and the available olefin moiety.[16] On the other hand, the transition metal catalyzed functionalization of C(sp^3)-H bonds, which is considered a powerful synthetic tool,[17] has been far less applied to the triterpenoid skeletons. Literature analysis on C(sp^3)-H activation in the PCT core has shown only a few examples (Figure 1). Thus, the Yu group[18] has reported site-selective C−H hydroxylation of different pentacyclic triterpenoids using Schönecker and Baran's Cu-mediated aerobic conditions ($Cu(OTf)_2$, O_2). In this case, the site-selectivity has been controlled by the transient pyridine-imino directing group, which was introduced using C(28) aldehyde. Baldwin's method[19] was successfully applied to introduce and modify a hydroxyl group on a nonactivated C(23) methyl group by several research groups.[20] Selective oxygenation of oleanolic C(23) using iridium catalyzed hydroxyl group-directed silylation/Tamao-Fleming oxidation sequence was explored by Hartwig.[21] Maulide group reported an approach for functionalization of the B ring in oleanane triterpenoids using a hydroxylated C(23) group as the key functionality for further linear reaction sequence.[22] Lu group developed an Ir-catalyzed C(sp^3)-H amination reaction using $TrocN_3$ as an easily transformable amine source at C(23) of oleanolic triterpenoid as an example of a topologically and functionally complex natural product substrate.[23] The betulin scaffold was also investigated in intramolecular metallonitrene-based C(sp^3)-H amination of sulfamate esters. White group discovered that [Mn(tBuPc)]SbF_6 catalyst preferentially forms C−N bond at the γ-C−H bond of the equatorial C(23) methyl group and provided oxathiazinane with high site- and

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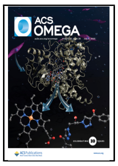

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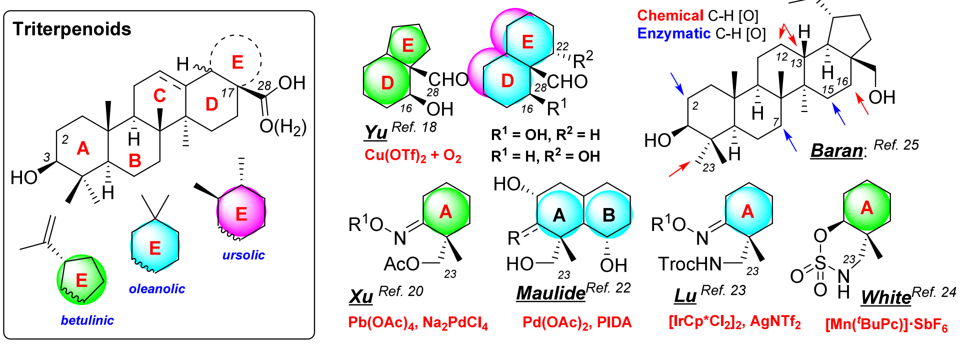

Figure 1. Previously reported C−H functionalized PCT.

diastereoselectivity.[24] Baran's group investigated different C−H oxidation methods on the betulin skeleton to improve the aqueous solubility of this natural product. The authors observed that nondirected or enzymatic oxidation of C−H bonds results in low selectivity and insufficient reaction yield.[25]

To the best of our knowledge, besides the aforementioned C−H hydroxylation and C−H amination examples, there are no reports on C−C bond forming C−H activation approaches within the pentacyclic terpenoid series; however, some successful examples of C(sp^3)-H arylation of smaller natural terpene molecules were reported.[26] Furthermore, since the beginning of this century, plenty of different methods for C(sp^3)-H arylation using different catalytic systems and directing groups suitable for the late-stage functionalization of complex molecules have been developed.[27] Hence, we report here an investigation of previously unexplored site-selective palladium-catalyzed C(sp^3)-H (het)arylation of pentacyclic triterpenoids.

■ RESULTS AND DISCUSSION

We started our investigation by preparing PCT derivatives bearing Daugulis directing groups[28] that are attached to the pentacyclic skeleton either by a native carboxylic amide **2a−d** or by a more flexible −CH$_2$−NH− linker **3a−d** (Figure 2). 8-Aminoquinoline amides **2a−d** were prepared by the coupling of betulonic, ursonic, and oleanonic acids with an 8-aminoquinoline, with pretransformation of acids into acid chlorides.[29] On the other hand, picolinamide[30] directing auxiliary was introduced by an amine reaction with picolinic acid.

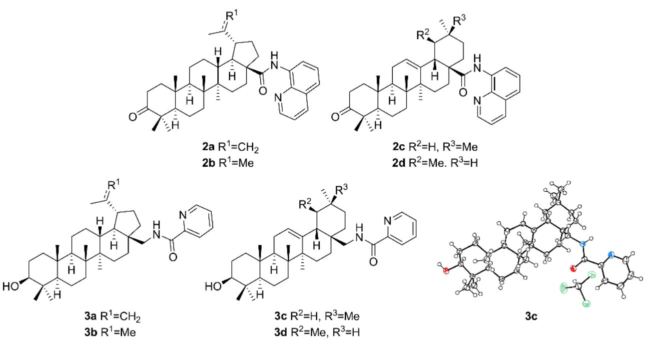

Figure 2. Triterpenic 8-aminoquinolinamides **2a−d** and picolinamides **3a−d**.

First, oxime **4a** was synthesized from commercially available betulin (**1a**) according to the literature procedure.[31] To explore and compare the possible reactivity of the isopropenyl moiety during the C−H activation, the saturated congener **4b** was also obtained (Scheme 1). Next, we proceeded with oxime **4a** and **4b** reduction using NaBH$_3$CN/TiCl$_4$ and amidation of the obtained primary amines by freshly generated picolinic chloride/Et$_3$N. Picolinic amides **3a** and **3b** were obtained over two steps with overall 81 and 60% yields, respectively. (Scheme 1).

Commercially available oleanolic and ursolic acids were converted into picolinamides **3c**[32] and **3d** in three steps.[33,34] In situ-generated activated esters were converted into amides **5a** and **5b**. Reduction of the latter with LiAlH$_4$ afforded primary amines that were converted into picolinamides using previously developed reaction conditions (Scheme 2).

With starting materials **2a** and **3a** in hand, we explored their ability to complex palladium and provide C−H deuteration products that would demonstrate the feasibility of the C−H activation event. We performed the C−H deuteration experiments in the presence of Pd(OAc)$_2$ and CsOAc using deuterated acetic acid as a solvent. Both of the tested directing groups provided C(16)/C(22) double-deuterated products (see Supporting Information Scheme S1 for C(sp^3)-H deuteration of **2a,c,d** and Scheme 8 for deuteration of **3a,c** (vide infra)). Inspired by the feasibility of the C−H activation event, we started to test possible conditions for the C−H arylation reaction. Surprisingly, no efficient reaction conditions for successful C-arylation were found in the case of quinolinamides **2a,c,d.**

To our delight, conformationally more flexible picolinamide **3a** was found to be a suitable starting material for the envisaged C−H arylation reactions. The reactive cocktail containing picolinamide **3a** (1 equiv), 4-iodoanisole (4 equiv), Pd(OAc)$_2$ (5 mol %), CuBr$_2$ (10 mol %)[35] and CsOAc (4 equiv) in toluene yielded a mixture of C(22)- and C(16)-regioisomers **6a** and **7a** in 92:8 ratio with 23% total yield (Table 1, entry 1). Changing the solvent to HFIP produced no product at all (entry 2). Then we switched to *t*AmOH and examined different bases, but CsOAc was found to be still the most efficient one (entry 6). It should be pointed out that the Ag(I) additive did not facilitate the reaction at a reasonable rate (entry 5). Gratifyingly, the use of Pd(OAc)$_2$ (5 mol %) in the presence of CuBr$_2$ (10 mol %) and CsOAc (4 equiv) in *t*AmOH gave C-arylated products **6a**/**7a** in 83% total isolated yield (entry 10). These appeared to be the best conditions, and any further variations of palladium source (entries 7,8) and

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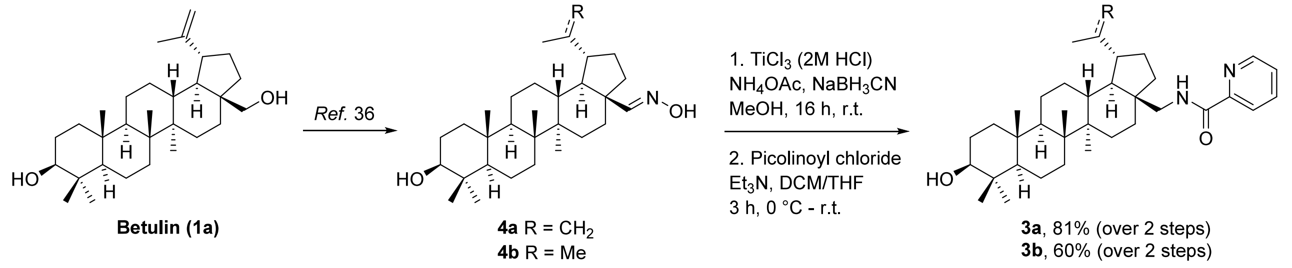
Scheme 1. Synthesis of Picolinic Amides 3a,b



Scheme 2. Synthesis of Picolinamides 3c,d

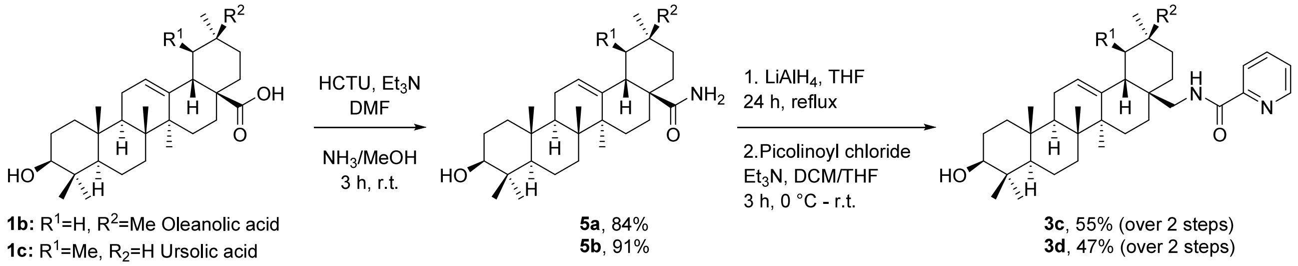
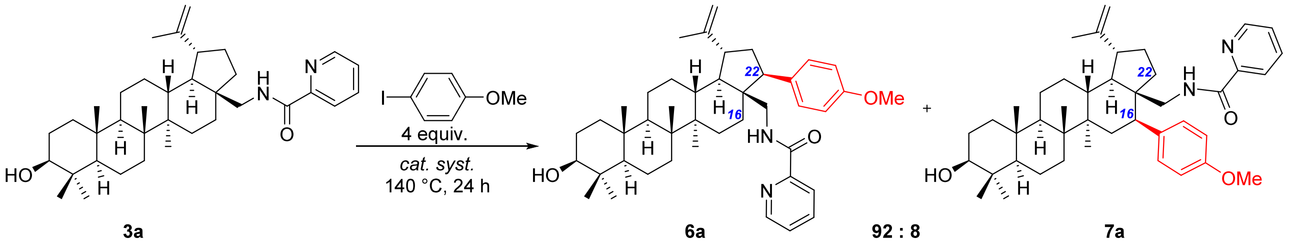


Table 1. Optimization of C(sp^3)-H Arylation Conditions for Reaction 3a → 6a + 7a

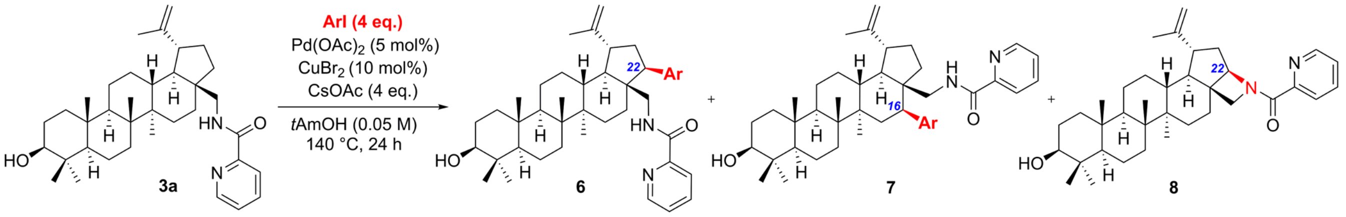


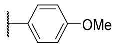
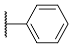
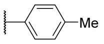
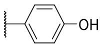
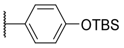
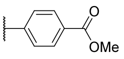
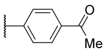
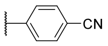
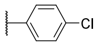
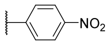
entry	catalyst (mol %)		additive (mol %)		base (4 equiv)	solvent	total isolated yield of 6a + 7a (92:8), %
1	$Pd(OAc)_2$	5	$CuBr_2$	10	CsOAc	Tol	23
2	$Pd(OAc)_2$	5	$CuBr_2$	10	CsOAc	HFIP	0
3	$Pd(OAc)_2$	5	$CuBr_2$	10	K_2CO_3	*t*AmOH	2
4	$Pd(OAc)_2$	5	$CuBr_2$	10	Cs_2CO_3	*t*AmOH	19
5	$Pd(OAc)_2$	5			AgOAc	*t*AmOH	17
6	$Pd(OAc)_2$	5			CsOAc	*t*AmOH	70
7	$Pd_2(dba)_3$	5	$CuBr_2$	10	CsOAc	*t*AmOH	76
8	$PdCl_2$	5	$CuBr_2$	10	CsOAc	*t*AmOH	78
9	$Pd(OAc)_2$	2.5	$CuBr_2$	5	CsOAc	*t*AmOH	21
10	**$Pd(OAc)_2$**	5	**$CuBr_2$**	10	**CsOAc**	***t*AmOH**	83
11	$Pd(OAc)_2$	7.5	$CuBr_2$	15	CsOAc	*t*AmOH	79
12	$Pd(OAc)_2$	10	$CuBr_2$	20	CsOAc	*t*AmOH	75
13	$Pd(OAc)_2$	20	$CuBr_2$	40	CsOAc	*t*AmOH	58
14	$Pd(OAc)_2$	5	$Cu(OAc)_2$	10	CsOAc	*t*AmOH	58
15	$Pd(OAc)_2$	5	$CuCl_2$	10	CsOAc	*t*AmOH	78

amount (entries 11–13), or Cu(II) source (entries 14,15) did not provide any improvement. We detected practically the same 92:8 ratio of regioisomers **6a**/**7a** by ^{1}H NMR in all crude reaction mixtures. We have also tested the influence of 4-iodoanisole excess on reaction outcome: the use of 2 equiv diminished the total isolated yield of products **6a** + **7a** to a 73–78% range. On the other hand, the use of 3 equiv of 4-iodoanisole in some experiments gave the total isolated yield of products **6a** + **7a** as high as 90%, yet the results had some dispersion, and a yield range of 83–90% was observed. Hence, we considered the iodoarene use in 4-fold excess as optimal.

Having found suitable C(sp^3)-H arylation conditions, we examined the scope of the aryl iodide components (Table 2). Reactions with aryl iodides possessing electron-rich aryl rings worked well, and C(sp^3)-H arylation products **6a–d**/**7a–d** were obtained in the summary yield range 50–83% (entries 1–4, Table 2). Two molecular structures of compounds **6a**[36] and **6b**[37] were unambiguously proven by their single crystal X-ray analysis (Figure 3). Once we started to perform reactions at a larger scale, the formation of C(22)-azetidine byproduct **8** was observed. Arylation employing iodoarenes with electron-withdrawing substituents proceeded poorly and provided both arylated regioisomers within a 29–54% yield range. On

Table 2. Scope and Isolated Yields of C(sp^3)-H Arylation Products of Picolinamide 3a



Ar	Yield of **6a-i** (%)	Yield of **7a-i** (%)	Yield of **8** (%)
	**6a**, 76	**7a**, 7	10
	**6b**, 64	**7b**, 9	26
	**6c**, 60	**7c**, 5	19
	**6d**, 45	**7d**, 6	10
	**6e**, 32	**7e**, 6	36
	**6f**, 32 (31)[a]	**7f**, 6 (3)[a]	56 (51)[a]
	**6g**, 22	**7g**, 7	40
	**6h**, 19	**7h**, 12	64
	**6i**, 42	**7i**, 12	44
	-	-	61

[a] Reaction time 48 h.

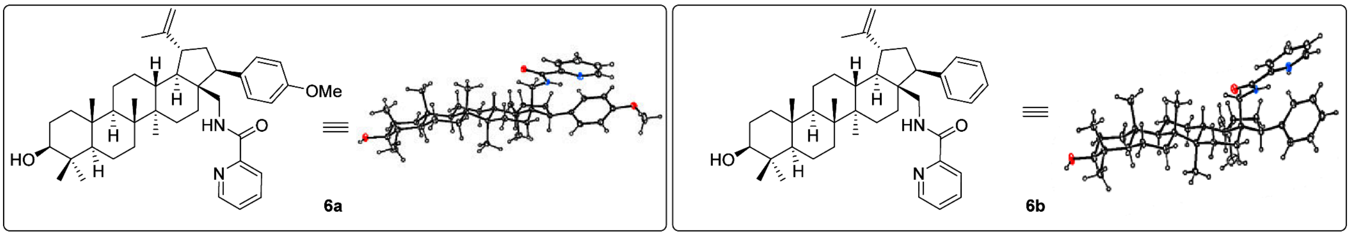
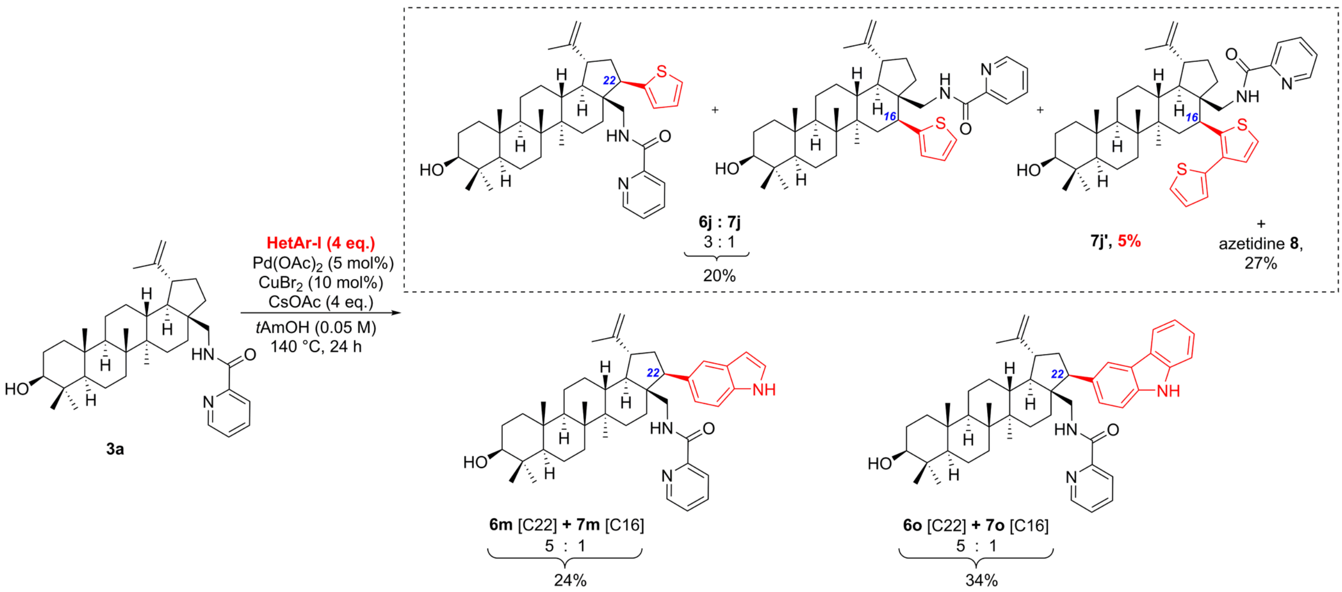


Figure 3. Single crystal X-ray diffraction analysis of **6a** and **6b**.

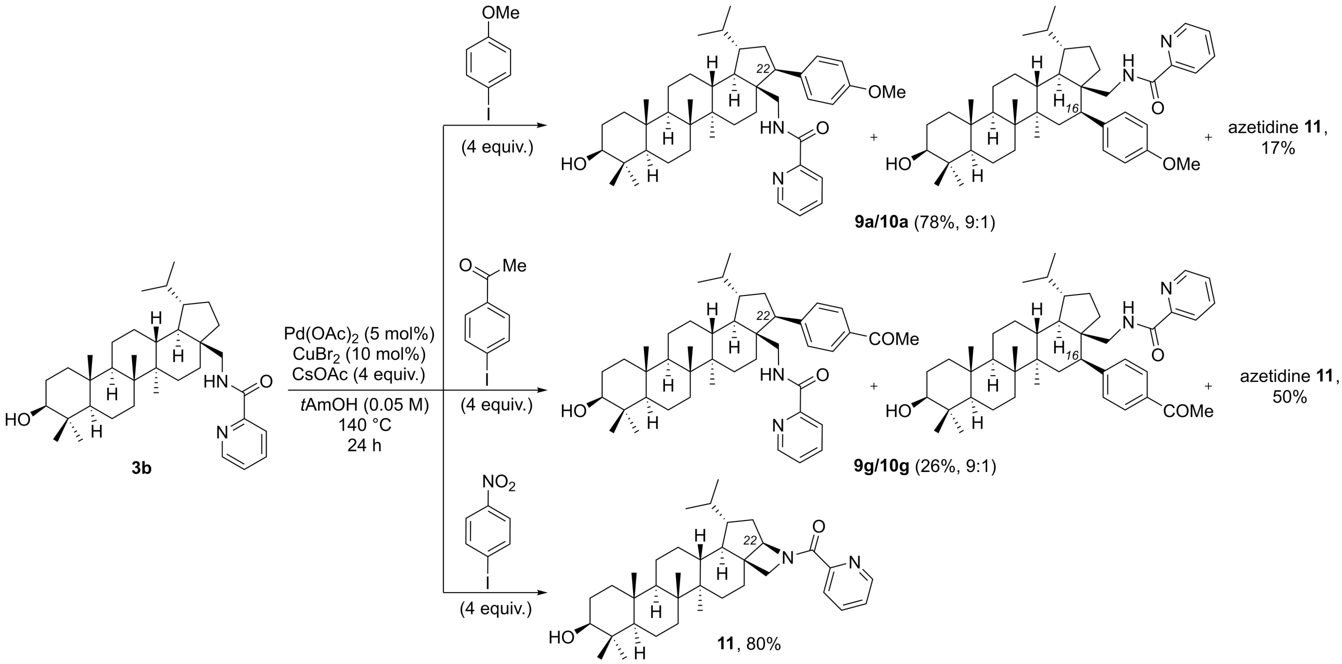
the other hand, iodobenzenes with substituents such as −COOMe, −C(O)Me, −CN, −Cl, $-NO_2$ (entries 6−10, Table 2) gave azetidine **8** as the major product in 40−64% yields. The highest azetidine yield was observed with $I-C_6H_4-CN$ (64%), but $I-C_6H_4-NO_2$ provided it as a single reaction product in 61% yield, which facilitated its isolation and purification. An additional experiment with methyl 4-iodobenzoate and extended reaction time to 48 h was performed, but it did not improve the C(sp^3)-H arylation outcome. Azetidines as C(sp^3)-H arylation byproducts have been reported before, and a targeted azetidination protocol employing AgOAc/C_6F_5I on simple model substrates has been previously reported by Wu and co-workers.[38] Additionally, it is known that azetidines can be formed in Pd-catalyzed and picolinamide-directed intramolecular C−H amination employing $PhI(OAc)_2$ as oxidant and Li_2CO_3 as a base.[39,40] However, in our hands, such a control experiment, which would lead to azetidine **8** as the main product, did not result in any conversion of starting material **3a**. It should be mentioned that the picolinamide directing group is instrumental also for the azetidination step, as a control experiment with free amine **4a′** (3β-hydroxy-lup-20(29)en-28-amine) did not result in azetidine formation. Also, control experiments run in the absence of ArI did not provide the azetidine product, and only the unchanged starting material was recovered.

We have also explored C(sp^3)-H (het)arylation reactions of **3a** with 4-iodo *N,N*-dimethyl aniline, 3-iodopyridine and 4-iodo-1-methyl-*1H*-pyrazole, but no conversion of starting

Scheme 3. C(sp^3)-H Hetarylation of Picolinamide 3a



Scheme 4. C(sp^3)-H Arylation and Azetidination of Lupane-Derived Picolinamide 3b

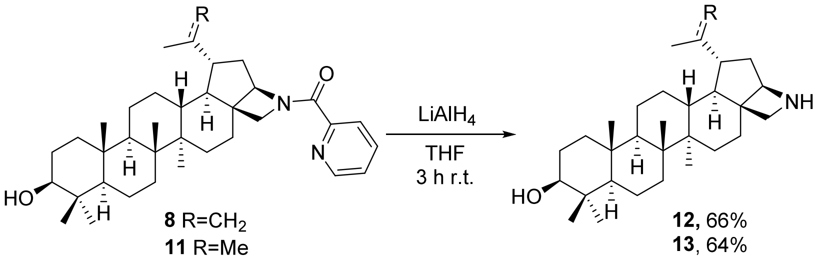


material was observed. Additionally, we have performed hetarylation with 5-iodo indole and 7-iodo carbazole (Scheme 3), and the expected products **6*m*/7m** and **6*o*/7o** were isolated in 24 and 34% yields, respectively, albeit without formation of azetidine. We also tested *N*-Cbz-protected 5-iodo indole and 7-iodo carbazole, but unexpectedly low conversion of a **3a** was observed that encumbered product isolation and characterization.

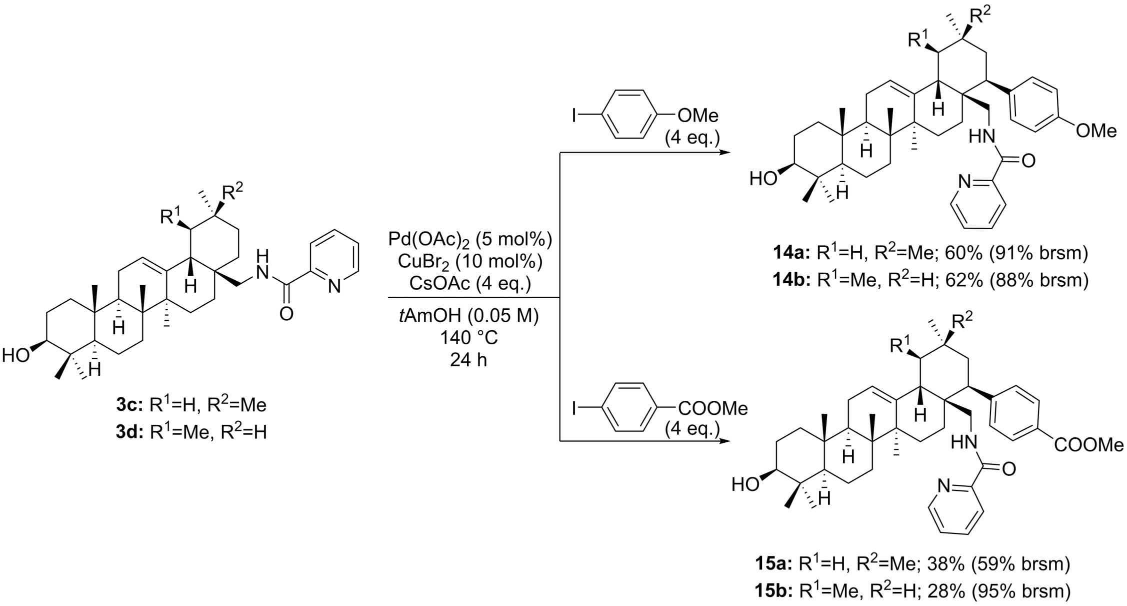
In all C(sp^3)-H (het)arylation cases discussed above, we have not detected any formation of diarylated products. Longer reaction time, higher concentration of an (het)aryl iodide component, as well as higher catalyst loading were found to be ineffective. The only exception was the reaction between **3a** and 2-iodo thiophene, which resulted in a detectable amount of diarylated product **7j′** (5%) besides monoaddition products **6*j*/7j** and azetidine **8**. However, the second C−H activation has taken place at the first installed thiophene moiety in product **7j** (Scheme 3).

In a parallel series of experiments reaction of saturated lupane-derived picolinamide **3b** with 4-iodoanisole leads to the formation of 9:1 regioisomers **9a/10a** in 78% total yield, along with 17% of azetidine **11** (Scheme 4). Next, a reaction between **3b** and 1-(4-iodophenyl)ethan-1-one gave 9:1 regioisomers **9g/10g** in 26% total yield along with 50% of azetidine **11**, but reaction with 1-iodo-4-nitrobenzene provided only azetidine **11** in very good 80% yield. Regardless of some differences in yields between the product series **6/7/8** and **9/10/11**, there are no notable differences in the reactivity between betulin-derived picolinic amide **3a** and saturated lupane-derived picolinamide **3b**.

Scheme 5. Synthesis of Unprotected Azetidines 12 and 13

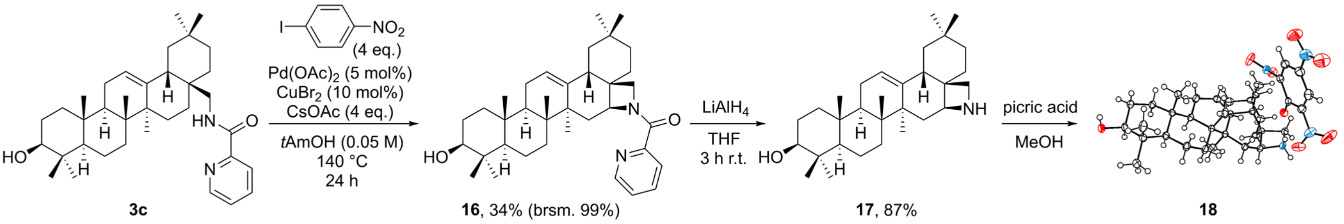


Scheme 6. C(sp^3)-H Arylation of Oleanolic and Ursolic Amides 3c,d[a]



[a]brsm = based on recovered starting material.

Scheme 7. Azetidine 17 Formation from Oleanolic Amide 3c

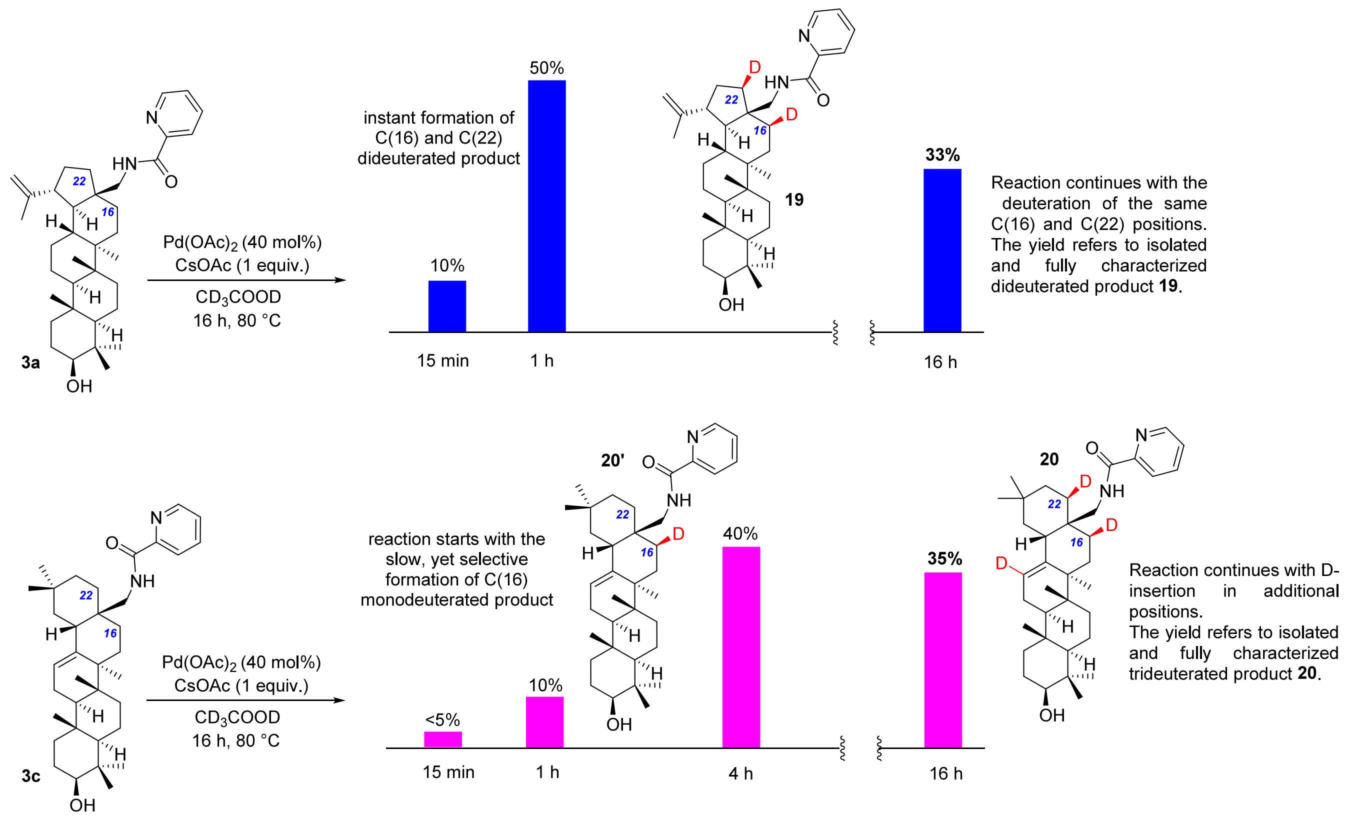


Azetidines **8** and **11** were observed as 1:1 mixtures of rotamers in their NMR spectra. In order to simplify the NMR characterization and to provide NH azetidines for further synthetic applications, we tested the cleavage of the picolinamide moiety. First, subjecting both **8** and **11** to alkaline hydrolysis conditions afforded no product. Consequently, reductive cleavage conditions employing LiAlH$_4$ in THF at room temperature afforded desired NH-azetidines **12** and **13** (Scheme 5).

Encouraged by the successful arylation of betulin and lupane core, we also have examined the arylation of oleanolic and ursolic acid-derived picolinamides **3c,d** employing 4-methoxyphenyl iodide and 4-iodobenzoic acid methyl ester (Scheme 6). Arylation of ursane and oleane cores resulted in higher 19:1 site-selectivity at C(22). Full conversion of **3c** and **3d** was not reached, but in most cases, reactions were quite clean, and after subtraction of the recovered unreacted starting material, high yields of products can be formally calculated. It is worth mentioning that analogously, as in previous cases, electron-deficient 4-iodobenzoic acid methyl ester provides significantly lower yields of arylation products **15a,b** than the reaction with 4-methoxyphenyl iodide. Interestingly, reactions of oleane and ursane starting materials **3c,d** → **14a,b**/**15a,b** did not provide the azetidine byproduct.

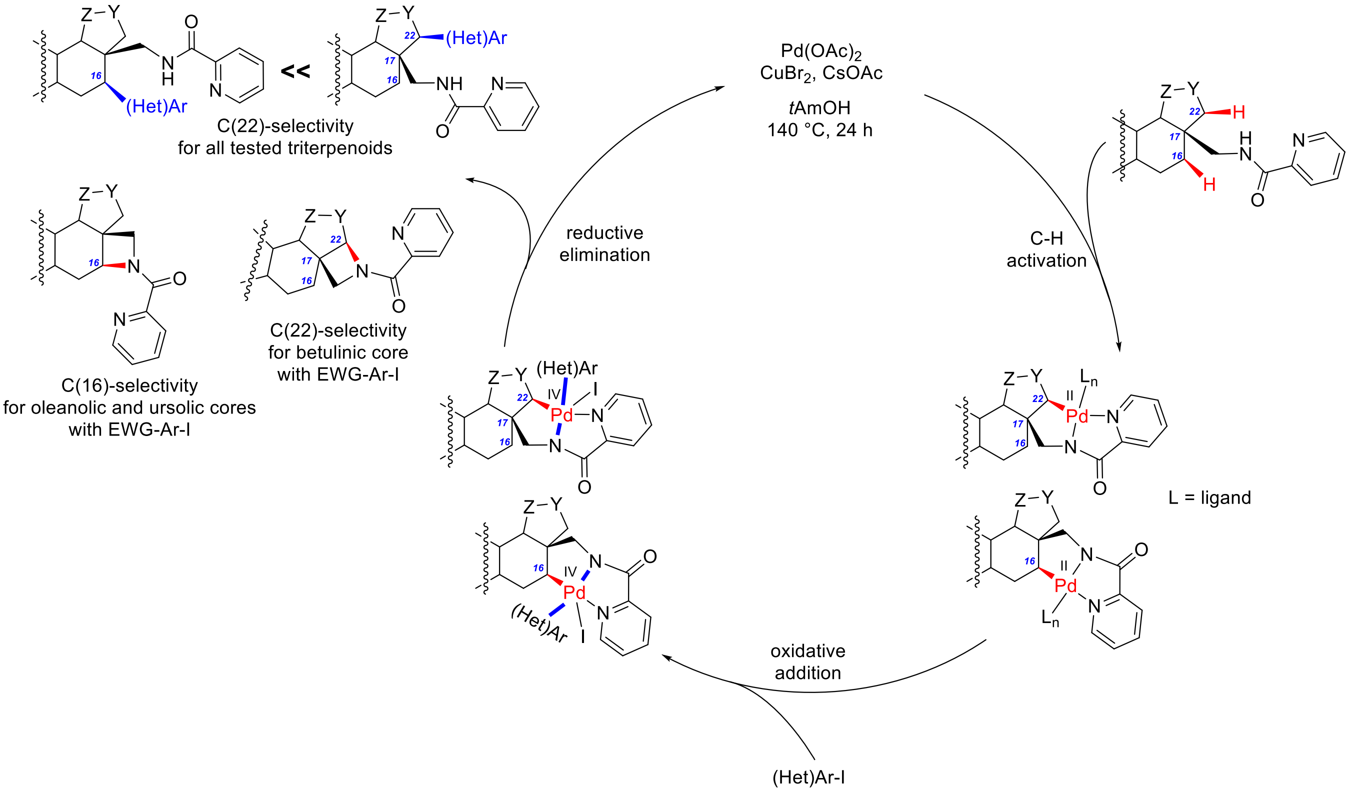
On the other hand, slow yet clean reaction between oleanolic amide **3c** and 1-iodo-4-nitrobenzene provided only azetidine **16**, which was isolated in 34% yield along with 65% of unreacted starting material (Scheme 7). Surprisingly, C−N bond formation in this case occurred at C(16) of the oleanolic core. Product **16** exists as a mixture of two stable rotamers in a 2:1 ratio. Further reductive cleavage of the directing group with LiAlH$_4$ released corresponding azetidine **17**, which was

Scheme 8. C−H Deuteration of Picolinamides 3a,c at Different Times[a]

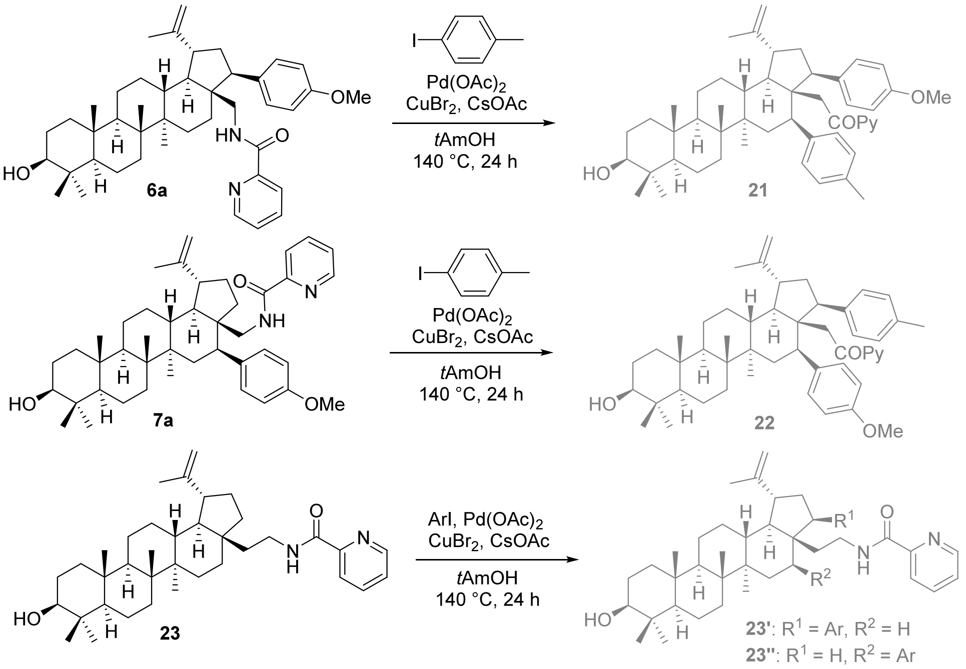


[a] D-insertion rate during reactions **3a** → **19** and **3c** → **20′** → **20** was established by integration of 2D HSQC NMR cross-peaks; depicted yields of final products **19** and **20** are the isolated yields.

Scheme 9. Plausible Pd-Catalyzed C(sp^3)-H Arylation and Azetidination Mechanism



Scheme 10. Arylation Attempts of Compounds 6a, 7a, and Extended Amide 23



further transformed into crystalline azetidinium picrate **18**. The molecular structure of the latter was unambiguously established by its single-crystal X-ray diffraction analysis.[41]

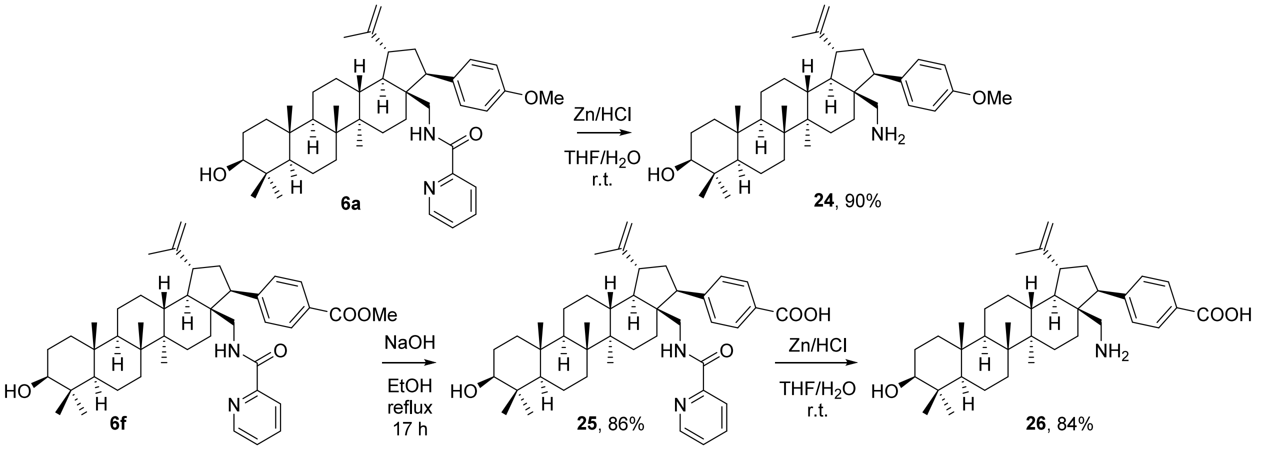
In order to explain the differences in C−H amination regioselectivity between betulin derived picolinamide **3a** and oleanolic acid derived picolinic amide **3c**, additional C−H deuteration experiments were carried out. In the beginning of our study we discovered that C−H deuteration of betulin derived picolinamide **3a** proceeded at both reaction sites C(16) and C(22) in 16 h at 80 °. Similar type of product was observed in the case of oleanolic acid derived picolinamide **3c** after 16 h reaction, but for this substrate also vinylic proton at C(12) was substituted with deuterium, yielding trideuterated product **20** (Scheme 8).

For clarity, the acidic −OH and −NH groups in Scheme 8 are depicted in their nondeuterated form as they undergo fast proton exchange during the isolation process. It was observed that the C(16)/C(22) C−H dideuteration of betulin core occurs without site selectivity, albeit with a higher rate. Thus, within 15 min already 10% conversion of starting material **3a** into dideuterated product **19** was observed. After 1 h, the conversion has reached 50%, and after 16 h, product **19** was isolated in 33% yield. On the other hand, picolinamide **3c** initially underwent C(16)-selective deuteration with a lower rate, providing only 10% conversion into monodeuterated intermediate **20′** after 1 h. After an additional 3 h (total reaction time 4 h), there was ∼ 40% conversion of starting material **3c** into C(16)-monodeuterated intermediate **20′**. Finally, after 16 h at 80 °C, trideuterated product **20** was isolated in 35% yield in the oleane series. From this, we can conclude that C(16)-H deuteration and C(22)-H deuteration rates for the betulin core are very similar, but the oleane molecular skeleton exhibits a certain kinetic preference for C(16)-H deuteration. A similar C(16)-H selectivity of oleanolic acid-derived quinoline amide was reported by Yuyong and co-workers.[42]

Based on the generally accepted concept, most likely, reductive elimination is the rate-limiting step in the C(sp^3)-H arylation process.[43] This assumption is also supported by the experiments with 8-aminoquinoline amide auxiliary that contains a less flexible CO-NH linker (compounds **2a,c,d**), which was able to ensure C(sp^3)-H deuteration, but failed in the arylation/azetidination experiments. Summing up the obtained regioselectivity patterns with more reactive starting materials bearing a flexible $-CH_2-NH-$ linker (compounds **3a−d**), we can conclude that reductive elimination occurs more slowly with palladium(IV) complexes bearing aryl substituents with electron-withdrawing substituents. In such complexes, at some point, reductive elimination forming the C−N bond is faster than that forming the C−C bond.[44,45] In the betulinic series, reductive elimination from C(22)-[Pd]-NC(O) system outperforms reductive elimination C(22)-[Pd]-Ar-EWG if $4-NO_2-C_6H_4I$ is used in the oxidative addition step (Scheme 9). This leads to the formation of azetidine. In the oleanolic series, the general rule for reductive elimination rates is the same: Ar-EDG > picolinamide > Ar-EWG. Only in this case, the C−H activation step is slower, C(16)-H-selective, and apparently kinetically comparable with the reductive elimination from the C(16)-[Pd]-NC(O) system. Therefore, starting material **3c** provides azetidine **16** at C (16) when treated with $4-NO_2-C_6H_4I$. Additionally, azetidine formation at C(22) in the oleanolic core would result in an unfavorable 1,3-diaxial interaction with one of the C(20)-geminal methyl groups, but such a steric constraint is absent in the betulin molecular skeleton. Radical scavengers TEMPO and galvinoxyl, which were used in the control experiments, did not influence the yield and selectivity of reaction **3a** → **6f** + **7f** + **8**, thus ruling out a single electron transfer mechanistic pathway for the C−Pd bond formation step (Scheme S2, Supporting Information).

Next, we explored the possibility of additional C−H arylation of previously obtained products **6a** and **7a** that, if successful, shall provide C(16),C(22)-bis-arylated products **21**

Scheme 11. Synthesis of Amine 24 and Amino Acid 26



and **22** (Scheme 10). Also, betulin amine homologue **23**, containing $-(CH_2)_2-$ linker between the terpene core and directing group, was explored as a starting material. In all these experiments, starting materials **6a**, **7a,** and **23** remained intact under our developed C−H arylation conditions.

Finally, the pyridyl amide was effectively removed from the arylated product **6a** in high yield by reductive cleavage with Zn/HCl to give the free amine **24**. The ester cleavage from compound **6f** and subsequent cleavage of the directing group gave novel betulin-derived amino acid **24** (Scheme 11).

■ SUMMARY

We have developed a palladium-catalyzed C(sp^3)-H arylation of different triterpenoid picolinamides with aryl iodides, which is the first C−C bond forming C−H activation protocol in the triterpenoid series. All three tested congeners possessing betulin, oleane, and ursane cores provided C(22)-arylation selectivity, and the aryl products were obtained in average to good yields. Oleane and ursane-derived picolinamides gave better C(22)/C16 selectivity up to 19:1, but betulin-derived picolinamides gave higher isolated yields − up to 83%. As expected, iodoarenes bearing electron-donating groups gave higher yields of C(sp^3)-arylation products, but in all cases azetidine side product was observed. On the other hand, switching to iodoarenes bearing electron-withdrawing groups shifted reactivity toward C(sp^3)- azetidination. The latter was the only detectable process when 4-$NO_2-C_6H_4I$ was used. Interestingly, the C(22)/C16 selectivity of the C(sp^3)-azetidination process was substrate-dependent. Thus, the betulin scaffold provided C(22)-azetidine, but the oleane scaffold gave C(16)-azetidine. The picolinamide directing group was successfully removed from the modified triterpenoids in the presence of Zn/HCl without any cationic rearrangements. Additionally, the obtained annulated betulin- and oleane-derived azetidines open broad possibilities for their further derivatization that may provide a novel approach to important terpenoid-based compounds in terms of medicinal chemistry.

■ EXPERIMENTAL SECTION

General Information. Solvents for the reactions were dried over standard drying agents and freshly distilled prior to use. All purchased chemicals (Fluka, Aldrich) were used as received. All reactions were followed by TLC on E. Merck Kieselgel 60 F_{254} and visualized by using a UV lamp. Column chromatography was performed on silica gel (60 Å, 40−63 μm, ROCC). Flash column chromatography was performed on a Büchi Sepacore system (Büchi-Labortechnik GmbH, Essen, Germany) with a Büchi Control Unit C-620, an UV detector Büchi UV photometer C-635, a Büchi fraction collector C-660, and two Pump Modules C-605. ^{1}H and ^{13}C NMR spectra were recorded on a Bruker 300 and 500 MHz, in $CDCl_3$, [D_6]DMSO, [D_8]THF, or [D_4]MeOD at 25 °C. Chemical shifts (δ) values are reported in ppm. The residual solvent peaks are used as internal reference ($CDCl_3$) 7.26 ppm, [D_6]DMSO 2.50 ppm, [D_8]THF 3.58 ppm, [D_4]MeOD 3.31 ppm for ^{1}H NMR, $CDCl_3$ 77.16 ppm, [D_6]DMSO 39.52 ppm, [D_8]THF 67.57 ppm, [D_4]MeOD 49.00 ppm for ^{13}C NMR), s (singlet), d (doublet), t (triplet), q (quartet), m (multiplet); *J* in hertz. High-resolution mass spectra (ESI) were performed on an Agilent 1290 Infinity series UPLC connected to an Agilent 6230 TOF mass spectrometer (calibration at *m*/*z* 121.050873 and *m*/*z* 922.009798).

*3β-Hydroxy-lup-20(29)en-28-amine (**4a′**).* Solution of oxime **4a** (5 g, 10.9 mmol, 1 equiv) and NH_4OAc (3.11 g, 40.4 mmol, 3.7 equiv) in MeOH (120 mL) was cooled to −10 °C, and $NaBH_3CN$ (1.99 g, 31.7 mmol, 2.9 equiv) was added portion-wise. The resulting reaction mixture was stirred at ambient temperature for 10 min, and then $TiCl_3$ solution in 2 M HCl (20% w/v, 21.8 mL, 43.6 mmol, 4 equiv) was added dropwise. After 1 h, the reaction mixture was heated up to room temperature and left stirring until complete conversion of the starting material was observed (TLC control). The reaction mixture was cooled to 0 °C, and 1 M NaOH aqueous solution (125 mL) was added dropwise, maintaining the temperature at 0−10 °C. The obtained precipitate was filtered through a Celite pad (H = 70 mm, d = 50 mm) and washed with a hot THF/MeOH 1:1 mixture (1000 mL). The filtrate was partially evaporated, and the obtained precipitate was filtered and subsequently washed with H_2O (20 mL) and MTBE (30 mL), then dried in an oven at 120 °C for 1 h to give a white amorphous solid (4.36 g, 90%), which was used without additional purification.

*3β-Hydroxy-lupan-28-amine (**4b′**).* Solution of oxime **4b** (5 g, 11.0 mmol, 1 equiv) and NH_4OAc (3.13 g, 40.7 mmol, 3.7 equiv) in MeOH (120 mL) was cooled to −10 °C, and $NaBH_3CN$ (2.00 g, 31.9 mmol, 2.9 equiv) was added portion-wise. The resulting mixture was stirred at ambient temperature for 10 min, and then $TiCl_3$ solution in 2 M HCl (22.0 mL, 44 mmol, 4 equiv) was added dropwise. After 1 h reaction was heated up to room temperature and left stirring until complete conversion of the starting material (TLC control). Reaction mixture was cooled to 0 °C, and 1 M NaOH aqueous solution (125 mL) was added dropwise, maintaining the temperature at 0−10 °C. Obtained precipitate was filtered through a Celite pad (H = 70 mm, d = 50 mm) and washed with a hot THF/MeOH 1:1 mixture (1000 mL). Filtrate was partially evaporated and obtained precipitate was filtered and subsequently washed with H_2O (20 mL) and MTBE (30 mL), then dried in oven at 120 °C for 1 h to give white amorphous solid (3.24 g, 67%), which was used directly for the next step without additional purification.

*3β-Hydroxy-olean-12(13)-ene-28-amine (**5a′**) or 3β-Hydroxy-urs-12(13)-ene-28-amine (**5b′**).* HCTU (1.08 g, 2.62 mmol) and Et_3N (0.44 g, 4.36 mmol) were added to a solution of oleanolic acid **1a** or ursolic acid **1b** (1g, 2.18 mmol) in DMF (5 mL) at room temperature. The resulting reaction mixture was stirred for 1 h; then, a saturated solution of NH_3 in EtOH (1 mL) was added at room temperature, and the obtained mixture was stirred for 12 h. The resulting mixture was diluted with water (15 mL) and filtered. The precipitate was washed with water (15 mL) and dried at 70 °C for 48 h to obtained amide **5a** or **5b** as a white solid (837 mg, 84% for **5a** and 908 mg, 91% for **5b**), which was used directly for the next step without additional purification. $LiAlH_4$ (140 mg, 3.68 mmol) was added portionwise to a solution of crude **5a** or **5b** (0.42 g, 0.92 mmol) in THF (3 mL) at 0 °C. Then the reaction mixture was stirred for 96 h at reflux temperature, cooled to 0 °C, and slowly quenched sequentially with water (1 mL), and 15% aqueous NaOH (2 mL). The obtained suspension was filtered, and the filtrate was evaporated to dryness and purified by silica column chromatography (DCM-MeOH 99:1−10:1) to yield pure oleanolic amine (0.26 g, 65%) or ursolic amine (0.21 g, 52%) after two steps.

General Procedure I for the Synthesis of Picolinic Amides. To a solution of picolinic acid (124 mg, 1 mmol, 1 equiv) in a mixture of anhydrous DCM (2 mL) and THF (2 mL), one drop of DMF and oxalyl chloride (127 mg, 1 mmol, 1 equiv) were subsequently added dropwise at 0 °C. Then the resulting reaction mixture was warmed up to room temperature and stirred for 1 h. The solution was concentrated in vacuo to remove excess oxalyl chloride and then redissolved back in DCM (6 mL) Then it was cooled to 0 °C and solution of triterpenoid amine (1.05 mmol, 1.05 equiv) and triethylamine (505 mg, 5 mmol, 5 equiv) in DCM (10 mL) was added dropwise during 30 min at ambient temperature. The resulting reaction mixture was warmed to room temperature and stirred for 5 h. Then it was diluted with DCM (50 mL) and washed with water (2 × 30 mL) and brine (2 × 30 mL), dried over anhydrous Na_2SO_4, filtered, and concentrated under reduced pressure. The obtained residue was purified by silica column chromatography (Hexanes-EtOAc 10:1−4:1) to yield picolinic amide as a white amorphous solid.

*3β-Hydroxy-28-picolinamido-lup-20(29)ene (**3a**).* According to GP I, compound **3a** was prepared from the corresponding amine (390 mg, 0.882 mmol, 1.05 equiv), picolinic acid (103 mg, 0.841 mmo, 1 equiv), oxalyl chloride (86 μL, 1.009 mmol, 1 equiv), Et_3N (293 μL, 2.106 mmol, 5 equiv), $DCM_{anh.}$ (15 mL), $THF_{anh.}$ (30 mL). Yield 457 mg, 90%. HRMS (ESI): *m*/*z* calc. for $[C_{36}H_{54}N_2O_2 + H]^+$ 547.4258; found 547.4273. ^1H NMR (500 MHz, $CDCl_3$) δ 8.54 (d, ^3J = 4.8 Hz, 1H, H−C(6′), 8.21 (d, ^3J = 7.8 Hz, 1H, H−C(3′)), 8.03 (t, ^3J = 6.5 Hz, 1H, H−N), 7.84 (td, ^3J = 7.8 Hz, ^4J = 1.7 Hz, 1H, H−C(4′), 7.41 (dd, ^3J = 7.8, 4.8 Hz, 1H, H−C(5′)), 4.72 (d, ^4J = 2.3 Hz, 1H, H_a-C (29)), 4.60 (s, 1H, H_b-C (29)), 3.71 (dd, ^2J = 13.8 Hz, ^3J = 6.5 Hz, 1H, H_a-C (28)), 3.24 (dd, ^2J = 13.8 Hz, ^3J = 6.5 Hz, 1H, H_b-C (28)), 3.18 (dd, ^3J = 11.3, 4.8 Hz, 1H, H−C (3)), 2.55 (td, ^3J = 11.2, 5.6 Hz, 1H, H−C (19)), 2.18 −2.07, m, 1H, H_a-C (21)), 1.90 (ddd, ^2J = 13.7 Hz, ^3J = 13.6 Hz, 4.4 Hz, 1H, H_a-C (15)), 1.83 (td, ^3J = 12.0, 3.4 Hz, 1H, H−C (13)), 1.80−1.76 (m, 1H, H_a-C (16)), 1.76−1.71 (m, 1H, H_a-C (22)), 1.70 (s, 3H, H_3−C (30)), 1.69−1.47 (m, 5H, H_a-C (16), H_a-C (12), H_2−C (2), H_a-C (1)), 1.47−1.36 (m, 6H, H_b-C (6), H_a-C (11), H_b-C (21), H_2−C (7), H−C (18)), 1.34−1.22 (m, 3H, H_b-C (11), H_b-C (16), H−C (9)), 1.14−1.03 (m, 6H, H_3−C (26), H_b-C (12), H_b-C (15), H_b-C (22)), 0.99 (s, 3H, H_3−C (27)), 0.97 (s, 3H, H_3−C (23)), 0.93−0.86 (m, 1H, H_b-C (1)), 0.84 (s, 3H, H_3−C (25)), 0.76 (s, 3H, H_3−C (25)), 0.72−0.66 (m, 1H, H−C (5)). ^{13}C NMR (126 MHz, $CDCl_3$) δ 164.71 (N−C = O), 150.43 (C20), 150.17 (C2′), 148.14 (C6′), 137.51 (C4′), 126.17 (C5′), 122.37 (C3′), 109.92 (C29), 79.13 (C3), 55.47 (C5), 50.56 (C9), 49.17 (C18), 47.57 (C19), 47.33 (C17), 42.88 (C14), 41.08 (C8), 39.01 (C4), 38.86 (C1), 37.48 (C13), 37.43 (C28), 37.31 (C10), 35.22 (C22), 34.30 (C7), 30.51 (C16), 29.94 (C21), 28.13 (C23), 27.56 (C2), 27.41 (C15), 25.37 (C12), 20.98 (C11), 19.46 (C30), 18.43 (C6), 16.24 (C25), 16.20 (C26), 15.51 (C24), 14.96 (C27).

*3β-Hydroxy-28-picolinamido-lupane (**3b**).* According to GP I, compound **3b** was prepared from the corresponding amine (400 mg, 0.901 mmol, 1.05 equiv), picolinic acid (106 mg, 0.858 mmo, 1 equiv), oxalyl chloride (88 μL, 1.029 mmol, 1 equiv), Et_3N (300 μL, 2.145 mmol, 5 equiv), $DCM_{anh.}$ (15 mL), $THF_{anh.}$ (30 mL). Yield 405 mg, 86%. HRMS (ESI): *m*/*z* calc. for $[C_{36}H_{56}N_2O_2 + H]^+$ 549.4415; found 549.4416. ^1H NMR (500 MHz, $CDCl_3$) δ 8.54 (d, ^3J = 4.8 Hz, 1H, H−C(6′), 8.20 (d, ^3J = 7.8 Hz, 1H, H−C(3′)), 8.00 (dd, ^3J = 6.5, 6.0 Hz, 1H, H−N), 7.84 (t, ^3J = 7.8 Hz, 1H, H−C(4′), 7.41 (dd, ^3J = 7.8, 4.8 Hz, 1H, H−C(5′)), 3.74 (dd, ^2J = 13.8 Hz, ^3J = 6.5 Hz, 1H, H_a-C (28)), 3.25−3.11 (m, 2H, H−C (3), H_b-C (28)), 1.97−1.81 (m, 4H, H_a-C (15), H−C (20), H−C (13), H−C (19)), 1.80−1.46 (m, 10H, H_2−C (21), H_a-C (6), H_a-C (11), H_2−C (2), H_a-C (16), H_a-C (12), H_a-C (22), H_a-C (1)), 1.47−1.17 (m, 8H, H_b-C (6), H_b-C (11), H_b-C (12), H_b-C (16), H_2−C (7), H_b-C (18), H_b-C (9)), 1.13 (s, 3H, H_3−C (26)), 1.08−1.02 (m, 1H, H_b-C (15)), 0.97 (s, 6H, H_3−C (23), H_3−C (27)), 0.96−0.87 (m, 2H, H_b-C (22), H_b-C (1)), 0.92 (d, ^3J = 6.8 Hz, 3H, H−C (30)), 0.85 (s, 3H, H_3−C (25)), 0.78 (d, ^3J = 6.0 Hz, 3H, H_3−C (29)), 0.77 (s, 3H, H_3−C (24)), 0.72−0.66 (m, 1H, H−C (5)). ^{13}C NMR (126 MHz, $CDCl_3$) δ 164.66 (C═O), 150.24 (C2′), 148.14 (C6′), 137.50 (C4′), 126.13 (C5′), 122.36 (C3′), 79.16 (C3), 55.43 (C5), 50.24 (C9), 48.50 (C18), 47.43 (C17), 44.43 (C19), 43.04 (C14), 41.12 (C8), 39.02 (C4), 38.86 (C1), 37.51 (C28), 37.28 (C10), 37.05 (C13), 35.36 (C22), 34.37 (C7), 30.61 (C16), 29.60 (C20), 28.14 (C23), 27.55 (C2), 27.30 (C15), 27.00 (C12), 23.10 (C30), 21.97 (C21), 20.98 (C11), 18.45 (C6), 16.20 (C25 + C26), 15.53 (C24), 15.14 (C29), 14.85 (C27).

*3β-28-Picolinamido-olean-12(13)-ene (**3c**).* According to GP I, compound **3c** was prepared from the corresponding amine (1.04 g, 2.354 mmol, 1.05 equiv), picolinic acid (276 mg, 2.242 mmo, 1 equiv), oxalyl chloride (230 μL, 2.690 mmol, 1 equiv), Et_3N (780 μL, 5.605 mmol, 5 equiv), $DCM_{anh.}$ (15 mL), $THF_{anh.}$ (5 mL). Yield 1.083 g, 88%. HRMS (ESI): *m*/*z* calc. for $[C_{36}H_{54}N_2O_2 + H]^+$ 547.4258; found 547.4254.

^{1}H NMR (500 MHz, CDCl$_3$) δ 8.54 (d, ^{3}J = 4.8 Hz, 1H, H−C(6′), 8.20 (d, ^{3}J = 7.8 Hz, 1H, H−C(3′)), 8.10 (dd, ^{3}J = 7.5, 5.6 Hz, 1H, H−N), 7.83 (td, ^{3}J = 7.8 Hz, ^{4}J = 1.7 Hz, 1H, H−C(4′), 7.41 (dd, ^{3}J = 7.8, 4.8 Hz, 1H, H−C(5′)), 5.27 (d, ^{3}J = 3.7 Hz, 1H, H−C (12)), 3.74 (dd, ^{2}J = 13.7 Hz, ^{3}J = 7.5 Hz, 1H, H$_a$-C (28)), 3.22 (dd, ^{3}J = 10.9, 4.8 Hz, 1H, H−C (3)), 2.97 (dd, ^{2}J = 13.7 Hz, ^{3}J = 5.6 Hz, 1H, H$_b$-C (28)), 2.08 (dd, ^{3}J = 13.5, 4.5 Hz, 1H, H−C (18)), 2.00−1.83 (m, 4H, H$_2$−C (11), H$_a$-C (16), H$_a$-C (15)), 1.75 (dd, ^{2}J = 13.6 Hz, ^{3}J = 13.5 Hz, 1H, H$_a$-C (19)), 1.68−1.47 (m, 7H, H$_a$-C (6), H$_2$−C (2), H$_a$-C (7), H$_a$-C (22), H$_a$-C (1), H−C (9)), 1.47−1.22 (m, 4H, H$_b$-C (6), H$_b$-C (7), H$_b$-C (22), H$_a$-C (21)), 1.22−1.18 (m, 1H, H$_b$-C (21)), 1.18 (s, 3H, H$_3$−C (27)), 1.14−1.09 (m, 2H, H$_b$-C (16), H$_b$-C (19)), 1.09 (s, 3H, H$_3$−C (26)), 1.04 −1.00 (m, 1H, H$_b$-C (15)), 0.99 (s, 3H, H$_3$−C (23)), 0.99−0.96 (m, 1H, H$_a$-C (1)), (s, 3H, H$_3$−C (25)), 0.89 (s, 3H, H$_3$−C (30)), 0.88 (s, 3H, H$_3$−C (29)), 0.79 (s, 3H, H$_3$−C (24)), 0.77−0.72 (m, 1H, H−C (5)). ^{13}C NMR (126 MHz, CDCl$_3$) δ 164.39 (C = O), 150.29 (C2′), 148.13 (C6′), 143.97 (C13), 137.46 (C4′), 126.09 (C5′), 122.99 (C12), 122.39 (C3′), 79.17 (C3), 55.35 (C5), 47.80 (C9), 47.41 (C28), 46.68 (C19), 44.78 (C18), 41.93 (C14), 40.04 (C8), 38.93 (C4), 38.78 (C1), 37.09 (C10), 36.83 (C17), 34.24 (C21), 33.34, (C30), 32.60 (C7), 32.14 (C22), 31.08 (C20), 28.24 (C13), 27.39 (C2), 26.24 (C27), 25.99 (C15), 23.77 (C11), 23.70 (C29), 22.59 (C16), 18.47 (C6), 16.86 (C26), 15.73 (C24), 15.67 (C25).

*3β-28-Picolinamido-urs-12(13)-ene (**3d**).* According to GP I, compound **3d** was prepared from the corresponding amine (230 mg, 0.498 mmol, 1.05 equiv), picolinic acid (62 mg, 0.504 mmo, 1 equiv), oxalyl chloride (56 μL, 0.504 mmol, 1 equiv), Et$_3$N (120 μL, 1.261 mmol, 5 equiv),DCM$_{anh.}$ (5 mL). Yield 208 mg, 80%. HRMS (ESI): *m*/*z* calc. for [C$_{36}$H$_{54}$N$_2$O$_2$ + H]$^+$ 547.4258; found 547.4267. ^{1}H NMR (500 MHz, CDCl$_3$) δ 8.55 (d, ^{3}J = 4.7 Hz, 1H, H−C(6′)), 8.20 (d, ^{3}J = 7.8 Hz, 1H, H−C(3′)), 8.06 (dd, ^{3}J = 7.6, 5.4 Hz, 1H, H−N), 7.83 (td, ^{3}J = 7.8 Hz, ^{4}J = 1.8 Hz, 1H, H−C(4′)), 7.40(dd, ^{3}J = 7.8, 4.7 Hz, 1H, H−C(5′)), 5.23 (t, ^{3}J = 3.6 Hz, 1H, H−C (12)), 3.75 (dd, ^{2}J = 13.7 Hz, ^{3}J = 7.6 Hz, 1H, H$_a$-C (28)), 3.23 (dd, ^{3}J = 11.0, 4.9 Hz, 1H, H−C (3)), 2.91 (dd, ^{2}J = 13.7 Hz, ^{3}J = 5.4 Hz, 1H, H$_b$-C (28)), 2.06−1.92 (m, 4H, H$_2$−C (11), H$_a$-C (16), H$_a$-C (15)), 1.77−1.50 (m, 7H, H$_a$-C (6), H$_2$−C (2), H$_a$-C (7), H$_a$-C (22), H$_a$-C (1), H−C (9)), 1.50−1.34 (m, 6H, H$_b$-C (6), H$_a$-C (22), H$_b$-C (7), H$_b$-C (22), H−C (19), H−C (18)), 1.28−1.20 (m, 1H, H$_b$-C (21)), 1.19-1.14 (m, 1H, H$_b$-C (16)), 1.13 (s, 3H, H$_3$−C (26)), 1.12 (s, 3H, H$_3$−C (26)), 1.06−0.99 (m, 2H, H$_b$-C (15), H$_b$-C (1)), 1.00 (s, 3H, H$_3$−C (23)), 0.96 (s, 3H, H$_3$−C (25)), 0.95−0.91 (m, 4H, H$_3$−C (30), H−C (20)), 0.83 (d, ^{3}J = 5.6 Hz, 3H, H$_3$−C (29)), 0.80 (s, 3H, H$_3$−C (24)), 0.74 (d, ^{3}J = 11.5 Hz, 1H, H−C (5)). ^{13}C NMR (126 MHz, CDCl$_3$) δ 164.37 (C=O), 150.35 (C2′), 148.13 (C6′), 138.44 (C13), 137.44 (C4′), 126.06 (C5′), 125.77 (C12), 122.39 (C3′), 79.20 (C3), 56.51 (C18), 55.36 (C5), 47.89 (C9), 47.67 (C28), 42.27 (C14), 40.26 (C8), 39.64 (C19), 39.52 (C20), 38.98 (C4), 38.93 (C1), 37.88 (C17), 37.04 (C10), 36.29 (C22), 32.89 (C7), 30.80 (C21), 28.27 (C23), 27.43 (C2), 26.47 (C15), 23.93 (C16), 23.64 (C11), 23.53 (C27), 21.43 (C30), 18.45 (C6), 17.52 (C29), 16.96 (C26), 15.84 (C25), 15.77 (C24).

*(17R)-17-(2-(Picolinamido)ethyl)-28-norlup-20(29)-en-3β-ol (**23**).* According to GP I, compound **23** was prepared from the corresponding amine (860 mg, 4.492 mmol, 1.05 equiv), picolinic acid (221 mg, 1.797 mmo, 1 equiv), oxalyl chloride (185 μL, 2.156 mmol, 1.2 equiv), Et$_3$N (626 μL, 4.492 mmol, 2.5 equiv), DCM$_{anh.}$ (40 mL)), THF$_{anh.}$ (60 mL). Yield 849 mg, 84%. HRMS (ESI): *m*/*z* calc. for [C$_{37}$H$_{56}$N$_2$O$_2$ + H]$^+$ 561.4415; found 561.4398. ^{1}H NMR (500 MHz, CDCl$_3$) δ 8.55 (d, J = 4.7 Hz, 1H, H−C(6′)), 8.21 (d, J = 7.7 Hz, 1H, H−C(3′)), 8.00 (t, ^{3}J = 5.7 Hz, 1H, H−N), 7.85 (td, J = 7.7, 1.8 Hz, 1H, H−C(4′)), 7.42 (ddd, ^{3}J = 7.7, 4.7 Hz, ^{4}J = 1.8 Hz, 1H, H−C(5′)), 4.67 (d, ^{4}J = 2.4 Hz, 1H, H$_a$-C (29)), 4.57 (s, 1H, H$_b$-C (29)), 3.45 (dddd, ^{2}J = 12.8 Hz, ^{3}J = 11.6, 5.9, 5.7 Hz, 1H, H$_a$-C(28′)) 3.38 (dddd, ^{2}J = 12.8 Hz, ^{3}J = 11.1, 5.7, 5.3 Hz, 1H, H$_b$-C(28′)), 3.18 (dd, ^{3}J = 11.4, 4.7 Hz, 1H, H−C (3), 2.41 (td, ^{3}J = 11.1, 5.6 Hz, 1H, H−C (19)), 1.97 (dtd, ^{2}J = 14.0, ^{3}J = 10.6, 8.2 Hz, 1H, H$_a$-C (21)), 1.86 (ddd, ^{2}J = 12.5 Hz, ^{3}J = 12.4 Hz, 6.1 Hz, 1H, H$_a$-C (28)), 1.82−1.70 (m, 3H, H$_a$-C (16), H$_a$-C (22), H−C (13)), 1.68 (s, 3H, H−C (30)), 1.67−1.57 (m, 4H, H$_a$-C (12), H$_a$-C (2), H$_a$-C (15), H$_a$-C (1)), 1.57−1.35 (m, 8H, H$_2$−C (6), H$_a$-C (11), H$_b$-C (2), H$_b$-C (21), H$_2$−C (7), H−C (18)), 1.35−1.17 (m, 4H, H$_b$-C (28), H$_b$-C (11), H$_b$-C (16), H−C (9)), 1.12−1.06 (m, 2H, H$_b$-C (22), H$_b$-C (12)), 1.06−1.02 (m, 4H, H$_3$−C (26), H$_b$-C (15)), 0.97 (s, 3H, H$_3$−C (27)), 0.96 (s, 3H, H$_3$−C (23)), 0.93−0.89 (m, 1H, H$_b$-C (1)), 0.82 (s, 3H, H$_3$−C (25)), 0.76 (s, 3H, H$_3$−C (24)), 0.68 (d, ^{3}J = 9.3 Hz, 1H, H−C (5)). ^{13}C NMR (126 MHz, CDCl$_3$) δ 164.32 (N−C=O), 150.79 (C20), 150.27 (C2′), 148.14 (C6′), 137.52 (C4′), 126.20 (C5′), 122.32 (C3′), 109.71 (C29), 79.14 (C3), 55.46 (C5), 50.61 (C9), 50.15 (C18), 47.49 (C19), 45.29 (C17), 42.70 (C14), 41.03 (C8), 39.02 (C1), 38.85 (C4), 37.35 (C13), 37.32 (C10), 35.99 (C28′), 35.95 (C22), 34.35 (C7), 31.33 (C16), 30.15 (C21), 28.13 (C23), 27.68 (C2), 27.55 (C28), 27.48 (C15), 25.24 (C12), 21.08 (C11), 19.44 (C30), 18.45 (C6), 16.29 (C25), 16.25 (C26), 15.51 (C24), 15.06 (C27).

General Procedure II for Arylation Reaction. A solution of picolinic amide (0.20 mmol, 1 equiv), iodo (het)arene (0.80 mmol, 4 equiv), Pd(OAc)$_2$ (2 mg, 0.01 mmol, 0.05 equiv), CuBr$_2$ (4 mg, 0.02 mmol, 0.1 equiv), and CsOAc (154 mg, 0.80 mmol, 4 equiv) in *t*-AmOH (2 mL) was stirred in a pressure vessel under a nitrogen atmosphere for 24 h at 140 °C. The resulting reaction mixture was cooled to room temperature and filtered through a Celite pad (H = 50 mm, d = 15 mm), followed by washing with THF/EtOAc 1:1 (10 mL). The filtrate was concentrated under reduced pressure, and the crude mixture was purified by column chromatography on silica gel (Hexanes-EtOAc 10:1 → 1:1), yielding desired arylation products as a white amorphous solid.

*(22S)-22-(4-Methoxyphenyl)-3β-hydroxy-28-picolinamido-lup-20(29)en (**6a**) and (16R)-16-(4-Methoxyphenyl)-3β-hydroxy-28-picolinamido-lup-20(29)ene (**7a**).* According to GP II, compounds **6a** and **7a** were prepared from picolinic amide **3a** (50 mg, 0.091 mmol, 1 equiv), 1-iodo-4-methoxybenzene (86 mg, 0.366 mmol, 4 equiv), Pd(OAc)$_2$ (1 mg, 0.004 mmol, 0.05 equiv), CuBr$_2$ (2 mg, 0.009 mmol, 0.1 equiv), and CsOAc (70 mg, 0.366 mmol, 4 equiv) in *t*-AmOH (2 mL). Yield 46 mg, 83%. HRMS (ESI): *m*/*z* calc. for [C$_{43}$H$_{60}$N$_2$O$_3$ + H]$^+$ 653.4677; found 653.4676.

*(22S)-22-(4-Methoxyphenyl)-3β-hydroxy-28-picolinamido-lup-20(29)ene (**6a**).* ^{1}H NMR (500 MHz, CDCl$_3$) δ 8.20 (dd, ^{3}J = 5.3 Hz, ^{4}J = 1.8 Hz, 1H, H−C(6′)), 8.00 (d, ^{3}J = 7.7 Hz, 1H, H−C(3′)), 7.70 (td, ^{3}J = 7.7 Hz, ^{4}J = 1.8 Hz, 1H, H−C(4′)), 7.28−7.24 (m, 3H, H−C(5′), H−C(3″), H−C(5″)), 6.92 (d, ^{3}J = 9.3 Hz, 1H, H−N), 6.87 (d, ^{3}J = 8.7 Hz, 2H, H−C(2″), H−C(6″)), 4.80 (d, ^{4}J = 2.2 Hz, 1H, H$_a$-C (29)), 4.66 (s, 1H, H$_b$-C (29)), 4.14 (dd, ^{2}J = 14.2, ^{3}J = 9.3 Hz, 1H, H$_a$-C (28)), 3.78 (s, 3H, CH$_3$−O) 3.19 (dd, ^{3}J = 11.3, 4.8 Hz, 1H,

H−C (3)), 2.96 (dd, ^2J = 14.2, ^3J = 2.8 Hz, 1H, H$_b$-C (28)), 2.88 (dd, ^3J = 10.0, 8.3 Hz, 1H, H−C (22)), 2.64 (ddd, ^2J = 13.6 Hz, ^3J = 11.5, 10.0 Hz, H$_a$-C (21)), 2.61 (ddd, ^3J = 11.5, 10.9, 4.2 Hz, 1H, H−C (19)), 2.02 (td, ^3J = 12.0, 3.5 Hz, 1H, H−C (13)), 1.89 (dd, ^3J = 12.0, 10.9 Hz, 1H, H−C (18)), 1.84 (ddd, ^2J = 13.1 Hz, ^3J = 6.9, 3.5 Hz, 1H, H$_a$-C (16)), 1.76 (s, 3H, H−C (30)), 1.76−1.70 (m, 4H, H$_a$-C (12), H$_a$-C (7), H$_a$-C (15), H$_a$-C (1)), 1.65−1.23 (m, 10H, H$_2$−C (2), H$_2$−C (6), H$_2$−C (11), H$_b$-C (16) H$_b$-C (7), H$_b$-C (21), H−C (9)), 1.17 (s, 3H, H$_3$−C (26)), 1.15−1.07 (m, 1H, H$_b$-C (12)), 1.03 (s, 3H, H$_3$−C (27)), 1.03−0.97 (m, 1H, H$_b$-C (15)), 0.96 (s, 3H,H$_3$−C (23)), 0.94−0.85 (m, 1H, H$_b$-C (1)), 0.84 (s, 3H, H$_3$−C (25)), 0.76 (s, 3H, H$_3$−C (24)), 0.71−0.64 (m, 1H, H−C (5)). ^{13}C NMR (126 MHz, CDCl$_3$) δ 163.98 (C=O), 158.95 (C4″) 150.14 (C20), 149.97 (C2′), 147.61 (C6′), 136.96 (C4′), 132.01 (C1″), 128.62 (C2″ + C6″), 125.69 (C5′), 121.78 (C3′), 114.40 (C3″ + C5″), 110.38 (C29), 79.20 (C3), 55.53 (C5), 55.29 (O−CH$_3$) 53.98 (C22), 50.68 (C9), 50.46 (C18), 50.14 (C17), 46.23 (C19), 42.73 (C14), 41.02 (C8), 39.02 (C1), 38.90 (C4), 37.68 (C13), 37.34 (C10), 35.91 (C28), 34.22 (C7), 34.09 (C21), 30.21 (C16), 28.13 (C23), 27.59 (C2), 27.41 (C15), 25.21 (C12), 20.99 (C11), 19.30 (C30), 18.37 (C6), 16.21 (C25), 16.06 (C26), 15.50 (C24), 15.14 (C27).

*(16R)-16-(4-Methoxyphenyl)-3β-hydroxy-28-picolinamido-lup-20(29)ene (**7a**).* ^{1}H NMR (500 MHz, CDCl$_3$) δ 8.21 (d, ^3J = 4.5 Hz, 1H, H−C(6′), 7.99 (d, ^3J = 7.8 Hz, 1H, H−C(3′), 7.71 (td, ^3J = 7.8 Hz, ^4J = 1.8 Hz, 1H, H−C(4′)), 7.29 (dd, ^3J = 7.8, 4.5 Hz, 1H, H−C(5′)), 7.24 (d, ^3J = 8.7 Hz, 2H, H−C(3″), H−C(5″)), 7.03 (d, ^3J = 9.9 Hz, 1H, H−N), 6.86 (d, ^3J = 8.7 Hz, 2H, H−C(2″), H−C(6″)), 4.74 (d, ^3J = 2.4 Hz, 1H, H$_a$-C (29)), 4.62 (s, 1H, H$_b$-C (29)), 3.79 (s, 3H, O−CH$_3$), 3.70 (dd, ^2J = 14.3, ^3J = 9.9 Hz, 1H, H$_a$-C (28)), 3.46 (d, ^2J = 14.3 Hz, 1H, H$_b$-C (28)), 3.20 (dd, ^3J = 11.4, 4.9 Hz, 1H, H−C (3)), 2.88 (dd, ^3J = 13.2, 3.5 Hz, 1H, H−C (16)), 2.69 (td, ^3J = 11.2, 4.2 Hz, 1H, H−C (19)), 2.41 (dd, ^2J = 13.4 Hz, ^3J = 13.2 Hz, 1H, H$_a$-C (15)), 2.01 (dddd, ^2J = 13.7 Hz, ^3J = 11.2, 10.4, 6.5 Hz, 1H, H$_a$-C (21)), 1.89 (dd, ^3J = 12.0, 11.2 Hz, 1H, H−C (18)), 1.80 (td, ^3J = 12.0, 3.5 Hz, 1H, H−C (13)), 1.75 (s, 3H, H−C (30)), 1.74−1.58 (m, 5H, H$_a$-C (12), H$_2$−C (2), H$_a$-C (22), H$_a$-C (1)), 1.58−1.23 (m, 10H, H$_2$−C (6), H$_2$−C (11), H$_b$-C (21), H$_b$-C (15), H$_2$−C (7), H$_b$-C (22), H−C (9)), 1.18 (s, 3H, H$_3$−C (26)), 1.13−1.07 (m, 4H, H$_3$−C (27), H$_b$-C (12)), 0.98 (s, 3H, H$_3$−C (23)), 0.96−0.90 (m, 1H, H$_b$-C (1)), 0.88 (s, 3H, H$_3$−C (25)), 0.78 (s, 3H, H$_3$−C (24)), 0.73−0.69 (m, 1H, H−C (5)). ^{13}C NMR (126 MHz, CDCl$_3$) δ 164.11 (C=O), 158.72 (C4″), 150.47 (C20), 149.85 (C2′), 147.68 (C6′), 137.02 (C4′), 135.77 (C1″), 128.60 (C2″ + C6″), 125.77 (C5′), 121.80 (C3′), 114.19 (C3″ + C5″), 109.64 (C29), 79.15 (C3), 55.48 (C5), 55.34 (CH$_3$−O), 51.32 (C17), 51.13 (C18), 50.62 (C9), 47.73 (C16), 46.93 (C19), 43.38 (C14), 41.44 (C8), 39.04 (C1), 38.93 (C4), 37.37 (C10), 37.09 (C13), 36.38 (C28), 35.14 (C22), 34.50 (C7), 32.49 (C15), 30.11 (C21), 28.16 (C23), 27.57 (C2), 25.71 (C12), 21.08 (C11), 20.22 (C30), 18.45 (C6), 16.41 (C26), 16.37 (C25), 15.58 (C24), 15.54 (C27).

*(22S)-22-Phenyl-3β-hydroxy-28-picolinamido-lup-20(29)-ene (**6b**) and (16R)-16-Phenyl-3β-hydroxy-28-picolinamido-lup-20(29)ene (**7b**).* According to GP II, compounds **6b** and **7b** were prepared from picolinic amide **3a** (100 mg, 0.183 mmol, 1 equiv), iodobenzene (149 mg, 0.731 mmol, 4 equiv), Pd(OAc)$_2$ (2 mg, 0.009 mmol, 0.05 equiv), CuBr$_2$ (4 mg, 0.018 mmol, 0.1 equiv), and CsOAc (140 mg, 0.731 mmol, 4 equiv) in *t*-AmOH (2 mL). Yield 83 mg, 73%. HRMS (ESI): *m*/*z* calc. for $[C_{42}H_{58}N_2O_2 + H]^+$ 623.4571; found 623.4574.

*(22S)-22-Phenyl-3β-hydroxy-28-picolinamido-lup-20(29)-ene (**6b**).* ^{1}H NMR (500 MHz, CDCl$_3$) δ 8.17 (dd, ^3J = 4.8 Hz, ^4J = 1.7 Hz, 1H, H−C (6)), 7.99 (d, ^3J = 7.8, Hz, 1H, H−C(3′)), 7.69 (td, ^3J = 7.8 Hz, ^4J = 1.7 Hz, 1H, H−C(4′)), 7.36−7.28 (m, 4H, H−C(2″), H−C(3″), H−C(5″), H−C(6″)), 7.27−7.23 (m, 2H, H−C(4″), H−C(5′)), 6.92 (d, ^3J = 9.3 Hz, 1H, H−N), 4.81 (d, ^4J = 2.2 Hz, 1H, H$_a$-C (29)), 4.66 (s, 1H, H$_b$-C (29)), 4.15 (dd, ^2J = 14.2, ^3J = 9.3 Hz, 1H, H$_a$-C (28)), 3.19 (dd, ^3J = 11.4, 4.8 Hz, 1H, H−C (3)), 3.02 (dd, ^2J = 14.2, ^3J = 2.7 Hz, 1H, H$_b$-C (28)), 2.93 (dd, ^3J = 10.3 9.3 Hz, 1H, H−C (22)), 2.70 (ddd, ^2J = 13.6 Hz, ^3J = 11.1, 10.3 Hz, 1H, H$_a$-C (21)), 2.64 (ddd, ^3J = 11.3, 11.1, 4.6 Hz, 1H, H−C (19)), 2.03 (td, ^3J = 12.0, 3.6 Hz, 1H, H−C (13)), 1.91 (dd, ^3J = 12.0, 11.3 Hz, 1H, H−C (18)), 1.84 (ddd, ^2J = 13.1 Hz, ^3J = 7.0, 3.6 Hz, 1H, H$_a$-C (16)), 1.77 (s, 3H, H−C (30)), 1.76−1.65 (m, 4H, H$_a$-C (12), H$_b$-C (21), H$_a$-C (1), H$_a$-C (15)), 1.65−1.23 (m, 10H, H$_2$−C (2), H$_2$−C (6), H$_2$−C (11), H$_b$-C (16) H$_2$−C (7), H−C (9)), 1.17 (s, 3H, H$_3$−C (26)), 1.14−1.07 (m, 1H, H$_b$-C (12)), 1.03 (s, 3H, H$_3$−C (27)), 1.02−0.96 (m, 1H, H$_b$-C (15)), 0.96 (s, 3H,H$_3$−C (23)), 0.96−0.89 (m, 1H, H$_b$-C (1)), 0.84 (s, 3H, H$_3$−C (25)), 0.76 (s, 3H, H$_3$−C (24)), 0.71−0.66 (m, 1H, H−C (5)). ^{13}C NMR (126 MHz, CDCl$_3$) δ 164.01 (C=O), 150.06 (C20), 149.91 (C2′), 147.43 (C6′), 140.10 (C1″), 136.95 (C4′), 129.01 (C3″ + C5″), 127.92 (C2″ + C6″), 126.67 (C4″), 125.60 (C5′), 121.75 (C3′), 110.43 (C29), 79.19 (C3), 55.53 (C5), 54.83 (C22), 50.68 (C9), 50.66 (C18), 50.39 (C17), 46.23 (C19), 42.72 (C14), 41.02 (C8), 39.02 (C4), 38.90 (C1), 37.69 (C13), 37.34 (C10), 35.90 (C28), 34.09 (C7 + C21), 30.25 (C16), 28.13 (C23), 27.59 (C2), 27.40 (C15), 25.21 (C12), 21.00 (C11), 19.29 (C30), 18.37 (C6), 16.21 (C25), 16.07 (C26), 15.50 (C24), 15.15 (C27).

*(16R)-16-Phenyl-3β-hydroxy-28-picolinamido-lup-20(29)-ene (**7b**).* ^{1}H NMR (500 MHz, CDCl$_3$) δ 8.17 (dd, ^3J = 4.8 Hz, ^4J = 1.7 Hz, 1H, H−C (6)), 7.98 (d, ^3J = 7.8, Hz, 1H, H−C(3′)), 7.71 (td, ^3J = 7.8 Hz, ^4J = 1.7 Hz, 1H, H−C(4′)), 7.35−7.24 (m, 6H, H−C(2″), H−C(3″), H−C(5″), H−C(6″), H−C(4″), H−C(5′)),7.06 (d, ^3J = 9.3 Hz, 1H, H−N), 4.75 (d, ^4J = 2.3 Hz, 1H, H$_a$-C (29)), 4.62 (s, 1H, H$_b$-C (29)), 3,73 (dd, ^2J = 14.2 Hz, ^3J = 9.3 Hz, 1H, H$_a$-C (28)), 3.40 (d, ^2J = 14.2 Hz, 1H, H$_b$-C (28)), 3.20 (dd, ^3J = 11.4, 4.9 Hz, 1H, H−C (3)), 2.92 (dd, ^3J = 13.0, 3.5 Hz, 1H, H−C (16)), 2.70 (td, ^3J = 10.9, 4.5 Hz, 1H, H−C (19)), 2.47 (dd, ^2J = 13.3 Hz, ^3J = 13.0 Hz, 1H, H$_a$-C (15)), 2.02 (dddd, ^2J = 12.8 Hz, ^3J = 12.5, 10.9, 7.5 Hz, 1H, H$_a$-C (21)), 1.91 (dd, ^3J = 11.9, 10.9 Hz, 1H, H−C (18)), 1.82 (td, ^3J = 11.9, 3.7 Hz, 1H, H−C (13)), 1.77 (s, 3H, H−C (30)), 1.76−1.65 (m, 3H, H$_a$-C (12), H$_b$-C (22), H$_a$-C (1)), 1.65−1.40 (m, 8H, H$_2$−C (6), H$_a$-C (11), H$_2$−C (2), H$_b$-C (22), H$_2$−C (7)), 1.40- 1.23 (m, 4H, H$_b$-C (11), H$_b$-C (21), H$_b$-C (15), H−C (9)), 1.19 (s, 3H, H$_3$−C (26)), 1.14−1.08 (m, 4H, H$_b$-C (12), H$_3$−C (27)), 0.98 (s, 3H,H$_3$−C (23)), 0.96−0.89 (m, 1H, H$_b$-C (1)), 0.88 (s, 3H, H$_3$−C (25)), 0.78 (s, 3H, H$_3$−C (24)), 0.74−0.67 (m, 1H, H−C (5)). ^{13}C NMR (126 MHz, CDCl$_3$) δ 164.14 (C=O), 150.44 (C20), 149.82 (C2′), 147.54 (C6′), 143.76 (C1″), 137.01 (C4′), 128.83 (C3″ + C5″), 127.82 (C2″ + C6″), 126.51 (C4″), 125.69 (C5′), 121.76 (C3′), 109.66 (C29), 79.14 (C3), 55.48 (C5), 51.33 (C18), 51.30 (C17), 50.62 (C9), 48.73 (C16), 46.94 (C19), 43.38 (C14), 41.45 (C8), 39.03 (C4), 38.92 (C1), 37.37 (C10), 37.11 (C13), 36.38 (C28), 35.06 (C22), 34.49 (C7), 32.33 (C15), 30.13 (C21),

28.15 (C23), 27.56 (C2), 25.71 (C12), 21.08 (C11), 20.24 (C30), 18.44 (C6), 16.41 (C25), 16.36 (C26), 15.57 (C24), 15.53 (C27).

*(22S)-22-Tolyl-3β-hydroxy-28-picolinamido-lup-20(29)-ene (**6c**) and (16R)-16-Tolyl-3β-hydroxy-28-picolinamido-lup-20(29)ene (**7c**).* According to GP II, compounds **6c** and **7c** were prepared from picolinic amide **3a** (100 mg, 0.183 mmol, 1 equiv), 1-iodo-4-methylbenzene (159 mg, 0.731 mmol, 4 equiv), Pd(OAc)$_2$ (2 mg, 0.009 mmol, 0.05 equiv), CuBr$_2$ (4 mg, 0.018 mmol, 0.1 equiv), and CsOAc (140 mg, 0.731 mmol, 4 equiv) in *t*-AmOH (2 mL). Yield 75 mg, 65%. HRMS (ESI): *m/z* calc. for [C$_{43}$H$_{60}$N$_2$O$_2$ + H]$^+$ 637.4728; found 637.4726.

*(22S)-22-Tolyl-3β-hydroxy-28-picolinamido-lup-20(29)-ene (**6c**).* ^{1}H NMR (500 MHz, CDCl$_3$) δ 8.18 (dd, 1H, ^3J = 5.3 Hz, ^4J = 1.8 Hz, H−C(6′)), 8.01 (d, ^3J = 7.8 Hz, 1H, H−C(3′)), 7.70 (td, ^3J = 7.8 Hz, ^4J = 1.8 Hz, 1H, H−C(4′)), 7.28−7.24 (m, 1H, H−C(5′)), 7.23 (d, ^3J = 7.9 Hz, 2H, H−C(2″), H−C(6″)), 7.13 (d, ^3J = 7.9 Hz, 2H, H−C(3″), H−C(5″)), 6.90 (d, ^3J = 9.4 Hz, 1H, H−N), 4.80 (d, ^4J = 2.2 Hz, 1H, H$_a$-C (29)), 4.66 (s, 1H, H$_b$-C (29)), 4.13 (dd, ^2J = 14.2, ^3J = 9.4 Hz, 1H, H$_a$-C (28)), 3.19 (dd, ^3J = 11.3, 4.8 Hz, 1H, H−C (3)), 3.00 (dd, ^2J = 14.4, ^3J = 2.8 Hz, 1H, H$_b$-C (28)), 2.89 (dd, ^3J = 10.1, 9.1 Hz, 1H, H−C (22)), 2.73−2.58 (m, 2H, H$_a$-C (21), H−C (19)), 2.33 (s, 3H, H$_3$C-Ph), 2.02 (td, ^3J = 12.0, 3.6 Hz, 1H, H−C (13)), 1.89 (dd, ^3J = 12.0, 11.2 Hz, 1H, H−C (18)), 1.84 (ddd, ^2J = 13.1 Hz, ^3J = 6.9, 3.5 Hz, 1H, H$_a$-C (16)), 1.76 (s, 3H, H−C (30)), 1.76−1.65 (m, 4H, H$_a$-C (12), H$_a$-C (7), H$_a$-C (1), H$_a$-C (15)), 1.65−1.23 (m, 10H, H$_2$−C (2), H$_2$−C (6), H$_2$−C (11), H$_b$-C (16) H$_b$-C (7), H$_b$-C (21), H−C (9)), 1.16 (s, 3H, H$_3$−C (26)), 1.14−1.08 (m, 1H, H$_b$-C (12)), 1.03 (s, 3H, H$_3$−C (27)), 1.03−0.96 (m, 1H, H$_b$-C (15)), 0.96 (s, 3H,H$_3$−C (23)), 0.96−0.85 (m, 1H, H$_b$-C (1)), 0.84 (s, 3H, H$_3$−C (25)), 0.76 (s, 3H, H$_3$−C (24)), 0.71−0.66 (m, 1H, H−C (5)). ^{13}C NMR (126 MHz, CDCl$_3$) δ 164.02 (C=O), 150.12 (C20), 150.05 (C2′), 147.52 (C6′), 136.94 (C4′ + C1″), 136.33 (C4″), 129.62 (C3″ + C5″), 127.71 (C2″+ C6″), 125.57 (C5′), 121.88 (3′), 110.36 (C29), 79.17 (C3), 55.52 (C5), 54.40 (C22), 50.67 (C9), 50.59 (C18), 50.18 (C17), 46.25 (C19), 42.70 (C14), 41.00 (C8), 39.00 (C1), 38.88 (C4), 37.67 (C13), 37.33 (C10), 35.95 (C28), 34.14 (C7), 34.09 (C21), 30.23 (C16), 28.11 (C23), 27.57 (C2), 27.40 (C15), 25.19 (C12), 21.22 (CH$_3$−Ph), 20.99 (C11), 19.29 (C30), 18.36 (C6), 16.20 (C25), 16.05 (C26), 15.49 (C24), 15.13 (C27).

*(16R)-16-Tolyl-3β-hydroxy-28-picolinamido-lup-20(29)-ene (**7c**).* ^{1}H NMR (500 MHz, CDCl$_3$) δ 8.19 (d, ^3J = 4.5 Hz, 1H, H−C(6′), 8.00 (d, ^3J = 7.8 Hz, 1H, H−C(3′), 7.72 (td, ^3J = 7.8, ^4J = 1.8 Hz, 1H, H−C(4′)), 7.29−7.26 (m, 1H, H−C(5′)), 7.21 (d, ^3J = 7.9 Hz, 2H, H−C(2″), H−C(6″)), 7.12 (d, ^3J = 7.9 Hz, 2H, H−C(3″), H−C(5″)), 7.04 (d, ^3J = 9.5 Hz, 1H, H−N), 4.74 (d, ^3J = 2.4 Hz, 1H, H$_a$-C (29)), 4.62 (s, 1H, H$_b$-C (29)), 3.72 (dd, ^2J = 14.4, ^3J = 9.5 Hz, 1H, H$_a$-C (28)), 3.38 (d, ^2J = 14.4 Hz, 1H, H$_b$-C (28)), 3.20 (dd, ^3J = 11.4, 4.9 Hz, 1H, H−C (3)), 2.88 (dd, ^3J = 13.2, 3.2 Hz, 1H, H−C (16)), 2.69 (td, ^3J = 11.0, 4.4 Hz, 1H, H−C (19)), 2.44 (dd, ^2J = 13.4 Hz, ^3J = 13.2 Hz, 1H, H$_a$-C (15)), 2.06−1.96 (m, 1H, H$_a$-C (21)), 1.89 (dd, ^2J = 12.0 Hz, ^3J = 11.4 Hz, 1H, H−C (18)), 1.80 (td, ^3J = 12.0, 3.5 Hz, 1H, H−C (13)), 1.75 (s, 3H, H−C (30)), 1.74−1.67 (m, 3H, H$_a$-C (12), H$_a$-C (22), H$_a$-C (1)), 1.66−1.23 (m, 12H, H$_2$−C (2), H$_2$−C (6), H$_2$−C (11), H$_b$-C (21), H$_b$-C (15), H$_2$−C (7), H$_b$-C (22), H−C (9)), 1.18 (s, 3H, H$_3$−C (26)), 1.13−1.07 (m, 4H, H$_3$−C (27), H$_b$-C (12)), 0.97 (s, 3H, H$_3$−C (23)), 0.96−0.90 (m, 1H, H$_b$-C (1)), 0.87 (s, 3H, H$_3$−C (25)), 0.78 (s, 3H, H$_3$−C (24)), 0.73−0.69 (m, 1H, H−C (5)). ^{13}C NMR (126 MHz, CDCl$_3$) δ 164.16 (C=O), 150.48 (C20), 149.97 (C2′), 147.63 (C6′), 140.68 (C1″), 137.03 (C4′), 136.15 (C4″), 129.45 (C3″ + C5″), 127.63 (C2″+ C6″), 125.68 (C5′), 121.90 (3′), 109.64 (C29), 79.14 (C3), 55.48 (C5), 50.62 (C9), 50.22 (C18), 50.21 (C17), 48.28 (C16), 46.95 (C19), 43.37 (C14), 41.44 (C8), 39.04 (C1), 38.92 (C4), 37.37 (C13), 37.10 (C10), 36.42(C28), 35.08 (C22), 34.46 (C7), 32.39 (C15), 30.13 (C21), 28.16 (C23), 27.57 (C2), 25.71 (C12), 21.22 (CH$_3$−Ph), 21.08 (C11), 20.21 (C30), 18.45 (C6), 16.41 (C25), 16.36 (C26), 15.57 (C24), 15.54 (C27).

*(22S)-22-(4-Hydroxyphenyl)-3β-hydroxy-28-picolinamido-lup-20(29)ene (**6d**) and (**7d**).* According to GP II, compounds **6d** and **7d** were prepared from picolinic amide **3a** (100 mg, 0.183 mmol, 1 equiv), 4-iodophenol (161 mg, 0.731 mmol, 4 equiv), Pd(OAc)$_2$ (2 mg, 0.009 mmol, 0.05 equiv), CuBr$_2$ (4 mg, 0.018 mmol, 0.1 equiv), and CsOAc (140 mg, 0.731 mmol, 4 equiv) in *t*-AmOH (2 mL). Yield 58 mg, 50%. HRMS (ESI): *m/z* calc. for [C$_{42}$H$_{58}$N$_2$O$_3$ + H]$^+$ 639.4520; found 639.4504.

*(22S)-22-(4-Hydroxyphenyl)-3β-hydroxy-28-picolinamido-lup-20(29)ene (**6d**).* ^{1}H NMR (500 MHz, CDCl$_3$) δ 8.34 (dd, 1H, ^3J = 5.1 Hz, ^4J = 1.8 Hz, H−C(6′)), 8.00 (d, ^3J = 7.7 Hz, 1H, H−C(3′)), 7.70 (td, ^3J = 7.7 Hz, ^4J = 1.8 Hz, 1H, H−C(4′)), 7.29−7.23 (m, 1H, H−C(5′)), 7.20 (d, ^3J = 8.6 Hz, 2H, H−C(2″), H−C(6″)), 7.03 (d, ^3J = 9.0 Hz, 1H, H−N), 6.83 (d, ^3J = 8.6 Hz, 2H, H−C(3″), H−C(5″)), 4.79 (d, ^4J = 2.3 Hz, 1H, H$_a$-C (29)), 4.66 (s, 1H, H$_b$-C (29)), 4.16 (dd, ^2J = 14.1, ^3J = 9.0 Hz, 1H, H$_a$-C (28)), 3.49 (s, 1H, OH) 3.19 (dd, ^3J = 11.4, 4.8 Hz, 1H, H−C (3)), 2.94 (dd, ^2J = 14.1, ^3J = 2.4 Hz, 1H, H$_b$-C (28)), 2.87 (dd, ^3J = 10.1, 8.7 Hz, 1H, H−C (22)), 2.69−2.55 (m, 2H, H$_a$-C (21), H−C (19)), 1.99 (td, ^3J = 11.9, 4.2 Hz, 1H, H−C (13)), 1.88 (dd, ^3J = 11.9, 10.9 Hz, 1H, H−C (18)), 1.82 (ddd, ^2J = 13.1 Hz, ^3J = 6.8, 3.5 Hz, 1H, H$_a$-C (16)), 1.76 (s, 3H, H−C (30)), 1.76−1.65 (m, 4H, H$_a$-C (12), H$_a$-C (7), H$_a$-C (1), H$_a$-C (15)), 1.65−1.23 (m, 9H, H$_2$−C (2), H$_2$−C (6), H$_2$−C (11), H$_b$-C (16) H$_b$-C (7), H$_b$-C (21), H−C (9)), 1.15 (s, 3H, H$_3$−C (26)), 1.13−1.05 (m, 1H, H$_b$-C (12)), 1.02 (s, 3H, H$_3$−C (27)), 1.01−0.97 (m, 1H, H$_b$-C (15)), 0.96 (s, 3H,H$_3$−C (23)), 0.94−0.88 (m, 1H, H$_b$-C (1)), 0.83 (s, 3H, H$_3$−C (25)), 0.76 (s, 3H, H$_3$−C (24)), 0.71−0.65 (m, 1H, H−C (5)). ^{13}C NMR (126 MHz, CDCl$_3$) δ 164.19 (C=O), 155.25 (C4″), 150.08 (C20), 149.74 (C2′), 147.95 (C6′), 137.02 (C4′), 131.85 (C1″), 128.87 (C2″ + C6″), 125.75 (C5′), 121.75 (C3′), 115.94 (C3″ + C5″), 110.40 (C29), 79.26 (C3), 55.52 (C5), 53.97 (C22), 50.66 (C9), 50.42 (C18), 50.11 (C17), 46.20 (C19), 42.72 (C14), 40.99 (C8), 39.01 (C4), 38.88 (C1), 37.68 (C13), 37.33 (C10), 35.97 (C28), 34.21 (C7), 34.08 (C21), 30.20 (C16), 28.12 (C23), 27.55 (C2), 27.40 (C15), 25.20 (C12), 20.98 (C11), 19.31 (C30), 18.37 (C6), 16.21 (C25), 16.07 (C26), 15.50 (C24), 15.13 (C27).

*(22S)-22-(4-(tert-Butyldimethylsilyl)oxyphenyl)-3β-hydroxy-28-picolinamido-lup-20(29)ene (**6e**) and (16R)-16-(4-(tert-Butyldimethylsilyl)oxyphenyl)-3β-hydroxy-28-picolinamido-lup-20(29)ene (**7e**).* According to GP II, compounds **6e** and **7e** were prepared from picolinic amide **3a** (100 mg, 0.183 mmol, 1 equiv), *tert*-butyl(4-iodophenoxy)dimethylsilane (244 mg, 0.731 mmol, 4 equiv), Pd(OAc)$_2$ (2 mg, 0.009 mmol, 0.05 equiv), CuBr$_2$ (4 mg, 0.018 mmol, 0.1 equiv), and CsOAc (140 mg, 0.731 mmol, 4 equiv) in *t*-AmOH (2 mL). Yield 45

mg, 33%. HRMS (ESI): m/z calc. for $[\mathrm{C_{48}H_{72}N_2O_3Si + H}]^+$ 753.5385; found 753.5368.

*(22S)-22-(4-(tert-Butyldimethylsilyl)oxyphenyl)-3β-hydroxy-28-picolinamido-lup-20(29)ene (**6e**).* ^{1}H NMR (500 MHz, CDCl$_3$) δ 8.32 (d, 1H, ^3J = 4.7 Hz, H−C(6′)), 8.00 (d, ^3J = 7.7 Hz, 1H, H−C(3′)), 7.69 (td, ^3J = 7.7 Hz, ^4J = 1.7 Hz, 1H, H−C(4′)),7.25 (dd, ^3J = 7.7, 4.7 Hz, 1H, H−C(5′)), 7.19 (d, ^3J = 8.1 Hz, 2H, H−C(2″), H−C(6″)), 6.98 (d, ^3J = 9.8 Hz, 1H, H−N), 6.81 (d, ^3J = 8.1 Hz, 2H, H−C(3″), H−C(5″)), 4.79 (d, ^4J = 2.2 Hz, 1H, H$_a$-C (29)), 4.65 (s, 1H, H$_b$-C (29)), 4.14 (dd, ^2J = 14.1 Hz, ^3J = 9.8 Hz 1H, H$_a$-C (28)), 3.18 (dd, ^3J = 11.3, 4.8 Hz, 1H, H−C (3)), 2.95 (d, ^2J = 14.1 Hz, 1H, H$_b$-C (28)), 2.86 (dd, ^3J = 9.6, 9.2 Hz, 1H, H−C (22), 2.66 −2.57 (m, 2H, H$_a$-C (21), H−C (19)), 2.01 (td, ^3J = 12.2, 3.4 Hz, 1H, H−C (13)), 1.91−1.80 (m, 2H, H−C (18), H$_a$-C (16)), 1.76 (s, 3H, H$_3$−C (30)), 1.75−1.64 (m, 4H, H$_a$-C (22), H$_a$-C (15), H$_b$-C (21), H$_a$-C (1)), 1.65−1.24 (m, 10H, H$_2$−C (2), H$_2$−C (6), H$_2$−C (11), H$_b$-C (16), H$_2$−C (7), H−C (9)), 1.17 (s, 3H, H$_3$−C (26)), 1.15−1.08 (m, 1H, H$_b$-C (15)), 1.02 (s, 3H, H$_3$−C (27)), 1.00 (s, 9H, (CH$_3$)$_3$C), 1.00−0.96 (m, 1H, H$_b$-C (15)), 0.96 (s, 3H, H$_3$−C (23)), 0.95−0.90 (m, 1H, H$_b$-C (1)), 0.84 (s, 3H, H$_3$−C (25)), 0.76 (s, 3H, H$_3$−C (24)), 0.68 (d, ^3J = 10.5 Hz, 1H, H−C (5)), 0.17 (s, 3H, H$_3$−C-Si), 0.16 (s, 3H, H$_3$−C-Si). ^{13}C NMR (126 MHz, CDCl$_3$) δ 164.07 (C═O), 154.96 (C4′), 150.16 (C20), 149.97 (C2′), 147.97 (C6′), 136.92 (C4′), 132.49 (C1″), 128.66 (C2″ + C6″), 125.56 (C5′), 121.69 (C3′), 120.49 (C3″ + C5″), 110.38 (C29), 79.20 (C3), 55.54 (C5), 54.08 (C22), 50.68 (C9), 50.48 (C18), 50.16 (C17), 46.24 (C19), 42.72 (C14), 41.01 (C8), 39.02 (C4), 38.90 (C1), 37.69 (C13), 37.35 (C10), 35.90 (C28), 34.28 (C21), 34.09 (C7), 30.23 (C16), 28.13 (C23), 27.59 (C2), 27.42 (C15), 25.81 (C12), 25.20 ((CH$_3$)$_3$C), 21.00 (C11), 19.26 (C30), 18.37 (C6), 18.25 (C(CH$_3$)$_3$), 16.21 (C25), 16.06 (C26), 15.50 (C24), 15.15 (C27), −4.32 ((CH$_3$)$_2$Si).

*(16R)-16-(4-(tert-Butyldimethylsilyl)oxyphenyl)-3β-hydroxy-28-picolinamido-lup-20(29)ene (**7e**).* ^{1}H NMR (500 MHz, CDCl$_3$) δ 8.32 (d, 1H, ^3J = 4.7 Hz, H−C(6′)), 7.99 (d, ^3J = 7.7 Hz, 1H, H−C(3′)), 7.71 (td, ^3J = 7.7 Hz, ^4J = 1.7 Hz, 1H, H−C(4′)), 7.26 (dd, ^3J = 7.7, 4.7 Hz, 1H, H−C(5′)), 7.18 (d, ^3J = 8.1 Hz, 2H, H−C(2″), H−C(6″)), 7.09 (d, ^3J = 9.7 Hz, 1H, H−N), 6.79 (d, ^3J = 8.1 Hz, 2H, H−C(3″), H−C(5″)), 4.74 (d, ^4J = 2.2 Hz, 1H, H$_a$-C (29)), 4.62 (s, 1H, H$_b$-C (29)), 3.71 (dd, ^2J = 14.3 Hz, ^3J = 9.7 Hz, 1H, H$_a$-C (28)), 3.33 (d, ^2J = 14.3 Hz, 1H, H$_b$-C (28)), 3.20 (dd, ^3J = 11.3, 4.8 Hz, 1H, H−C (3)), 2.86 (dd, ^3J = 13.0, 3.2 Hz, 1H, H−C (16)), 2.69 (td, ^3J = 11.0, 4.4 Hz, 1H, H−C (19)), 2.39 (dd, ^2J = 13.6 Hz, ^3J = 13.0 Hz, 1H, H$_a$-C (15)), 2.08−1.96 (m, 2H, H$_a$-C (21), H$_a$-C (2)), 1.88 (dd, ^3J = 11.9, 11.0 Hz, 1H, H−C (18)), 1.79 (td, ^3J = 11.9, 3.7 Hz, 1H, H−C (13)), 1.74 (s, 3H, H−C (30)), 1.76−1.20 (m, 15H, H$_2$−C (12), H$_2$−C (22), H$_a$-C (1), H$_b$-C (2), H$_2$−C (11), H$_2$−C (6), H$_2$−C (7), H$_b$-C (15), H$_b$-C (21), H−C (9)), 1.17 (s, 3H, H$_3$−C (26)), 1.09 (s, 3H, H$_3$−C (27)), 1.01 (s, 9H, (H$_3$C)$_3$C), 0.98 (s, 3H,H$_3$−C (23)), 0.97−0.90 (m, 1H, H$_b$-C (1)), 0.88 (s, 3H, H$_3$−C (25)), 0.78 (s, 3H, H$_3$−C (24)), 0.74−0.69 (m, 1H, H−C (5)), 0.18 (s, 3H, H$_3$−C-Si), 0.17 (s, 3H, H$_3$−C-Si).^{13}C NMR (126 MHz, CDCl$_3$) δ 164.20 (N−C═O), 154.71 (C4″), 150.50 (C20), 149.87 (C2′), 148.02 (C6′), 136.97 (C4′), 136.25 (C1″), 128.56 (C2″ + C6″), 125.65 (C5′), 121.71 (C3′), 120.25 (C3″ + C5″), 109.61 (C29), 79.15 (C3), 55.48 (C5), 51.31 (C18), 51.17 (C17), 50.62 (C9), 47.86 (C16), 46.94 (C19), 43.38 (C14), 41.44 (C8), 39.04 (C4), 38.93 (C1), 37.37 (C13), 37.09 (C10), 36.39 (C28), 35.13 (C22), 34.51 (C7), 32.51 (C15), 30.13 (C21), 28.16 (C23), 27.57 (C2), 25.82 ((CH$_3$)$_3$), 25.71 (C12), 21.09 (C11), 20.25 (C30), 18.44 (C6), 18.28 (C((CH$_3$)$_3$C), 16.40 (C25), 16.36 (C26), 15.54 (C24), 14.27 (C27), −4.28 ((CH$_3$)Si), −4.31 ((CH$_3$)Si).

*(22S)-22-(4-Methoxycarbonylphenyl)-3β-hydroxy-28-picolinamido-lup-20(29)ene (**6f**) and (16R)-16-(4-Methoxycarbonylphenyl)-3β-hydroxy-28-picolinamido-lup-20(29)ene (**7f**).* According to GP II, compounds **6f** and **7f** were prepared from picolinic amide **3a** (100 mg, 0.183 mmol, 1 equiv), methyl 4-iodobenzoate (161 mg, 0.731 mmol, 4 equiv), Pd(OAc)$_2$ (2 mg, 0.009 mmol, 0.05 equiv), CuBr$_2$ (4 mg, 0.018 mmol, 0.1 equiv), and CsOAc (140 mg, 0.731 mmol, 4 equiv) in *t*-AmOH (2 mL). Yield 47 mg, 38%. HRMS (ESI): m/z calc. for $[\mathrm{C_{44}H_{60}N_2O_4 + H}]^+$ 681.4626; found 681.4606.

*(22S)-22-(4-Methoxycarbonylphenyl)-3β-hydroxy-28-picolinamido-lup-20(29)ene (**6f**).* ^{1}H NMR (500 MHz, CDCl$_3$) δ 8.05 (dd, 1H, ^3J = 4.9 Hz, ^4J = 1.6 Hz, H−C(6′)), 7.96 (d, ^3J = 7.7 Hz, 1H, H−C(3′)), 7.95 (d, ^3J = 8.2 Hz, 2H, H−C(3″), H−C(5″)), 7.68 (td, ^3J = 7.7 Hz, ^4J = 1.6 Hz, 1H, H−C(4′)), 7.40 (d, ^3J = 8.2 Hz, 2H, H−C(2″), H−C(6″)), 7.22 (dd, ^3J = 7.7, 4.9 Hz, 1H, H−C(5′)),), 6.87 (d, ^3J = 9.0 Hz, 1H, H−N), 4.81 (d, ^4J = 2.3 Hz, 1H, H$_a$-C (29)), 4.68 (s, 1H, H$_b$-C (29)), 4.06 (dd, ^2J = 14.3, ^3J = 9.0 Hz, 1H, H$_a$-C (28)), 3.90 (s, 3H, O−CH$_3$) 3.20 (dd, ^3J = 11.4, 4.7 Hz, 1H, H−C (3)), 2.94 (dd, ^2J = 14.3, ^3J = 2.4 Hz, 1H, H$_b$-C (28)), 2.87 (dd, ^3J = 9.8, 9.6 Hz, 1H, H−C (22)), 2.73 (ddd, ^2J = 13.6 Hz, ^3J = 11.2, 9.8 Hz, 1H H$_a$-C (21)), 2.68−2.53 (m, 2H, H−C (19), OH), 2.00 (td, ^3J = 11.7, 3.5 Hz, 1H, H−C (13)), 1.93 (dd, ^3J = 11.7, 11.0 Hz, 1H, H−C (18)), 1.86 (ddd, ^2J = 13.1 Hz, ^3J = 6.7, 3.5 Hz, 1H, H$_a$-C (16)), 1.77 (s, 3H, H−C (30)), 1.76−1.65 (m, 4H, H$_a$-C (12), H$_a$-C (7), H$_a$-C (1), H$_a$-C (15)), 1.65−1.23 (m, 10H, H$_2$−C (2), H$_2$−C (6), H$_2$−C (11), H$_b$-C (16) H$_b$-C (7), H$_b$-C (21), H−C (9)), 1.14 (s, 3H, H$_3$−C (26)), 1.13−1.05 (m, 1H, H$_b$-C (12)), 1.04 (s, 3H, H$_3$−C (27)), 1.01−0.97 (m, 1H, H$_b$-C (15)), 0.96 (s, 3H,H$_3$−C (23)), 0.94−0.88 (m, 1H, H$_b$-C (1)), 0.84 (s, 3H, H$_3$−C (25)), 0.76 (s, 3H, H$_3$−C (24)), 0.73−0.66 (m, 1H, H−C (5)). ^{13}C NMR (126 MHz, CDCl$_3$) δ 167.26 (O−C═O), 164.12 (N−C═O), 149.66 (C20), 149.41 (C2′), 147.54 (C6′), 145.88 (C1″), 137.05 (C4′), 130.23 (C3″ + C5″), 128.61 (C4″), 127.81 (C2″ + C6″), 125.84 (C5′), 121.84 (C3′), 110.68 (C29), 79.26 (C3), 55.51 (C5), 54.81 (C22), 52.12 (O−CH$_3$), 50.87 (C17), 50.79 (C18), 50.64 (C9), 46.16 (C19), 42.68 (C14), 41.00 (C8), 39.00 (C4), 38.88 (C1), 37.69 (C13), 37.32 (C10), 36.00 (C28), 34.11 (C7), 33.85 (C21), 30.27 (C16), 28.11 (C23), 27.51 (C2), 27.37 (C15), 25.20 (C2), 20.97 (C11), 19.36 (C30), 18.36 (C6), 16.21 (C25), 16.03 (C26), 15.49 (C24), 15.15 (C27).

*(16R)-16-(4-Methoxycarbonylphenyl)-3β-hydroxy-28-picolinamido-lup-20(29)ene (**7f**).* ^{1}H NMR (500 MHz, CDCl$_3$) δ 8.07 (d, ^3J = 4.7 Hz, 1H, H−C(6′), 7.96 (d, ^3J = 7.7 Hz, 1H, H−C(3′)), 7.94 (d, ^3J = 8.2 Hz, 2H, H−C(3″, H−C(5″)), 7.70 (td, ^3J = 7.7, ^4J = 1.7 Hz, 1H, H−C(4′)), 7.39 (d, J = 8.2 Hz, 2H, H−C(2″), H−C(6″)), 7.24 (dd, ^3J = 7.7, 4.7 Hz, 1H, H−C(5′)), 6.99 (d, ^3J = 9.0 Hz, 1H, H−N), 4.75 (d, ^3J = 2.2 Hz, 1H, H$_a$-C (29)), 4.64 (s, 1H, H$_b$-C (29)), 3.92 (s, 3H, O−CH$_3$), 3.64 (dd, ^2J = 14.5 Hz, ^3J = 9.0 Hz, 1H, H$_a$-C (28)), 3.45 (dd, ^2J = 14.5 Hz, ^3J = 3.2 Hz, 1H, H$_b$-C (28)), 3.20 (dd, ^3J = 11.3, 4.9 Hz, 1H, H−C (3)), 2.97 (dd, ^3J = 13.0, 3.4 Hz, 1H, H−C (16)), 2.68 (td, ^3J = 11.1, 4.5 Hz, 1H H−C (19)),

2.48 (dd, ^2J = 13.2 Hz, ^3J = 13.0 Hz, 1H, H$_a$-C (15)), 2.03 (ddd, ^2J = 13.6 Hz, ^3J = 11.0, 7.6 Hz, 1H, H$_a$-C (21)), 1.92 (dd, ^3J = 12.0, 11.1 Hz, 1H, H−C (18)), 1.82 (td, ^3J = 12.0, 3.6 Hz, 1H, H−C (13)), 1.75 (s, 3H, H$_3$−C (30)), 1.75−1.58 (m, 5H, H$_a$-C (12), H$_2$−C (2), H$_a$-C (22), H$_a$-C (1)), 1.58−1.42 (m, 6H, H$_2$−C (6), H$_a$-C (21), H$_b$-C (22), H$_2$−C (7)), 1.42−1.23 (m, 4H, H$_b$-C (11), H$_b$-C (21), H$_b$-C (16), H−C (9)), 1.21 (s, 3H, H$_3$−C (26)), 1.14−1.07 (m, 4H, H$_3$−C (27), H$_b$-C (12)), 0.98 (s, 3H, H$_3$−C (27)), 0.97−0.90 (m, 1H, H$_b$-C (1)), 0.88 (s, 3H, H$_3$−C (25)), 0.78 (s, 3H, H$_3$−C (24)), 0.75−0.68 (m, 1H, H−C (5)). ^{13}C NMR (126 MHz, CDCl$_3$) δ 167.32 (O−C═O), 164.20 (N−C═O), 150.17 (C20), 149.46 (C2′), 149.35 (C1″), 147.62 (C6′), 137.11 (C4′), 130.07 (C3″ + C5″), 128.44 (C4″), 127.77 (C2″ + C6″), 125.88 (C5′), 121.82 (C3′), 109.86 (C29), 79.18 (C3), 55.48 (C5), 52.15 (O−CH$_3$), 51.49 (C17), 51.38 (C18), 50.59 (C9), 48.81 (C16), 46.86 (C19), 43.39 (C14), 41.45 (C8), 39.03 (C4), 38.92 (C1), 37.37 (C10), 37.11 (C13), 36.35 (C28), 35.06 (C22), 34.51 (C7), 32.12 (C15), 30.04 (C21), 28.14 (C23), 27.53 (C2), 25.65 (C12), 21.04 (C11), 20.20 (C30), 18.43 (C6), 16.43 (C26), 16.36 (C25), 15.60 (C27), 15.54 (C24).

*(22S)-22-(4-Methylcarbonylphenyl)-3β-hydroxy-28-picolinamido-lup-20(29)ene (**6g**) and (16R)-16-(4-Methylcarbonylphenyl)-3β-hydroxy-28-picolinamido-lup-20(29)ene (**7g**).* According to GP II, compounds **6g** and **7g** were prepared from picolinic amide **3a** (100 mg, 0.183 mmol, 1 equiv), 1-(4-iodophenyl)ethan-1-one (180 mg, 0.731 mmol, 4 equiv), Pd(OAc)$_2$ (2 mg, 0.009 mmol, 0.05 equiv), CuBr$_2$ (4 mg, 0.018 mmol, 0.1 equiv), and CsOAc (140 mg, 0.731 mmol, 4 equiv) in *t*-AmOH (2 mL). Yield 35 mg, 29%. HRMS (ESI): m/z calc. for $[C_{44}H_{60}N_2O_3 + H]^+$ 665.4677; found 665.4658.

*(22S)-22-(4-Methylcarbonylphenyl)-3β-hydroxy-28-picolinamido-lup-20(29)ene (**6g**).* ^{1}H NMR (500 MHz, CDCl$_3$) δ 8.02 (d, ^3J = 4.7 Hz, 1H, H−C(6′)), 7.96 (d, ^3J = 7.7 Hz, 1H, H−C(3′)), 7.86 (d, ^3J = 8.2 Hz, 2H, H−C(3″), H−C(5″)), 7.69 (td, ^3J = 7.7, ^4J = 1.7 Hz, 1H, H−C(4′)), 7.42 (d, ^3J = 8.2 Hz, 2H, H−C(2″), H−C(6″)), 7.23 (dd, ^3J = 7.7, 4.7 Hz, 1H, H−C(5′)), 6.90 (dd, ^3J = 8.5, 4.7 Hz, 1H, H−N), 4.82 (d, ^4J = 2.2 Hz, 1H, H$_a$-C (29)), 4.68 (s, 1H, H$_b$-C (29)), 4.03 (dd, ^2J = 14.3 Hz, ^3J = 8.5 Hz, 1H, H$_a$-C (28)), 3.21 (dd, ^3J = 11.4, 4.7 Hz, 1H, H−C (3)), 3.12 (dd, ^2J = 14.3 Hz, ^3J = 4.7 Hz, 1H, H$_b$-C (28)), 2.97 (dd, ^3J = 9.9, 9.5 Hz, 1H, H−C (22)), 2.85−2.62 (m, 2H, H$_a$-C((21), H−C (19)), 2.50 (s, 3H, H$_3$C−C═O), 2.00 (td, ^3J = 11.8, 3.6 Hz, 1H, H−C (13)), 1.94 (dd, ^3J = 11.8, 10.9 Hz, 1H, H−C (18)), 1.88 (ddd, ^2J = 13.1 Hz, ^3J = 13.1, 3.6 Hz, 1H, H$_a$-C (16)), 1.77 (s, 3H, H−C (30)), 1.77−1.65 (m, 4H, H$_a$-C (12), H$_a$-C (7), H$_a$-C (1), H$_b$-C (21)), 1.65−1.44 (m, 6H, H$_a$-C (6), H$_a$-C (11), H$_a$-C (15), H$_2$−C (2), H$_b$-C (16)), 1.44−1.25 (m, 4H, H$_b$-C (7), H$_b$-C (6), H$_b$-C (11), H−C (9)), 1.13 (s, 3H, H$_3$−C (26)), 1.13−1.08 (m, 1H, H$_b$.C (12)), 1.07−1.02 (m, 4H, H$_3$−C (27), H$_b$-C (15)), 0.96 (s, 3H,H$_3$−C (23)), 0.95−0.88 (m, 1H, H$_b$-C (1)), 0.84 (s, 3H, H$_3$−C (25)), 0.76 (s, 3H, H$_3$−C (24)), 0.73−0.66 (m, 1H, H−C (5)). ^{13}C NMR (126 MHz, CDCl$_3$) δ 197.99 (C═O), 164.13 (N−C═O), 149.60 (C20), 149.32 (C2′), 147.55 (C6′), 146.23 (C1″), 137.15 (C4′), 135.76 (C4″), 128.99 (C3″ + C5″), 128.02 (C2″ + C6″), 126.02 (C5′), 121.88 (C3′), 110.73 (C29), 79.30 (C3), 55.51 (C5), 54.83 (C22), 50.85 (C17), 50.84 (C18), 50.64 (C9), 46.16 (C19), 42.69 (C14), 41.00 (C8), 39.00 (C4), 38.88 (C1), 37.71 (C13), 37.33 (C10), 36.05 (C28), 34.13 (C7), 33.88 (C21), 30.27 (C16), 28.11 (C23), 27.50 (C2), 27.37 (C15), 26.66 (CH$_3$−C═O)), 25.20 (C2), 20.98 (C11), 19.38 (C30), 18.36 (C6), 16.21 (C25), 16.03 (C26), 15.49 (C24), 15.17 (C27).

*(16R)-16-(4-Methylcarbonylphenyl)-3β-hydroxy-28-picolinamido-lup-20(29)ene (**7g**).* ^{1}H NMR (500 MHz, CDCl$_3$) δ 8.02 (dd, 1H, ^3J = 4.9 Hz, ^4J = 1.6 Hz, H−C(6′)), 7.97 (d, ^3J = 7.7 Hz, 1H, H−C(3′)), 7.86 (d, ^3J = 8.0 Hz, 2H, H−C(3″), H−C(5″)), 7.70 (td, ^3J = 7.7 Hz, ^4J = 1.6 Hz, 1H, H−C(4′)), 7.41 (d, ^3J = 8.0 Hz, 2H, H−C(2″), H−C(6″)), 7.24 (dd, ^3J = 7.7, 4.9 Hz, 1H, H−C(5′))), 7.00 (dd, ^3J = 8.5, 3.6 Hz, 1H, H−N), 4.76 (d, ^4J = 2.2 Hz, 1H, H$_a$-C (29)), 4.64 (s, 1H, H$_b$-C (29)), 3.61 (dd, ^2J = 14.5 Hz, ^3J = 8.5 Hz, 1H, H$_a$-C (28)), 3.50 (dd, ^2J = 14.5 Hz, ^3J = 3.5 Hz, 1H, H$_b$-C (28)), 3.20 (dd, ^3J = 11.4, 4.9 Hz, 1H, H−C (3)), 2.98 (dd, ^3J = 13.1, 3.5 Hz, 1H, H−C (16)), 2.68 (td, ^3J = 11.0, 4.4 Hz, 1H H−C (19)), 2.49 (dd, ^2J = 13.5 Hz, ^3J = 13.1 Hz, 1H, H$_a$-C (15)), 2.53 (s, 3H, H$_3$C−C═O), 2.09−1.97 (m, 1H, H$_a$-C (21)), 1.93 (dd, ^3J = 11.9, 11.0 Hz, 1H, H−C (18)), 1.82 (td, ^3J = 11.9, 3.6 Hz, 1H, H−C (13)), 1.76 (s, 3H, H$_3$−C (30)), 1.75−1.58 (m, 5H, H$_a$-C (12), H$_2$−C (2), H$_a$-C (22), H$_a$-C (1)), 1.58−1.42 (m, 6H, H$_2$−C (6), H$_a$-C (21), H$_b$-C (22), H$_2$−C (7)), 1.42−1.23 (m, 4H, H$_b$-C (11), H$_b$-C (21), H$_b$-C (16), H−C (9)), 1.21 (s, 3H, H$_3$−C (26)), 1.14−1.07 (m, 4H, H$_3$−C (27), H$_b$-C (12)), 0.98 (s, 3H, H$_3$−C (23)), 0.97−0.90 (m, 1H, H$_b$-C (1)), 0.88 (s, 3H, H$_3$−C (25)), 0.78 (s, 3H, H$_3$−C (24)), 0.75−0.68 (m, 1H, H−C (5)). ^{13}C NMR (126 MHz, CDCl$_3$) δ 198.00 (O═C−CH$_3$), 164.12 (N−C═O), 150.13 (C20), 149.68 (C2′), 149.49 (C1″), 147.61 (C6′), 137.14 (C4′), 135.60 (C4″), 128.80 (C3″ + C5″), 127.97 (C2″ + C6″), 125.98 (C5′), 121.85 (C3′), 109.89 (C29), 79.16 (C3), 55.48 (C5), 51.47 (C17), 51.40 (C18), 50.60 (C9), 48.83 (C16), 46.86 (C19), 43.38 (C14), 41.45 (C8), 39.03 (C4), 38.92 (C1), 37.38 (C10), 37.10 (C13), 36.34 (C28), 35.06 (C22), 34.51 (C7), 32.17 (C15), 30.04 (C21), 28.14 (C23), 27.54 (C2), 26.70 (CH$_3$−C═O), 25.65 (C12), 21.04 (C11), 20.20 (C30), 18.43 (C6), 16.44 (C26), 16.36 (C25), 15.61 (C27), 15.54 (C24).

*(22S)-22-(4-Cyanophenyl)-3β-hydroxy-28-picolinamido-lup-20(29)ene (**6h**) and (16R)-16-(4-Cyanophenyl)-3β-hydroxy-28-picolinamido-lup-20(29)ene (**7h**).* According to GP II, compounds **6h** and **7h** were prepared from picolinic amide **3a** (100 mg, 0.183 mmol, 1 equiv), 4-iodobenzonitrile (167 mg, 0.731 mmol, 4 equiv), Pd(OAc)$_2$ (2 mg, 0.009 mmol, 0.05 equiv), CuBr$_2$ (4 mg, 0.018 mmol, 0.1 equiv), and CsOAc (140 mg, 0.731 mmol, 4 equiv) in *t*-AmOH (2 mL). Yield 37 mg, 31%. HRMS (ESI): m/z calc. for $[C_{43}H_{57}N_3O_2 + H]^+$ 648.4524; found 648,4512.

*(22S)-22-(4-Cyanophenyl)-3β-hydroxy-28-picolinamido-lup-20(29)ene (**6h**).* ^{1}H NMR (500 MHz, CDCl$_3$) δ 8.29 (d, ^3J = 4.7 Hz, 1H, H−C(6′)), 7.99 (d, ^3J = 7.8 Hz, 1H, H−C(3′)), 7.74 (td, ^3J = 7.7, ^4J = 1.7 Hz, 1H, H−C(4′)), 7.55 (d, ^3J = 7.8 Hz, 2H, H−C(3″), H−C(5″)), 7.42 (d, ^3J = 7.8 Hz, 2H, H−C(2″), H−C(6″)), 7.34 (dd, ^3J = 7.7, 4.8 Hz, 1H, H−C(5′)), 6.82−6.73 (dd, ^3J = 8.4, 3.8 Hz, 1H, H−N), 4.82 (s, 1H, H$_a$-C (29)), 4.69 (s, 1H, H$_b$-C (29)), 4.02 (dd, ^2J = 14.4 Hz, ^3J = 8.4 Hz, 1H, H$_a$-C (28)), 3.19 (dd, ^3J = 11.4, 4.7 Hz, 1H, H−C (3)), 3.10 (dd, ^2J = 14.4, ^3J = 3.8 Hz, 1H, H$_b$-C (28)), 2.95 (dd, ^3J = 10.1, 8.3 Hz, 1H, H−C (22)), 2.76−2.62 (m, 2H, H−C (19), H$_a$-C (21)), 1.99 (td, ^3J = 12.0, 3.5 Hz, 1H, H−C (13)), 1.93 (dd, ^3J = 12.0, 10.9 Hz, 1H, H−C (18)), 1.81−1.77 (m, 1H, H$_a$-C (15)), 1.77 (s, 3H, H$_3$−C (30)), 1.76−1.65 (m, 3H, H$_a$-C (12), H$_b$-C(C21), H$_a$-C (1)), 1.65−1.44 (m, 5H, H$_a$-C (6), H$_a$-C (11), H$_2$−C (2), H$_b$-C (16)), 1.44−1.35 (m, 4H, H$_b$-C (6), H$_2$−C (7)), 1.34−1.24 (m, 2H, H$_b$-C (11), H−C (9)), 1.14 (s, 3H, H$_3$−C (26)), 1.14−1.10 (m, 1H, H$_b$-C

(12)), 1.10−1.04 (m, 1H, H_b-C (15)), 1.04 (s, 3H, H_3−C (27)), 0.96 (s, 3H, H_3−C (23)), 0.95−0.89 (m, 1H, H_b-C (1)), 0.84 (s, 3H, H_3−C (25)), 0.76 (s, 3H, H_3−C (24)), 0.68 (d, ^3J = 9.9 Hz, 1H, H−C (5)). ^{13}C NMR (126 MHz, $CDCl_3$) δ 163.86 (N−C=O), 149.44 (C20), 149.40 (C2′), 147.75 (C6′), 146.26 (C1″), 137.25 (C4′), 132.56 (C3″ + C5″), 128.58 (C2″ + C6″), 126.24 (C5′), 121.85 (C3′), 119.16 (C4″), 110.85 (C29), 110.31 (CN), 79.15 (C3), 55.52 (C5), 54.90 (C22), 51.05 (C9), 50.87 (C18), 50.63 (C17), 46.03 (C19), 42.67 (C14), 41.02 (C8), 39.02 (C4), 38.89 (C1), 37.67 (C13), 37.33 (10), 35.78 (C28), 34.13 (C7), 33.72 (C21), 30.25 (C16), 28.12 (C23), 27.56 (C2), 27.36 (C15), 25.21 (C12), 20.96 (C11), 19.41 (C30), 18.36 (C6), 16.22 (C26), 16.06 (C25), 15.49 (C24), 15.17 (C27).

*(16R)-16-(4-Cyanophenyl)-3β-hydroxy-28-picolinamido-lup-20(29)ene (**7h**).* ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.30 (d, 1H, ^3J = 4.7 Hz, H−C(6′)), 7.99 (d, ^3J = 7.7 Hz, 1H, H−C(3′)), 7.75 (td, ^3J = 7.7 Hz, ^4J = 1.7 Hz, 1H, H−C(4′)), 7.53 (d, ^3J = 8.1 Hz, 2H, H−C(3″), H−C(5″)), 7.41 (d, ^3J = 8.1 Hz, 2H, H−C(2″), H−C(6″)), 7.34 (dd, ^3J = 7.7, 4.7 Hz, 1H, H−C(5′)), 6.90 (dd, ^3J = 8.2, 4.1 Hz, 1H, H−N), 4.75 (d, ^4J = 2.2 Hz, 1H, H_a-C (29)), 4.64 (s, 1H, H_b-C (29)), 3.57 (dd, ^2J = 14.6 Hz, ^3J = 8.2 Hz, 1H, H_a-C (28)), 3.50 (dd, ^2J = 14.6 Hz, ^3J = 4.1 Hz, 1H, H_b-C (28)), 3.19 (dd, ^3J = 11.3, 4.8 Hz, 1H, H−C (3)), 2.96 (dd, ^3J = 13.1, 3.4 Hz, 1H, H−C (16)), 2.67 (td, ^3J = 11.0, 4.4 Hz, 1H, H−C (19)), 2.46 (dd, ^2J = 13.3 Hz, ^3J = 13.1 Hz, 1H, H_a-C (15)), 2.06 (dddd, ^2J = 13.2 Hz, ^3J = 11.5, 11.0, 6.3 Hz, 1H, H_a-C (21)), 1.91 (dd, ^3J = 11.9, 11.0 Hz, 1H, H−C (18)), 1.82 (td, ^3J = 11.9, 3.7 Hz, 1H, H−C (13)), 1.76 (s, 3H, H−C (30)), 1.76−1.59 (m, 5H, H_a-C (12), H_a-C (22), H_a-C (1), H_2−C (2)), 1.58−1.43 (m, 6H, H_2−C (6), H_a-C (11), H_b-C (22), H_2−C (7)), 1.43- 1.23 (m, 4H, H_b-C (11), H_b-C (21), H_b-C (15), H−C (9)), 1.21 (s, 3H, H_3−C (26)), 1.16−1.09 (m, 4H, H_b.C (12), H_3−C (27)), 0.98 (s, 3H,H_3−C (23)), 0.97−0.90 (m, 1H, H_b-C (1)), 0.88 (s, 3H, H_3−C (25)), 0.78 (s, 3H, H_3−C (24)), 0.74−0.69 (m, 1H, H−C (5)). ^{13}C NMR (126 MHz, $CDCl_3$) δ 163.97 (N−C=O), 149.96 (C20), 149.61 (C1″), 149.40 (C2′), 147.84 (C6′), 137.27 (C4′), 132.37 (C3″ + C5″), 128.54 (C2″ + C6″), 126.27 (C5′), 121.85 (C3′), 119.21 (C4″), 110.15 (C29), 109.98 (CN), 79.09 (C3), 55.48 (C5), 51.53 (C17), 51.39 (C18), 50.57 (C9), 48.87 (C16), 46.81 (C19), 43.38 (C14), 41.44 (C8), 39.03 (C4), 38.92 (C1), 37.37 (C10), 37.07 (C13), 36.12 (C28), 35.04 (C22), 34.52 (C7), 32.00 (C15), 29.98 (C21), 28.14 (C23), 27.54 (C2), 25.61 (C12), 21.02 (C11), 20.20 (C30), 18.41 (C6), 16.45 (C25), 16.36 (C26), 15.61 (C24), 15.53 (C27).

*(22S)-22-(4-Chlorophenyl)-3β-hydroxy-28-picolinamido-lup-20(29)ene (**6i**) and (16R)-16-(4-Chlorophenyl)-3β-hydroxy-28-picolinamido-lup-20(29)ene (**7i**).* According to GP II, compounds **6i** and **7i** were prepared from picolinic amide **3a** (100 mg, 0.183 mmol, 1 equiv), 1-chloro-4-iodobenzene (174 mg, 0.731 mmol, 4 equiv), $Pd(OAc)_2$ (2 mg, 0.009 mmol, 0.05 equiv), $CuBr_2$ (4 mg, 0.018 mmol, 0.1 equiv), and CsOAc (140 mg, 0.731 mmol, 4 equiv) in *t*-AmOH (2 mL). Yield 65 mg, 54%. HRMS (ESI): *m/z* calc. for $[C_{42}H_{57}ClN_2O_2 + H]^+$ 657.4181; found 657.4170.

*(22S)-22-(4-Chlorophenyl)-3β-hydroxy-28-picolinamido-lup-20(29)ene (**6i**).* ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.32 (d, ^3J = 4.7 Hz, 1H, H−C(6′)), 7.97 (d, ^3J = 7.7 Hz, 1H, H−C(3′)), 7.69 (td, ^3J = 7.7, ^4J = 1.7 Hz, 1H, H−C(4′)), 7.31−7.16 (m, 5H, H−C(5′), H−C(2″), H−C(3″), H−C(5″), H−C(6″)), 6.89 (dd, ^3J = 9.5, 2.8 Hz, 1H, H−N), 4.78 (d, ^4J = 2.2 Hz, 1H, H_a-C (29)), 4.64 (s, 1H, H_b-C (29)), 4.10 (dd, ^2J = 14.2 Hz, ^3J = 9.5 Hz, 1H, H_a-C (28)), 3.16 (dd, ^3J = 11.4, 4.7 Hz, 1H, H−C (3)), 2.96 (dd, ^2J = 14.2 Hz, ^3J = 2.8 Hz, 1H, H_b-C (28)), 2.86 (dd, ^3J = 9.6, 9.1 Hz, 1H, H−C (22)), 2.68−2.54 (m, 2H, H_a-C((21), H−C (19)), 1.97 (td, ^3J = 11.9, 3.5 Hz, 1H, H−C (13)), 1.88 (dd, ^3J = 11.9, 10.9 Hz, 1H, H−C (18)), 1.80 (ddd, ^2J = 13.1 Hz, ^3J = 13.1, 3.6 Hz, 1H, H_a-C (16)), 1.74 (s, 3H, H−C (30)), 1.74−1.62 (m, 4H, H_a-C (12), H_a-C (15), H_a-C (1), H_b-C (21)), 1.62−1.51 (m, 2H, H_2−C (2)), 1.51−1.31 (m, 6H, H_2−C (6), H_a-C (11), H_b-C (16), H_2−C (7)), 1.31−1.22 (m, 2H, H_b-C (11), H−C (9)), 1.13 (s, 3H, H_3−C (26)), 1.12−1.05 (m, 1H, H_{b-}C (12)), 1.01−0.96 (m, 4H, H_3−C (27), H_b-C (15)), 0.93 (s, 3H,H_3−C (23)), 0.93−0.88 (m, 1H, H_b-C (1)), 0.81 (s, 3H, H_3−C (25)), 0.74 (s, 3H, H_3−C (24)), 0.70−0.63 (m, 1H, H−C (5)). ^{13}C NMR (126 MHz, $CDCl_3$) δ 164.06 (N−C=O), 149.77 (C20), 149.61 (C2′), 148.05 (C6′), 138.71 (C1″), 137.06 (C4′), 132.73 (C4″), 129.12 (C2″ + C6″), 129.09 (C3″ + C5″), 125.87 (C5′), 121.76 (C3′), 110.59 (C29), 79.20 (C3), 55.52 (C5), 54.17 (C22), 50.65 (C9), 50.61 (C18), 50.45 (C17), 46.12 (C19), 42.69 (C14), 41.01 (C8), 39.01 (C4), 38.89 (C1), 37.65 (C13), 37.33 (10), 35.84 (C28), 34.09 (C7), 34.03 (C21), 30.17 (C16), 28.12 (C23), 27.56 (C2), 27.37 (C15), 25.21 (C12), 20.97 (C11), 19.36 (C30), 18.36 (C6), 16.21 (C26), 16.04 (C25), 15.49 (C24), 15.14 (C27).

*(16R)-16-(4-Chlorophenyl)-3β-hydroxy-28-picolinamido-lup-20(29)ene (**7i**).* ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.36 (m, d, ^3J = 4.5 Hz, 1H, H−C(6′)), 8.00 (d, ^3J = 7.8 Hz, 1H, H−C(3′), 7.72 (td, ^3J = 7.8, ^4J = 1.8 Hz, 1H, H−C(4′)), 7.31 (dd, ^3J = 7.8, 4.5 Hz, 1H, H−C(5′)), 7.29−7.21 (m, 4H, H−C(2″), H−C(3″), H−C(5″), H−C(6″)), 7.05 (d, *J* = 9.3 Hz, 1H, H−N), 4.75 (d, ^3J = 2.4 Hz, 1H, H_a-C (29)), 4.63 (s, 1H, H_b-C (29)), 3.67 (dd, ^2J = 14.3, ^3J = 9.3 Hz, 1H, H_a-C (28)), 3.38 (d, ^2J = 14.3 Hz, 1H, H_b-C (28)), 3.21 (dd, ^3J = 11.4, 4.9 Hz, 1H, H−C (3)), 2.90 (dd, ^3J = 13.0, 3.5 Hz, 1H, H−C (16)), 2.68 (td, ^3J = 11.4, 4.4 Hz, 1H, H−C (19)), 2.41 (dd, ^2J = 13.4 Hz, ^3J = 13.0 Hz, 1H, H_a-C (15)), 2.05−1.96 (m, 1H, H_a-C (21)), 1.90 (dd, ^2J = 12.0 Hz, ^3J = 11.4 Hz, 1H, H−C (18)), 1.79 (td, ^3J = 12.0, 3.5 Hz, 1H, H−C (13)), 1.75 (s, 3H, H−C (30)), 1.74−1.67 (m, 5H, H_a-C (12), H_a-C (22), H_a-C (1), H_2−C (2)), 1.66−1.23 (m, 10H, H_2−C (6), H_2−C (11), H_b-C (21), H_b-C (15), H_2−C (7), H_b-C (22), H−C (9)), 1.18 (s, 3H, H_3−C (26)), 1.13−1.07 (m, 4H, H_3−C (27), H_b-C (12)), 0.98 (s, 3H, H_3−C (23)), 0.96−0.90 (m, 1H, H_b-C (1)), 0.88 (s, 3H, H_3−C (25)), 0.78 (s, 3H, H_3−C (24)), 0.73−0.68 (m, 1H, H−C (5)). ^{13}C NMR (126 MHz, $CDCl_3$) δ 164.01 (N−C=O), 149.94 (C20), 149.16 (C2′), 147.88 (C6′), 141.99 (C1″), 136.90 (C4′), 132.29 (C4″), 128.81 (C2″ + C6″), 128.64 (C3″ + C5″), 125.75 (C5′), 121.53 (C3′), 109.55 (C29), 78.94 (C3), 55.52 (C5), 51.03 (C17), 50.97 (C18), 50.34 (C9), 47.78 (C16), 46.59 (C19), 43.13 (C14), 41.17 (C8), 38.87 (C4), 38.66 (C1), 37.11 (C13), 36.82 (C10), 36.08(C28), 34.79 (C22), 34.26 (C7), 32.01 (C15), 29.77 (C21), 27.89 (C23), 27.26 (C2), 25.40 (C12), 20.78 (C11), 19.97 (C30), 18.17 (C6), 16.15 (C26), 16.10 (C25), 15.34 (C24), 15.28 (C27).

*(22S)-22-(Thiophen-2-yl)-3β-hydroxy-28-picolinamido-lup-20(29)ene (**6j**) and (16R)-16-(2-Thiophenyl)-3β-hydroxy-28-picolinamido-lup-20(29)ene (**7j**).* According to GP II, a mixture of compounds **6j**, **7j**, **7j′**, and **8** was prepared from picolinic amide **3a** (100 mg, 0.183 mmol, 1 equiv), 2-iodothiophene (80 μL, 0.731 mmol, 4 equiv), $Pd(OAc)_2$ (2 mg, 0.009 mmol, 0.05 equiv), $CuBr_2$ (4 mg, 0.018 mmol, 0.1

equiv), and CsOAc (140 mg, 0.731 mmol, 4 equiv) in *t*-AmOH (2 mL). Total yield of isomers **6j** and **7j** (3:1) 23 mg, 20% along with **7j′** (5%) and **8** (27%). HRMS (ESI) of **6j**: *m*/*z* calc. for [$C_{40}H_{56}N_2O_2S$ + H]$^+$ 629.4135; found 629.4114.

*(22S)-22-(2-Thiophenyl)-3β-hydroxy-28-picolinamido-lup-20(29)ene (**6j**).* ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.30 (d, ^3J = 4.8 Hz, 1H, H−C(6′)),8.04 (d, ^3J = 7.8 Hz, 1H, H−C(3′)), 7.72 (td, ^3J = 7.8 Hz, ^4J = 1.8 Hz, 1H, H−C(4′)), 7.29 (dd, ^3J = 7.8, 4.8 Hz, 1H, H−C(5′)), 7.19 (d, ^3J = 9.7 Hz, 1H, H−N), 7.17 (d, ^3J = 4.9 Hz, 1H, H−C(5″)), 7.01 (dd, ^3J = 4.9, 3.6 Hz, 1H, H−C(4″)), 6.97 (d, ^3J = 3.6 Hz, 1H, H−C(3″)), 4.79 (s, 1H, H_a-C (29)), 4.66 (s, 1H, H_b-C (29)), 4.17 (dd, ^2J = 14.2 Hz, ^3J = 9.7 Hz, 1H, H_a-C (28)), 3.19 (dd, ^3J = 11.3, 4.8 Hz, 1H, H−C (3)), 3.10 (dd, ^3J = 10.1, 9.3 Hz, 1H, H−C (22)), 3.00 (d, ^2J = 14.2 Hz, 1H, H_b-C (28)), 2.63 (ddd, ^3J = 11.1, 10.8, 4.6 Hz, 1H, H−C (19)), 2.58 (ddd, ^2J = 13.4 Hz, ^3J = 11.1, 10.1 Hz 1H, H_a-C (21)), 2.08−1.98 (m, 2H, H−C (13), H_a-C (16)), 1.92 (ddd, ^2J = 13.4 Hz, ^3J = 9.3, 4.6 Hz, 1H, H_b-C (21)), 1.85 (dd, ^3J = 11.6, 10.8 Hz, 1H, H−C (18)), 1.84−1.76 (m, 1H, H_a-C (15)), 1.75 (s, 3H, H−C (30)), 1.74−1.65 (m, 2H, H_a-C (12), H_a-C (1)), 1.64−1.53 (m, 2H, H_2−C (2)), 1.51−1.34 (m, 6H, H_2−C (6), H_a-C (11), H_b-C (16), H_2−C (7)), 1.33−1.22 (m, 2H, H_b-C (11), H−C (9)), 1.18 (s, 3H, H_3−C (26)), 1.12−1.07 (m, 1H, H_b-C (12)), 1.06−1.00 (m, 4H, H_3−C (27), H_b-C (15)), 0.96 (s, 3H,H_3−C (23)), 0.95−0.87 (m, 1H, H_b-C (1)), 0.84 (s, 3H, H_3−C (25)), 0.76 (s, 3H, H_3−C (24)), 0.71−0.66 (m, 1H, H−C (5)).^{13}C NMR (126 MHz, $CDCl_3$) δ 164.13 (N−C=O), 150.05 (C20), 149.67 (C2′), 147.64 (C6′), 144.36 (C2″), 137.04 (C4′), 127.35 (C4″), 125.70 (C5′), 123.90 (C3″), 123.76 (C5″), 121.90 (C3′), 110.68 (C29), 79.19 (C3), 55.53 (C5), 50.66 (C9), 50.32 (C18), 50.19 (C19), 50.03 (C17), 46.24 (C22), 42.75 (C14), 41.03 (C8), 39.02 (C4), 38.90 (C1), 37.73 (C13), 37.34 (C10), 36.86 (C21), 36.18 (C28), 34.11 (C7), 29.84 (C16), 28.13 (C23), 27.58 (C2), 27.45 (C15), 25.18 (C12), 20.97 (C11), 19.32 (C30), 18.38 (C6), 16.21 (C25), 16.08 (C26), 15.51 (C24), 15.07 (C27).

*(16R)-16-(2-Thiophenyl)-3β-hydroxy-28-picolinamido-lup-20(29)ene (**7j**).* ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.30 (d, ^3J = 4.8 Hz, 1H, H−C(6′)),8.02 (d, ^3J = 7.8 Hz, 1H, H−C(3′)), 7.74 (td, ^3J = 7.8 Hz, ^4J = 1.8 Hz, 1H, H−C(4′)), 7.33−7.27 (m, 2H, H−C(5′), H−N)), 7.16 (d, ^3J = 5.2 Hz, 1H, H−C(5″)), 6.98 (dd, ^3J = 5.2, 3.5 Hz, 1H, H−C(4″)), 6.94 (d, ^3J = 3.5 Hz, 1H, H−C(3″)), 4.75 (d, ^4J = 2.2 Hz, 1H, H_a-C (29)), 4.62 (s, 1H, H_b-C (29)), 3.75 (dd, ^2J = 14.6 Hz, ^3J = 9.8 Hz, 1H, H_a-C (28)), 3.36 (dd, ^2J = 14.6 Hz, ^3J = 2.9 Hz, 1H, H_b-C (28)) 3.20 (dd, ^3J = 11.4, 4.8 Hz, 1H, H−C (3)), 3.15 (dd, ^3J = 12.9, 3.7 Hz, 1H, H−C (16)), 2.72 (ddd, ^3J = 11.1, 10.7, 5.8 Hz, 1H, H−C (19)), 2.34 (dd, ^2J = 13.2 Hz, ^3J = 12.9 Hz, 1H, H_a-C (15)), 2.16−2.02 (m, 1H, H_a-C (21)), 1.99 (dd, ^2J = 10.8 Hz, ^3J = 7.8 Hz, 1H, H−C (22)), 1.88−1.78 (m, 2H, H−C (13), H−C (18)), 1.74 (s, 3H, H_3−C (30)), 1.72−1.60 (m, 4H, H_a-C (12), H_2−C (2), H_a-C (1)), 1.60−1.35 (m, 8H, H_2−C (6), H_a-C (11), H_b-C (21), H_2−C (7), H_b-C (22), H_b-C (15)), 1.42−1.23 (m, 2H, H_b-C (11), H−C (9)), 1.16 (s, 3H, H_3−C (26)), 1.12−1.07 (m, 4H, H_3−C (27), H_b-C (12)), 0.98 (s, 3H, H_3−C (23)), 0.93−0.88 (m, 1H, H_b-C (1)), 0.87 (s, 3H, H_3−C (25)), 0.78 (s, 3H, H_3−C (24)), 0.76−0.68 (m, 1H, H−C (5)).^{13}C NMR (126 MHz, $CDCl_3$) δ 164.32 (N−C=O), 150.19 (C20), 149.83 (C2′), 147.90 (C2″), 147.71 (C6′), 137.12 (C4′), 126.94 (C4″), 125.83 (C5′), 123.54 (C3″), 123.35 (C5″), 121.92 (C3′), 109.84 (C29), 79.16 (C3), 55.46 (C5), 51.30 (C17), 50.76 (C18), 50.53 (C9), 47.14 (C19), 44.85 (C16), 43.57 (C14), 41.34 (C8), 39.03 (C4), 38.90 (C1), 37.36 (C10), 36.91 (C13), 36.67 (C28), 35.02 (C22), 34.44 (C7), 34.38 (C15), 30.08 (C21), 28.15 (C23), 27.54 (C2), 25.52 (C12), 21.01 (C11), 20.06 (C30), 18.43 (C6), 16.37 (C26), 16.32 (C25), 15.66 (C27), 15.53 (C24).

*(16R)-16-([2,3′-Bisthiophen]-2′-yl)-3β-hydroxy-28-picolinamido-lup-20(29)ene (**7j′**).* ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.52 (d, ^3J = 4.8 Hz, 1H, H−C(6′)), 8.14 (d, ^3J = 7.8 Hz, 1H, H−C(3′)), 8.13 (t, ^3J = 5.6 Hz, 1H, H−N), 7.82 (td, ^3J = 7.8 Hz, ^4J = 1.8 Hz, 1H, H−C(4′)), 7.39 (dd, ^3J = 7.8, 4.8 Hz, 1H, H−C(5′)), 7.30 (d, ^3J = 5.1 Hz, 1H, C(5‴)), 7.16 (d, ^3J = 5.2 Hz, 1H, H−C(5″)), 7.06 (d, ^3J = 3.5 Hz, 1H, H−C(3‴)), 7.00 (dd, ^3J = 5.1, 3.5 Hz, 1H, H−C(4‴)), 6.91 (d, ^3J = 5.2 Hz, 1H, H−C(4″)), 4.73 (d, ^4J = 2.2 Hz, 1H, H_a-C (29)), 4.59 (s, 1H, H_b-C (29)), 3.80 (dd, ^2J = 13.6 Hz, ^3J = 5.6 Hz, 1H, H_a-C (28)), 3.63 (dd, ^2J = 13.6 Hz, ^3J = 5.6 Hz, 1H, H_b-C (28)) 3.18 (dd, ^3J = 11.4, 4.8 Hz, 1H, H−C (3)), 3.05−2.94 (m, 1H, H−C (16)), 2.17−1.93 (m, 2H, H−C (19), H_a-C (22)), 1.76 (dd, ^3J = 10.1, 7.8 Hz, 1H, H−C (18)), 1.68−1.56 (m, 5H, H_a-C (1), H_a-C (15), H_2−C (2), H_a-C (12)), 1.55 (s, 3H, H_3−C (30)), 1.53−1.47 (m, 2H, H_b-C (22), H_a-C (6)), 1.46−1.32 (m, 6H, H_b-C (6), H_a-C (11), H_2−C (21), H_a-C (7), H−C (13)), 1.31−1.22 (m, 2H, H_b-C (7), H−C (9)), 1.17 (dd, ^2J = 11.2 Hz, ^3J = 5.9 Hz, 1H, H_b-C (15)), 1.14−1.02 (m, 2H, H_b-C (11), H_b-C (12)), 0.97 (s, 3H, H_3−C (26), 0.94 (s, 3H, H_3−C (23)), 0.94−0.91 (m, 1H, H_b-C (1)), 0.83 (s, 3H, H_3−C (25)), 0.76 (s, 6H, H_3−C (27), H_3−C (24)), 0.72−0.66 (m, 1H, H−C (5)). ^{13}C NMR (126 MHz, $CDCl_3$) δ 164.45 (N−C=O), 149.91 (C2′), 149.39 (C20), 148.95 (C2″), 148.33 (C6′), 139.22 (C2‴), 137.39 (C4′), 133.92 (C4″), 130.63 (C3″), 127.71 (C3‴), 126.91 (C4‴), 126.17 (C5′), 125.78 (C5‴), 122.28 (C3′), 121.23 (C5″), 110.70 (C29), 79.21 (C3), 56.11 (C5), 53.59 (C13), 53.57 (C19), 51.61 (C9), 49.08 (C28), 47.79 (C14), 45.16 (C17), 44.62 (C16), 40.63 (C8), 39.24 (C4) 39.13 (C1), 38.09 (C18), 37.38 (C10), 35.22 (C7), 35.02 (C15), 31.91 (C22), 28.09 (C23), 27.53 (C2), 27.26 (C12), 27.19 (C21), 22.15 (C11), 19.49 (C27), 18.87 (C30), 18.42 (C6), 16.49 (C25), 15.91 (C26), 15.40 (C24).

*(22S)-22-(1H-5-Indolyl)-3β-hydroxy-28-picolinamido-lup-20(29)ene (**6m**) and (16R)-16-(1H-5-Indolyl)-3β-hydroxy-28-picolinamido-lup-20(29)ene (**7m**).* According to GP II, a mixture of compounds **6m** and **7m** was prepared from picolinic amide **3a** (100 mg, 0.183 mmol, 1 equiv), 5-iodo-1H-indole (173 mg, 0.731 mmol, 4 equiv), $Pd(OAc)_2$ (2 mg, 0.009 mmol, 0.05 equiv), $CuBr_2$ (4 mg, 0.018 mmol, 0.1 equiv), and CsOAc (140 mg, 0.731 mmol, 4 equiv) in *t*-AmOH (2 mL). Total yield of isomers **6m** and **7m** (5:1) 28 mg, 24%. HRMS (ESI): *m*/*z* calc. for [$C_{44}H_{59}N_3O_2$ + H]$^+$ 662.4680; found 662.4683.

*(22S)-22-(1H-5-Indolyl)-3β-hydroxy-28-picolinamido-lup-20(29)ene (**6m**).* 1H NMR (500 MHz, CDCl3) δ 8.17 (bs, 1H, H−N(1″)), 7.89 (d, ^3J = 7.7 Hz, 1H, H−C(3′)), 7.65 (s, 1H, H−C(4″), 7.58 (td, ^3J = 7.7, ^4J = 1.7 Hz, 1H, H−C(4′)), 7.44 (dd, ^3J = 4.7 Hz, ^4J = 1.5 Hz, 1H, H−C(6′)), 7.33 (d, ^3J = 8.4 Hz, 1H, H−C(6″), 7.22 (t, ^3J = 2.8 Hz, 1H, H−C(2″), 7.18 (d, ^3J = 8.4 Hz, 1H, H−C(7″)), 7.07 (dd, ^3J = 7.7, 4.7 Hz, 1H, H−C(5′)), 6.92 (d, ^3J = 9.7 Hz, 1H, H−N−C=O), 6.54 (dd, ^3J = 2.8 Hz, ^4J = 2.6 Hz, 1H, H−C(3″)), 4.82 (d, ^4J = 2.3 Hz, 1H, H_a-C (29)), 4.67 (s, 1H, H_b-C (29)), 4.18 (dd, ^2J = 14.0, ^3J = 9.7 Hz, 1H, H_a-C (28)), 3.20 (dd, ^3J = 11.4, 4.8 Hz, 1H, H−C (3)) 3.06 (dd, ^3J = 11.2, 10.1 Hz, 1H, H−C (22)),

3.02 (d, ^{2}J = 14.0 Hz, 1H, H_b-C (28)) 2.80 (dt, ^{2}J = 14.0, ^{3}J = 11.2 Hz, 1H, H_a-C (21)), 2.66 (td, ^{3}J = 11.2, 5.0 Hz, 1H, H−C (19)), 2.20−1.85 (m, 3H, H−C (13), H−C (18), H_a-C (16)), 1.79 (s, 3H, H_3−C (30)), 1.78−1.66 (m, 4H, H_a-C (12), H_b-C (21), H_a-C (1), H_a-C (15)), 1.66−1.21 (m, 10H, H_2−C (2), H_2−C (6), H_2−C (11), H_b-C (16), H−C (9), H_2−C (7), 1.17 (s, 3H, H_3−C (26)), 1.16−1.06 (m, 1H, H_b-C (12)), 1.05 (s, 3H, H_3−C (27)), 1.02−0.98 (m, 1H, H_b-C (15)), 0.96 (s, 3H, H_3−C (23)) 0.94−0.88 (m, 1H, H_b-C (1)), 0.84 (s, 3H, H_3−C (25)), 0.76 (s, 3H, H_3−C (24)), 0.73−0.66 (m, 1H, H−C (5)). 13C NMR (126 MHz, CDCl3) δ 164.07 (C═O), 150.36 (C20), 149.72 (C2′), 147.30 (C6′), 136.73 (C4′), 135.57 (C7a″), 131.25 (C5″), 129.00 (C3a″), 125.31 (C5′), 124.28 (C2″), 122.55 (C7″), 121.54 (C3′), 119.21 (C4″), 111.42 (C6″), 110.24 (C29), 103.10 (C3″), 79.25 (C3), 55.54 (C5), 54.83 (C22), 50.69 (C9), 50.47 (C18), 50.29 (C17), 46.30 (C19), 42.78 (C14), 41.02 (C8), 39.02 (C4), 38.89 (C1), 37.70 (C13), 37.34 (C10), 36.10 (C28), 34.50 (C7), 34.08 (C21), 30.36 (C16), 28.13 (C23), 27.58 (C2), 27.45 (C15), 25.26 (C12), 21.00 (C11), 19.38 (C30), 18.37 (C6), 16.21 (C25), 16.05 (C26), 15.50 (C24), 15.16 (C27).

*(16R)-16-(1H-5-Indolyl)-3β-hydroxy-28-picolinamido-lup-20(29)ene (**7m**).* ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.13 (bs, 1H, H−N(1″)), 7.89 (d, ^{3}J = 7.7 Hz, 1H, H−C(3′)), 7.63 (s, 1H, H−C(4″)), 7.60 (td, ^{3}J = 7.7 Hz, ^{4}J = 1.7 Hz, 1H, H−C(4′)), 7.49 (d, ^{3}J = 4.7 Hz, 1H, H−C(6′)), 7.32 (d, ^{3}J = 8.4 Hz, 1H, H−C(6″)), 7.23 (t, ^{3}J = 2.8 Hz, 1H, H−C(2″)), 7.16 (d, ^{3}J = 8.4 Hz, 1H, H−C(7″)), 7.08 (dd, ^{3}J = 7.7, 4.7 Hz, 1H, H−C(5′)), 7.05 (d, ^{3}J = 10.1 Hz, 1H, H−N−C═O), 6.54 (dd, ^{3}J = 2.8 Hz, ^{4}J = 2.6 Hz, 1H, H−C(3″)), 4.75 (s, 1H, H_a-C (29)), 4.62 (s, 1H, H_b-C (29)), 3.76 (dd, ^{2}J = 14.2 Hz, ^{3}J = 10.1 Hz, 1H, H_a-C (28)), 3.39 (d, ^{2}J = 14.2 Hz, 1H, H_b-C (28)), 3.20 (dd, ^{3}J = 11.2, 4.9 Hz, 1H, H−C (3)), 3.04 (dd, ^{3}J = 13.2, 3.1 Hz, 1H, H−C (16)), 2.71 (dt, ^{3}J = 11.2, 5.6 Hz, 1H, H−C (19)), 2.56 (dd, ^{2}J = 13.4 Hz, ^{3}J = 13.2 Hz, 1H, H_a-C (15)), 2.12−1.98 (m, 1H, H_a-C (21)), 1.94 (dd, ^{3}J = 11.8, 11.2 Hz, 1H, H−C (18)), 1.83 (td,^{3} J = 11.8, 3.2 Hz, 1H, H−C (13)), 1.76 (s, 3H, H−C (30)), 1.76−1.41 (m, 12H, H_2−C (6), H_a-C (11), H_a-C (12), H_2−C (2), H_b-C (15), H_2−C (7), H_2−C (22), H_a-C (1)), 1.38−1.24 (m, 3H, H_b-C (11), H_b-C (21), H−C (9)), 1.22 (s, 3H, H_3−C (26)), 1.13 (s, 3H, H_3−C (27)), 1.13−1.09 (m, 1H, H_a-C (12)) 0.98 (s, 3H, H_3−C (23)), 0.97−0.89 (m, 1H, H_b-C (1)), 0.89 (s, 3H, H_3−C (25)), 0.79 (s, 3H, H_3−C (24)), 0.75−0.69 (m, 1H, H−C (5)). ^{13}C NMR (126 MHz, $CDCl_3$) δ 164.12 (C═O), 150.66 (C20), 149.80 (C2′), 147.37 (C6′), 136.77 (C4′), 135.33 (C7a″), 131.07 (C5″), 128.86, (C3a″) 125.35 (C5′), 124.24 (C2″), 122.96 (C7″), 121.54 (C3′), 118.76 (C4″), 111.09 (C6″), 109.52 (C29), 103.20 (C3″), 79.17 (C3), 55.49 (C5), 51.61 (C17), 51.22 (C18), 50.67 (C9), 48.52 (C16), 46.99 (C19), 43.49 (C14), 41.50 (C8), 39.04 (C4), 38.94 (C1), 37.39 (C10), 37.17 (C13), 36.53 (C28), 35.29 (C22), 34.51 (C7), 32.83 (C15), 30.20 (C21), 28.16 (C23), 27.58 (C2), 25.77 (C12), 21.13 (C11), 20.28 (C30), 18.47 (C6), 16.44 (C25), 16.39 (C26), 15.65 (C27), 15.55 (C24).

*(22S)-22-(9H-3-Carbazolyl)-3β-hydroxy-28-picolinamido-lup-20(29)ene (**6o**) and (16R)-16-(9H-3-Carbazolyl)-3β-hydroxy-28-picolinamido-lup-20(29)ene (**7o**).* According to GP II, a mixture of compounds **6o** and **7o** was prepared from picolinic amide **3a** (100 mg, 0.183 mmol, 1 equiv), 3-iodo-9H-carbazole (214 mg, 0.731 mmol, 4 equiv), $Pd(OAc)_2$ (2 mg, 0.009 mmol, 0.05 equiv), $CuBr_2$ (4 mg, 0.018 mmol, 0.1 equiv), and CsOAc (140 mg, 0.731 mmol, 4 equiv) in *t*-AmOH (2 mL). Total yield of isomers **6o** and **7o** (5:1) 44 mg, 34%. HRMS (ESI): *m*/*z* calc. for $[C_{48}H_{61}N_3O_2 + H]^+$ 712.4837; found 712.4835.

*(22S)-22-(9H-3-Carbazolyl)-3β-hydroxy-28-picolinamido-lup-20(29)ene (**6o**).* ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.16 (s, 1H, H−N (9)), 8.06−8.03 (m, 2H, H−C(4″), H−C(5″)), 7.80 (d, ^{3}J = 7.8 Hz, 1H, H−C(3′)), 7.45−7.40 (m, 3H, H−C(8″), H−C(4′), H−C(7″)), 7.38 (dd, ^{3}J = 8.6, ^{4}J = 1.9 Hz, 1H, H−C(2″), 7.34 (d, J = 8.6 Hz, 1H, H−C(1″)), 7.23−7.17 (m, 2H, H−C(6′), H−C(6″), 6.92−6.86 (m, 2H, H−N−C═O, H−C(5′), 4.84 (d, ^{4}J = 2.4 Hz, 1H, H_a-C (29)), 4.69 (s, 1H, H_b-C (29)), 4.12 (dd, ^{2}J = 14.1, ^{3}J = 9.4 Hz, 1H, H_a-C (28)), 3.20 (dd, ^{3}J = 11.4, 4.8 Hz, 1H, H−C (3)), 3.12 (dd, ^{3}J = 11.3, 8.6 Hz, 1H, H−C (22)), 3.10 (dd, ^{2}J = 14.1 Hz, ^{3}J = 2.7 Hz, 1H, H_b-C (28)), 2.85 (ddd, ^{2}J = 14.0, ^{3}J = 11.3, 11.1 Hz, 1H, H_a-C (21)), 2.68 (td, ^{3}J = 11.1, 5.1 Hz, 1H, H−C (19)), 2.07−1.91 (m, 3H, H−C (13), H−C (18), H_a-C (16)), 1.86 (ddd, ^{2}J = 14.0, ^{3}J = 8.6, 5.1 Hz, 1H, H_b-C (21)), 1.80 (s, 3H, H−C (30)), 1.78−1.66 (m, 3H, H_a-C (12), H_a-C (1), H_a-C (15)), 1.66−1.23 (m, 10H, H_2−C (2), H_2−C (6), H_2−C (11), H_b-C (16), H−C (9), H_2−C (7),), 1.15 (s, 3H, H_3−C (26)), 1.14−1.06 (m, 1H, H_b-C (12)), 1.07 (s, 3H, H_3−C (27)), 1.05−0.98 (m, 1H, H_b-C (15)), 0.97 (s, 3H, H_3−C (23)), 0.95−0.86 (m, 1H, H_b-C (1)), 0.84 (s, 3H, H_3−C (25)), 0.76 (s, 3H, H_3−C (24)), 0.73−0.66 (m, 1H, H−C (5)). ^{13}C NMR (126 MHz, $CDCl_3$) δ 164.04 (C═O), 150.25 (C20), 149.60 (C2′), 147.12 (C6′), 139.96 (C9a″), 139.07 (C8a″), 136.48 (C4′), 130.97 (C3″), 126.00 (C2″), 125.87 (C7″), 125.21 (C5′), 124.30 (C4a″), 123.56 (C4b″), 121.39 (C3′), 120.62 (C5″), 119.46 (C6″), 118.87 (C4″), 110.95 (C1″), 110.54 (C8″), 110.33 (C29), 79.20 (C3), 55.53 (C5), 54.82 (C22), 50.68 (C9), 50.53 (C18), 50.22 (C17), 46.28 (C19), 42.76 (C14), 41.01 (C8), 39.01 (C4), 38.89 (C1), 37.70 (C13), 37.33 (C10), 36.10 (C28), 34.53 (C7), 34.09 (C21), 30.40 (C16), 28.13 (C23), 27.58 (C2), 27.45 (C15), 25.25 (C12), 21.00 (C11), 19.39 (C30), 18.37 (C6), 16.20 (C25), 16.07 (C26), 15.50 (C24), 15.17 (C27).

*(16R)-16-(9H-3-Carbazolyl)-3β-hydroxy-28-picolinamido-lup-20(29)ene (**7o**).* ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.06 (d, ^{3}J = 7.8 Hz, 1H, H−C(5″), 8.01 (s, 1H, H−C(4″)), 7.81 (bs, 1H, H−C(3′)), 7.53−7.39 (m, 3H, H-(C4′), H−C(7″), H−C(8″), 7.39−7.31 (m, 2H, H−C(2″), H−C(1″)), 7.22−7.17 (m, 2H, H−C(6′), H−C(6″), 7.08 (bs, 1H, H−N), 6.94−6.88 (m, 1H, H−C(5′)), 4.77 (d, ^{4}J = 2.2 Hz, 1H, H_a-C (29)), 4.64 (s, 1H, H_b-C (29)), 3.70 (dd, ^{2}J = 14.3, ^{3}J = 9.2 Hz, 1H, H_a-C (28)), 3.53 (d, ^{2}J = 14.3 Hz, 1H, H_b-C (28)), 3.21 (dd, ^{2}J = 11.5, 4.9 Hz, 1H, H−C (3)), 3.12 (dd, ^{3}J = 13.3, 3.5 Hz, 1H, H−C (16)), 2.71 (td, ^{3}J = 11.0, 4.5 Hz, 1H, H−C (19)), 2.62 (dd, ^{2}J = 13.3 Hz, ^{3}J = 13.3 Hz, 1H, H_a-C (15)), 2.11−2.00 (m, 1H, H_a-C (21)), 1.97 (dd, ^{3}J = 11.7, 11.2 Hz, 1H, H−C (18)), 1.93−1.80 (m, 1H, H−C (13)), 1.78 (s, 3H, H_3−C (30)), 1.78−1.66 (m, 3H, H_a-C (12), H_a-C (22)), H_a-C (1)), 1.67−1.45 (m, 9H, H_2−C (6), H_a-C (11), H_2−C (2), H_b-C (15), H_2−C (7), H_b-C (22)), 1.42−1.28 (m, 3H, H_b-C (11), H_b-C (21), H−C (9)), 1.26 (s, H_3−C (26)), 1.16 (s, 3H, H_3−C (27)), 1.16−1.09 (m, 1H, H_b-C (12)), 0.98 (s, 3H, H_3−C (23)), 0.98−0.93 (m, 1H, H_b-C (1)), 0.90 (s, 3H, H_3−C (25)), 0.80 (s, 3H, H_3−C (24)), 0.77−0.70 (m, 1H, H−C (5)). ^{13}C NMR (126 MHz, $CDCl_3$) δ 164.10 (C═O), 150.38 (C20), 149.23 (C2′), 147.02 (C6′), 139.78 (C9a″), 138.65 (C8a″), 136.55 (C4′), 134.85 (C3″), 126.23 (C2″), 125.76 (C7″), 125.25 (C5′), 124.01 (C4a″), 123.51 (C4b″), 121.39 (C3′), 120.58 (C5″), 119.35 (C6″), 118.40 (C4″), 110.51

(C1″), 110.37 (C8″), 109.52 (C29), 79.08 (C3), 55.36 (C5), 51.42 (C17), 51.17 (C18), 50.54 (C9), 48.55 (C16), 46.88 (C19), 43.45 (C14), 41.37 (C8), 38.91 (C4), 38.80 (C1), 37.26 (C10), 37.06 (C13), 36.55 (C28), 35.09 (C22), 34.39 (C7), 32.73 (C15), 30.00 (C21), 28.02 (C23), 27.42 (C2), 25.61 (C12), 20.97 (C11), 20.11 (C30), 18.33 (C6), 16.37 (C25), 16.26 (C26), 15.58 (C24), 15.42 (C27).

*(22S)-22-(4-Methoxyphenyl)-3β-hydroxy-28-picolinamido-lupane (**9a**) and (16R)-16-(4-Methoxyphenyl)-3β-hydroxy-28-picolinamido-lupane (**10a**).* According to GP II, compounds **9a** and **10a** were prepared from picolinic amide **3b** (30 mg, 0.055 mmol, 1 equiv), 1-iodo-4-methoxybenzene (51 mg, 0.218 mmol, 4 equiv), Pd(OAc)$_2$ (1 mg, 0.003 mmol, 0.05 equiv), CuBr$_2$ (2 mg, 0.005 mmol, 0.1 equiv), and CsOAc (42 mg, 0.218 mmol, 4 equiv) in *t*-AmOH (1 mL). Yield 28 mg, 78%. HRMS (ESI): m/z calc. for $[C_{43}H_{62}N_2O_3 + H]^+$ 655.4833; found 655.4839.

*(22S)-22-(4-Methoxyphenyl)-3β-hydroxy-28-picolinamido-lupane (**9a**).* ^{1}H NMR (500 MHz, CDCl$_3$) δ 8.18 (d, ^3J = 4.8 Hz, 1H, H−C(6′)), 8.00 (d, ^3J = 7.8 Hz, 1H, H−C(3′)), 7.69 (td, ^3J = 7.8 Hz, ^4J = 1.8 Hz, 1H, H−C(4′)), 7.29−7.21 (m, 3H, H−C(5′), H−C(2″), H−C(6″)), 6.97 (d, ^3J = 9.2 Hz, 1H, H−N), 6.86 (d, ^3J = 8.3 Hz, 2H, H−C(3″), H−C(5″)), 4.12 (dd, ^2J = 14.2, ^3J = 9.2 Hz, 1H, H$_a$-C (28)), 3.77 (s, 3H, CH$_3$−O) 3.20 (dd, ^3J = 11.3, 4.9 Hz, 1H, H−C (3)), 2.96 (dd, ^2J = 14.2, ^3J = 2.8 Hz, 1H, H$_b$-C (28)), 2.66 (dd, ^3J = 12.0, 8.1 Hz, 1H, H−C (22)), 2.30 (ddd, ^2J = 13.6 Hz, ^3J = 13.2, 11.2 Hz, 1H, H$_a$-C (21)), 2.09−1.45 (m, 14H, H$_2$−C (6), H$_a$-C (11), H−C (20), H−C (19), H−C (13), H$_b$-C (21), H$_2$−C (2), H$_a$-C (12), H$_a$-C (15), H$_a$-C (16), H$_a$-C (1), H−C (18)), 1.47−1.19 (m, 6H, H$_b$-C (11), H$_2$−C (7), H$_b$-C (16), H−C (9), H$_b$-C (12)), 1.18 (s, 3H, H$_3$−C (26)), 1.01 (s, 3H, H$_3$−C (27)), 1.01−0.97 (m, 1H, H$_b$-C (15)), 0.96 (s, 3H, H$_3$−C (23)), 0.93 (d, ^3J = 6.8 Hz, 3H, H$_3$−C (30)), 0.91−0.87 (m, 1H, H$_b$-C (1)), 0.85 (s, 3H, H$_3$−C (25)), 0.84 (d, ^3J = 6.7 Hz, 3H, H$_3$−C (29)), 0.76 (s, 3H, H$_3$−C (24)), 0.71−0.67 (m, 1H, H−C (5)). ^{13}C NMR (126 MHz, CDCl$_3$) δ 163.98 (C═O), 158.81 (C4″), 149.99 (C2′), 147.57 (C6′), 136.91 (C4′), 132.57 (C1″), 128.68 (C2″ + C6″), 125.63 (C5′), 121.76 (C3′), 114.31 (C3″ + C5″), 79.19 (C3), 55.48 (C5), 55.27 (O−CH$_3$), 53.67 (C22), 50.32 (C9), 50.24 (C17), 49.89 (C18), 42.90 (C14), 42.75 (C19), 41.04 (C8), 39.01 (C4), 38.88 (C1), 37.29 (C10), 37.27 (C13), 36.05 (C28), 34.15 (C7), 30.45 (C16), 29.63 (C20), 28.12 (C23), 27.54 (C2), 27.30 (C15), 27.00 (C12), 26.53 (C21), 23.14 (C30), 20.99 (C11), 18.37 (C6), 16.15 (C25), 16.04 (C26), 15.52 (C24), 15.09 (C29), 15.00 (C27).

*(16R)-16-(4-Methoxyphenyl)-3β-hydroxy-28-picolinamido-lupane (**10a**).* ^{1}H NMR (500 MHz, CDCl$_3$) δ 8.20 (dd, 1H, ^3J = 4.9 Hz, ^4J = 1.7 Hz, H−C(6′)), 7.99 (d, ^3J = 7.7 Hz, 1H, H−C(3′)), 7.71 (td, ^3J = 7.7 Hz, ^4J = 1.7 Hz, 1H, H−C(4′)), 7.27 (dd, ^3J = 7.7, 4.9 Hz, 1H, H−C(5′)), 7.23 (d, ^3J = 8.1 Hz, 2H, H−C(2″), H−C(6″)), 7.04 (dd, ^3J = 9.7, 2.2 Hz, 1H, H−N), 6.85 (d, ^3J = 8.1 Hz, 2H, H−C(3″), H−C(5″)), 3.79 (s, 3H, CH$_3$−O), 3.64 (dd, ^2J = 14.3 Hz, ^3J = 9.7 Hz, 1H, H$_a$-C (28)), 3.34 (dd, ^2J = 14.3 Hz, ^3J = 2.2 Hz, 1H, H$_b$-C (28)), 3.21 (dd, ^3J = 11.3, 4.8 Hz, 1H, H−C (3)), 2.66 (dd, ^3J = 13.0, 3.5 Hz, 1H, H−C (16)), 2.40 (dd, ^2J = 13.3 Hz, ^3J = 13.0 Hz, 1H, H$_a$-C (15)), 1.98 (ddd, ^3J = 10.6 Hz, 3.6, 2.6 Hz, 1H, H−C (19)), 1.88 (septd, ^3J = 6.8, 2.6 Hz, 1H, H−C (20)), 1.81 (td, ^3J = 12.1, 3.7 Hz, 1H, H−C (13)), 1.76−1.70 (m, 1H, H$_a$-C (1)), 1.70−1.39 (m, 12H, H$_2$−C (6), H$_a$-C (11), H$_2$−C (21), H$_2$−C (2), H$_a$-C (12), H$_2$−C (7), H$_a$-C (22), H−C (18)), 1.35−1.21 (m, 4H, H$_b$-C (11), H$_b$-C (12), H$_b$-C (15), H−C (9)), 1.19 (s, 3H, H$_3$−C (26)), 1.17−1.12 m, 1H, H$_b$-C (22)), 1.08 (s, 3H, H$_3$−C (27)), 0.98 (s, 3H, H$_3$−C (23)), 0.97−0.89 (m, 1H, H$_b$-C (1)), 0.89 (s, 3H, H$_3$−C (25)), 0.86 (d, ^3J = 6.8 Hz, 3H, H−C (30)), 0.83 (d, ^3J = 6.8 Hz, 3H, H$_3$−C (29)), 0.78 (s, 3H, H$_3$−C (25)), 0.72 (d, ^3J = 10.3 Hz, 1H, H−C (5)). ^{13}C NMR (126 MHz, CDCl$_3$) δ 164.10 (C═O), 158.67 (C4″), 149.87 (C2′), 147.68 (C6′), 137.02 (C4′), 135.84 (C1″), 128.63 (C2″ + C6″), 125.75 (C5′), 121.78 (C3′), 114.12 (C3″ + C5″), 79.18 (C3), 55.44 (C5), 55.33 (O−CH$_3$), 51.20 (C17), 50.72 (C18), 50.39 (C9), 47.69 (C16), 44.02 (C19), 43.47 (C14), 41.50 (C8), 39.04 (C4), 38.92 (C1), 37.34 (C10), 36.67 (C28), 36.65 (C13), 35.39 (C22), 34.58 (C7), 32.36 (C15), 29.70 (C20), 28.16 (C23), 27.54 (C2), 27.15 (C12), 23.10 (C30), 21.91 (C21), 21.11 (C11), 18.45 (C6), 16.43 (C26), 16.33 (C25), 15.55 (C24), 15.52 (C27), 15.30 (C29).

*(22S)-22-(4-Methylcarbonylphenyl)-3β-hydroxy-28−28-picolinamido-lupane (**9g**) and (16R)-16-(4-Methylcarbonylphenyl)-3β-hydroxy-28-picolinamido-lupane (**10g**).* According to GP II, compounds **9g** and **10g** were prepared from picolinic amide **3b** (100 mg, 0.183 mmol, 1 equiv), 1-(4-iodophenyl)ethan-1-one (179 mg, 0.731 mmol, 4 equiv), Pd(OAc)$_2$ (2 mg, 0.009 mmol, 0.05 equiv), CuBr$_2$ (4 mg, 0.018 mmol, 0.1 equiv), and CsOAc (140 mg, 0.731 mmol, 4 equiv) in *t*-AmOH (2 mL). Yield 31 mg, 26%. HRMS (ESI): m/z calc. for $[C_{44}H_{62}N_2O_3 + H]^+$ 667.4833; found 667.4815.

*(22S)-22-(4-Methylcarbonylphenyl)-3β-hydroxy-28−28-picolinamido-lupane (**9g**).* ^{1}H NMR (500 MHz, CDCl$_3$) δ 7.98 (d, ^3J = 4.8 Hz, 1H, H−C(6′)), 7.96 (d, ^3J = 7.8 Hz, 1H, H−C(3′)), 7.84 (d, ^3J = 8.1 Hz, 2H, H−C(3″), H−C(5″)), 7.67 (td, ^3J = 7.8 Hz, ^4J = 1.8 Hz, 1H, H−C(4′)), 7.41 (d, ^3J = 8.1 Hz, 2H, H−C(2″), H−C(6″)), 7.20 (dd, ^3J = 7.8, 4.8 Hz, 1H, H−C(5′)), 6.87 (dd, ^3J = 8.4, 3.7 Hz, 1H, H−N), 4.01 (dd, ^2J = 14.3 Hz, ^3J = 8.4 Hz, 1H, H$_a$-C (28)), 3.20 (dd, ^3J = 11.4, 4.7 Hz, 1H, H−C (3)), 3.11 (dd, ^2J = 14.3 Hz, ^3J = 3.7 Hz, 1H, H$_b$-C (28)), 2.74 (dd, ^3J = 11.8, 8.0 Hz, 1H, H−C (20)), 2.50 (s, 3H, H$_3$−C═O), 2.40 (ddd, ^2J = 13.6 Hz, ^3J = 11.8, 11.4 Hz, 1H, H$_a$-C (21)), 2.02 (td, ^3J = 12.1, 3.9 Hz, 1H, H−C (13)), 1.99−1.93 (m, 2H, H−C (20), H−C (19)), 1.88 (ddd, ^2J = 13.1 Hz, ^3J = 6.8, 3.5 Hz, 1H, H$_a$-C (16)), 1.85−1.75 (m, 2H, H$_b$-C (21), H$_a$-C (15)), 1.75−1.57 (m, 5H, H$_a$-C (12), H$_2$−C (2), H$_a$-C (1), H−C (18)), 1.56−1.44 (m, 3H, H$_a$-C (6), H$_a$-C (11), H$_b$-C (16)), 1.46−1.30 (m, 5H, H$_b$-C (11), H$_b$-C (6), H$_2$−C (7), H−C (9)), 1.30−1.22 (m, 1H, H$_b$-C (12)), 1.15 (s, 3H, H$_3$−C (26)), 1.06−1.00 (m, 4H, H$_3$−C (27), H$_b$-C (15)), 0.96 (s, 3H, H$_3$−C (23)), 0.94 (d, ^3J = 6.7 Hz, 3H, H−C (30)), 0.94−0.89 (m, 1H, H$_b$-C (1)), 0.86 (d, ^3J = 6.9 Hz, 3H, H$_3$−C (29)), 0.85 (s, 3H, H$_3$−C (25)), 0.76 (s, 3H, H$_3$−C (24)), 0.69 (d, ^3J = 9.3 Hz, 1H, H−C (5)). ^{13}C NMR (126 MHz, CDCl$_3$) δ 197.94(O═C−CH$_3$), 163.88 (O═C-NH$_2$), 149.66 (C2′), 147.46 (C6′), 146.89 (C1″), 136.99 (C4′), 135.58 (C4″), 128.87 (C3″ + C5″), 128.00 (C2″ + C6″), 125.80 (C5′), 121.77 (C3′), 79.15 (C3), 55.47 (C5), 54.59 (C22), 51.04 (C17), 50.29 (C9 + C18), 42.87 (C14), 42.78 (C19), 41.05 (C8), 39.01 (C4), 38.87 (C1), 37.29 (C10), 37.28 (C13), 36.06 (C28), 34.19 (C7), 30.54 (C6), 29.58 (C20), 28.13 (C23), 27.54 (C2), 27.28 (C15), 26.98 (C12), 26.66 (CH$_3$−C═O), 26.29 (C21), 23.10 (C30), 20.98 (C11), 18.37 (C6), 16.16 (C25), 16.05 (C26), 15.52 (C24), 15.09 (C29), 15.03 (C27).

*(16R)-16-(4-Methylcarbonylphenyl)-3β-hydroxy-28-picolinamido-lupane (**10g**).* ^{1}H NMR (500 MHz, CDCl$_3$^{1}H NMR

(500 MHz, $CDCl_3$) δ 8.02 (d, ^3J = 4.8 Hz, 1H, H−C(6′)), 7.97 (d, ^3J = 7.8 Hz, 1H, H−C(3′)), 7.84 (d, ^3J = 8.1 Hz, 2H, H−C(3″), H−C(5″)), 7.70 (td, ^3J = 7.8 Hz, ^4J = 1.8 Hz, 1H, H−C(4′)), 7.39 (d, ^3J = 8.1 Hz, 2H, H−C(2″), H−C(6″)), 7.24 (dd, ^3J = 7.8, 4.8 Hz, 1H, H−C(5′)), 7.01 (bs, 1H, H−N), 3.57 (m, 2H, H_2−C (28)), 3.22 (dd, ^3J = 11.3, 4.8 Hz, 1H, H−C (3)), 2.92 (dd, ^3J = 13.0, 3.6 Hz, 1H, H−C (16)), 2.52 (s, 3H, H_3C−C=O), 2.47 (dd, ^2J = 13.3 Hz, ^3J = 13.0 Hz, 1H, H_a-C (15)), 1.97 (ddd, ^3J = 10.5 Hz, 3.5, 2.6 Hz, 1H, H−C (19)), 1.88 (septd, ^3J = 6.8, 2.6 Hz, 1H, H−C (20)), 1.85 (td, ^3J = 12.1, 3.7 Hz, 1H, H−C (13)), 1.76−1.70 (m, 1H, H_a-C (1)), 1.70−1.43 (m, 12H, H_2−C (6), H_a-C (11), H_2−C (21), H_2−C (2), H_a-C (12), H_2−C (7), H_a-C (22), H−C (18)), 1.39−1.31 (m, 3H, H_b-C (11), H_b-C (15), H−C (9)), 1.28−1.23 (m, 2H, H_b-C (12), H_b-C (12)), 1.23 (s, 3H, H_3−C (26)), 1.09 (s, 3H, H_3−C (27)), 0.98 (s, 3H, H_3−C (23)), 0.97−0.90 (m, 1H, H_b-C (1)), 0.90 (s, 3H, H_3−C (25)), 0.87 (d, ^3J = 6.8 Hz, 3H, H−C (30)), 0.84 (d, ^3J = 6.8 Hz, 3H, H_3−C (29)), 0.79 (s, 3H, H_3−C (25)), 0.72 (d, ^3J = 10.3 Hz, 1H, H−C (5)). ^{13}C NMR (126 MHz, $CDCl_3$) δ 198.06 (O=C−CH_3), 164.15 (O=C-NH_2), 149.74 (C2′), 149.42 (C1″), 147.62 (C6′), 137.17 (C4′), 135.54 (C4″), 128.75 (C3″ + C5″), 128.01 (C2″ + C6″), 126.00 (C5′), 121.85 (C3′), 79.21 (C3), 55.44 (C5), 51.34 (C17), 51.01 (C18), 50.36 (C9), 48.81 (C16), 43.97 (C19), 43.47 (C14), 41.50 (C8), 39.03 (C4), 38.92 (C1), 37.34 (C10), 36.67 (C13), 36.64 (C28), 35.30 (C22), 34.59 (C7), 32.02 (C15), 29.68 (C20), 28.14 (C23), 27.50 (C2), 27.08 (C12), 26.69 (CH_3−C=O), 23.06 (C30), 21.89 (C21), 21.06 (C11), 18.43 (C6), 16.45 (C26), 16.33 (C25), 15.55 (C24), 15.53 (C27), 15.28 (C29).

*(22S)-22-(4-Methoxyphenyl)-3β-28-picolinamido-olean-12(13)-ene (**14a**).* According to GP II, compound **14a** was prepared from picolinic amide **3c** (100 mg, 0.183 mmol, 1 equiv), 1-iodo-4-methoxybenzene (171 mg, 0.731 mmol, 4 equiv), $Pd(OAc)_2$ (2 mg, 0.009 mmol, 0.05 equiv), $CuBr_2$ (4 mg, 0.018 mmol, 0.1 equiv), and CsOAc (140 mg, 0.731 mmol, 4 equiv) in *t*-AmOH (2 mL). Yield 72 mg, 60% (brsm 91%). HRMS (ESI): *m/z* calc. for $[C_{43}H_{60}N_2O_3 + H]^+$ 653.4677; found 653.4678. ^1H NMR (500 MHz, $CDCl_3$) δ 8.32 (d, 1H, ^3J = 4.7 Hz, 1H, H−C(6′)), 8.08 (d, ^3J = 7.7 Hz, 1H, H−C(3′)), 7.75 (t, ^3J = 7.7 Hz, 1H, H−C(4′)), 7.69−7.63 (m, 1H, H−N), 7.32 (dd, ^3J = 7.7, 4.7 Hz, 1H, H−C(5′)), 7.16 (d,^3J = 8.2 Hz, 2H, H−C(2″), H−C(6″)), 6.79 (d, ^3J = 8.2 Hz, 2H, H−C(3″), H−C(5″)), 5.31 (d, ^3J = 3.6 Hz, 1H, H−C (12)), 3.73 (s, 3H, O−CH_3), 3.62 (dd, ^2J = 14.2 Hz, ^3J = 7.6 Hz, 1H, H_a-C (28)), 3.21 (dd, ^3J = 11.0, 4.8 Hz, 1H, H−C (3)), 3.11 (dd, ^2J = 14.2 Hz, ^3J = 3.7 Hz, 1H, H_b-C (28)), 2.86 (dd, ^3J = 13.7, 3.2 Hz, 1H, H−C (22)), 2.26 (dd, ^3J = 13.8, 4.0 Hz, 1H, H−C (18)), 1.91−1.78 (m, 3H, H_a-C (19), H_a-C (11), H_a-C (16)), 1.88 (dd, ^3J = 5.4, 5.0 Hz, 1H, H_b-C (11)), 1.82 (dd, ^3J = 13.7 Hz, ^2J = 13.5 Hz, 1H, H_a-C (21)), 1.67−1.46 (m, 7H, H_a-C (6), H_a-C (15), H_2−C (2), H_a-C (7), H_a-C (1), H−C (9)), 1.44−1.33 (m, 2H, H_b-C (6), H_b-C (16)), 1.33−1.24 (m, 3H, H_b-C (7), H_b-C (21), H_b-C (19)), 1.23 (s, 3H, H_3−C (27)), 1.04 (s, 3H, H_3−C (26)), 1.03 (s, 3H, H_3−C (29)), 1.02−0.99 (m, 1H, H_b-C (15)), 0.99−0.96 (m, 4H, H_3−C (23), H_b-C (1)), 0.96 (s, 3H, H_3−C (30)), 0.93 (s, 3H, H_3−C (25)), 0.77 (s, 3H, H_3−C (24)), 0.75−0.70 (m, 1H, H−C (5)). ^{13}C NMR (126 MHz, $CDCl_3$) δ 163.82 (C=O), 158.49 (C4″), 150.27 (C2′), 147.81 (C6′), 143.85 (C13), 137.07 (C4′), 135.18 (C1″), 130.35 (C2″ + C6″), 125.74 (C5′), 123.44 (C12), 121.87 (C3′), 113.77 (C3″ + C5″), 79.20 (C3), 55.34 (C5), 55.25 (O−CH_3), 47.81 (C22), 47.78 (C9), 46.70 (C19), 46.08 (C28), 45.46 (C18), 42.80 (C21), 41.72 (C14), 40.44 (C17), 39.96 (C8), 38.92 (C4), 38.82 (C1), 37.06 (C10), 33.56 (C30), 32.56 (C7), 31.39 (C20), 28.23 (C23), 27.39 (C2), 26.39 (C27), 25.64 (C15), 24.30 (C29), 23.85 (C11), 18.70 (C16), 18.42 (C6), 16.83 (C26), 15.71 (C24), 15.65 (C25).

*(22S)-22-(4-Methoxyphenyl)-3β-28-picolinamido-urs-12(13)-ene (**14b**).* According to GP II, compound **14b** was prepared from picolinic amide **3d** (100 mg, 0.183 mmol, 1 equiv), 1-iodo-4-methoxybenzene (171 mg, 0.731 mmol, 4 equiv), $Pd(OAc)_2$ (2 mg, 0.009 mmol, 0.05 equiv), $CuBr_2$ (4 mg, 0.018 mmol, 0.1 equiv), and CsOAc (140 mg, 0.731 mmol, 4 equiv) in *t*-AmOH (2 mL). Yield 74 mg, 62% (brms. 88%). HRMS (ESI): *m/z* calc. for $[C_{43}H_{60}N_2O_3 + H]^+$ 653.4677; found 653.4669. ^1H NMR (500 MHz, $CDCl_3$) δ 8.36 (d, ^3J = 4.7 Hz, 1H, H−C(6′)), 8.09 (d, ^3J = 7.9 Hz, 1H, H−C(3′)), 7.76 (t, ^3J = 7.7, 1H, H−C(4′)), 7.68 (bs, 1H, H−N), 7.36−7.31 (m, 1H, H−C(5′)), 7.15 (d, ^3J = 8.1 Hz, 2H, H−C(2″), H−C(6″)), 6.78 (d, ^3J = 8.1 Hz, 2H, H−C(3″), H−C(5″)), 5.26 (t, ^3J = 3.6 Hz, 1H, H−C (12)), 3.72(s, 3H, H_3C−O), 3.54 (dd, ^2J = 14.2 Hz, ^3J = 7.2 Hz, 1H, H_a-C (28)), 3.22 (dd, ^3J = 11.2, 4.9 Hz, 1H, H−C (3)), 3.13 (dd, ^2J = 14.2 Hz, ^3J = 3.9 Hz, 1H, H_b-C (28)), 2.82 (dd, ^3J = 12.6, 3.3 Hz, 1H, H−C (22)), 2.09−1.91 (m, 3H, H_2−C (11), H_a-C (16)), 1.77 (dt, ^2J = 12.8 Hz, ^3J = 12.7 Hz, 1H, H_a-C (21)), 1.70−1.58 (m, 6H, H_a-C (15), H_2−C (2), H_a-C (1), H−C (19), H−C (18)), 1.58−1.34 (m, 6H, H_2−C (6), H_b-C (16), H_a-C (7), H_b-C (21), H−C (9)), 1.32- 1.25 (m, 1H, H_b-C (7)), 1.22−1.13 (m, 4H, H−C (20), H_3−C (27)), 1.05 (s, 3H, H_3−C (26)), 1.05−9.99 (m,2H, H_b-C (15), H_b-C (1)), 0.99 (d, ^3J = 6.9 Hz, 3H, H_3−C (30)), 0.98 (s, 3H, H_3−C (23)), 0.94 (s, 3H, H_3−C (25)), 0.90 (d, ^3J = 5.4 Hz, 3H, H_3−C (29)), 0.77 (s, 3H, H_3−C (24)), 0.72 (dd, ^3J = 11.4, 1.8 Hz, 1H, H−C (5)). ^{13}C NMR (126 MHz, $CDCl_3$) δ 163.87 (C = O), 158.42 (C4″), 150.32 (C2′), 147.87 (C6′), 138.20 (C13), 137.11 (C4′), 135.29 (C1″), 130.23 (C2″ + C6″), 126.34 (C12), 125.76 (C5′), 121.89 (C3′), 113.69 (C3″ + C5″), 79.24 (C3), 57.10 (C18), 55.36 (C5), 55.23 (O−CH_3), 51.98 (C22), 47.92 (C9), 45.77 (C28), 42.19 (C14), 41.09 (C17), 40.14 (C8), 39.76 (C19), 39.70 (C20), 39.02 (C4), 38.92 (C1), 38.76 (C21), 37.03 (C10), 32.93 (C7), 28.26 (C23), 27.41 (C2), 26.06 (C15), 23.70 (C11), 23.48 (C27), 21.36 (C30), 20.32 (C16), 18.40 (C6), 17.94 (C29), 17.00 (C26), 15.85 (C25), 15.75 (C24).

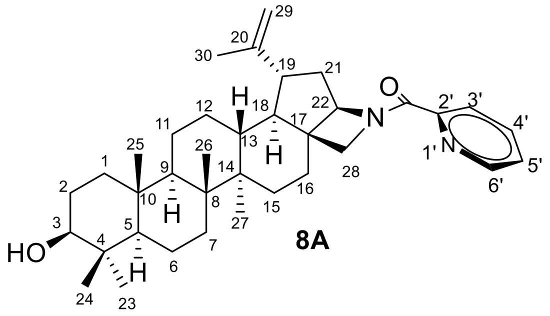
*(22S)-22-(4-Methoxycarbonylphenyl)-3β-28-picolinamido-olean-12(13)-ene (**15a**).* According to GP II, compound **15a** was prepared from picolinic amide **3c** (100 mg, 0.183 mmol, 1 equiv), methyl 4-iodobenzoate (161 mg, 0.731 mmol, 4 equiv), $Pd(OAc)_2$ (2 mg, 0.009 mmol, 0.05 equiv), $CuBr_2$ (4 mg, 0.018 mmol, 0.1 equiv), and CsOAc (140 mg, 0.731 mmol, 4 equiv) in *t*-AmOH (2 mL). Yield 46 mg, 37% (brsm. 57%). HRMS (ESI): *m/z* calc. for $[C_{44}H_{60}N_2O_4 + H]^+$ 681.4626; found 681.4609. ^1H NMR (500 MHz, $CDCl_3$) δ 8.21 (d, 1H, ^3J = 4.7 Hz, 1H, H−C(6′)), 8.06 (d, ^3J = 7.7 Hz, 1H, H−C(3′)), 7. 87 (d, ^3J = 8.1 Hz, 2H, H−C(3″), H−C(5″)), 7.74 (dt, ^3J = 7.7, 1.7 Hz, 1H, H−C(4′)), 7.55 (bs, 1H, H−N), 7.31 (d, ^3J = 8.1 Hz, 2H, H−C(2″), H−C(6″)), 7.28 (dd, ^3J = 7.7, 4.7 Hz, 1H, H−C(5′)), 5.32 (d, ^3J = 3.7 Hz, 1H, H−C (12)), 3.88 (s, 3H, O−CH_3), 3.57 (dd, ^2J = 14.2 Hz, ^3J = 7.0 Hz, 1H, H_a-C (28)), 3.22 (dd, ^3J = 11.0, 4.7 Hz, 1H, H−C (3)), 3.18 (dd, ^2J = 14.2 Hz, ^3J = 4.5 Hz, 1H, H_b-C (28)), 2.97 (dd, ^3J = 13.8, 3.2 Hz, 1H, H−C (22)), 2.27 (dd, ^3J = 13.8, 3.7 Hz, 1H, H−C (18)), 2.05 (ddd, ^2J = 13.7 Hz, ^3J =

13.5, 4.6 Hz, 1H, H$_a$-C (16)), 2.04−1.91 (m, 2H, H$_a$-C (19), H$_a$-C (11)), 1.92−1.82 (m, 2H H$_b$-C (11), H$_a$-C (21)), 1.68−1.45 (m, 7H, H$_a$-C (6), H$_a$-C (15), H$_2$−C (2), H$_a$-C (7), H$_a$-C (1), H−C (9)), 1.44−1.34 (m, 2H, H$_b$-C (6), H$_b$-C (16)), 1.33−1.22 (m, 6H, H$_b$-C (7), H$_b$-C (21), H$_b$-C (19), H$_3$−C (27)), 1.06−1.00 (m, 7H, H$_3$−C (26), H$_3$−C (29), H$_b$-C (15)), 0.99−0.96 (m, 7H, H$_3$−C (23), H$_3$−C (30), H$_b$-C (1)), 0.93 (s, 3H, H$_3$−C (25)), 0.77 (s, 3H, H$_3$−C (24)), 0.75−0.70 (m, 1H, H−C (5)). ^{13}C NMR (126 MHz, CDCl$_3$) δ 167.25 (O−C=O), 163.87 (N−C=O), 150.00 (C2′), 148.86 (C1″), 147.74 (C6′), 143.56 (C13), 137.12 (C4′), 129.65 (C3″ + C5″), 129.50 (C2″ + C6″), 128.32 (C4″), 125.79 (C5′), 123.72 (C12), 121.90 (C3′), 79.19 (C3), 55.33 (C5), 52.06 (O−CH$_3$), 48.94 (C22), 47.78 (C9), 46.62 (C19), 46.03 (C28), 45.51 (C18), 42.39 (C21), 41.70 (C14), 40.71 (C17), 39.98 (C8), 38.92 (C4), 38.82 (C1), 37.06 (C10), 33.49 (C30), 32.55 (C7), 31.37 (C20), 28.23 (C23), 27.38 (C2), 26.38 (C27), 25.65 (C15), 24.23 (C29), 23.84 (C11), 18.82 (C16), 18.41 (C6), 16.81 (C26), 15.71 (C24), 15.66 (C25).

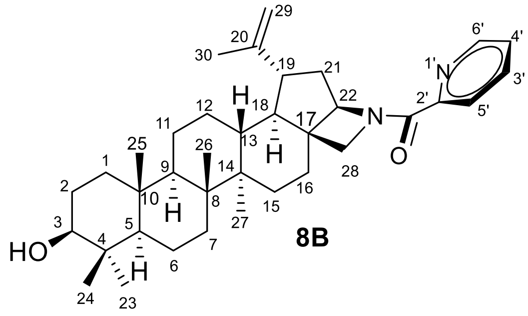
*(22S)-22-(4-Methoxycarbonylphenyl)-3β-28-picolinamido-urs-12(13)-ene (**15b**).* According to GP II, compound **15b** was prepared from picolinic amide **3d** (100 mg, 0.183 mmol, 1 equiv), methyl 4-iodobenzoate (191 mg, 0.731 mmol, 4 equiv), Pd(OAc)$_2$ (2 mg, 0.009 mmol, 0.05 equiv), CuBr$_2$ (4 mg, 0.018 mmol, 0.1 equiv), and CsOAc (140 mg, 0.731 mmol, 4 equiv) in *t*-AmOH (2 mL). Yield 35 mg, 28% (brsm. 95%). HRMS (ESI): *m/z* calc. for [C$_{44}$H$_{60}$N$_2$O$_4$ + H]$^+$ 681.4626; found 681.4608.^{1}H NMR (500 MHz, CDCl$_3$) δ 8.26 (d, ^3J = 4.7 Hz, 1H, H−C(6′)), 8.06 (d, ^3J = 7.8 Hz, 1H, H−C(3′)), 7.86 (d, ^3J = 8.1 Hz, 2H, H−C(3″), H−C(5″)), 7.76 (td, ^3J = 7.7, ^4J = 1.7 Hz, 1H, H−C(4′)), 7.61 (dd, ^3J = 6.6, 4.9 Hz, 1H, H−N), 7.33−7.28 (m, 3H, H−C(5′), H−C(2″), H−C(6″)), 5.28 (t, ^3J = 3.6 Hz, 1H, H−C (12)), 3.87 (s, 3H, H$_3$C−O), 3.50 (dd, ^2J = 14.3 Hz, ^3J = 6.6 Hz, 1H, H$_a$-C (28)), 3.23 (dd, ^3J = 11.4, 4.9 Hz, 1H, H−C (3)), 3.20 (dd, ^2J = 14.3 Hz, ^3J = 4.9 Hz, 1H, H$_b$-C (28)), 2.82 (dd, ^3J = 13.2, 3.3 Hz, 1H, H−C (22)), 2.11 (ddd, ^2J = 13.6 Hz, ^3J = 13.6, 4.8 Hz, 1H, H$_a$-C (16)), 2.03−1.93 (m, 2H, H$_2$−C (11)), 1.81 (ddd, ^2J = 13.2 Hz, ^3J = 13.2, 12.8 Hz, 1H, H$_a$-C (21)), 1.71−1.58 (m, 6H, H$_a$-C (15), H$_2$−C (2), H$_a$-C (1), H−C (19), H−C (18)), 1.58−1.43 (m, 5H, H$_a$-C (6), H$_b$-C (16), H$_a$-C (7), H$_b$-C (21), H−C (9)), 1.40−1.34 (m, 1H, H$_b$-C (6)), 1.32- 1.25 (m, 1H, H$_b$-C (7)), 1.22- 1.13 (m, 4H, H−C (20), H$_3$−C (27)), 1.09−1.03 (m, 1H, H$_b$-C (15)), 1.02 (s, 3H, H$_3$−C (26)), 1.02−0.98 (m, 4H, H$_b$-C (1), H$_3$−C (30)), 0.98 (s, 3H, H$_3$−C (23)), 0.94 (s, 3H, H$_3$−C (25)), 0.91 (d, ^3J = 5.5 Hz, 3H, H$_3$−C (29)), 0.77 (s, 3H, H$_3$−C (24)), 0.73 (dd, ^3J = 11.8, 1.8 Hz, 1H, H−C (5)). ^{13}C NMR (126 MHz, CDCl$_3$) δ 167.24 (O−C=O), 164.00 (N−C=O), 149.85 (C2′), 148.87 (C1″), 147.80 (C6′), 137.91 (C13), 137.23 (C4′), 129.59 (C3″ + C5″), 129.36 (C2″ + C6″), 128.29 (C4″), 126.66 (C12), 125.89 (C5′), 121.97 (C3′), 79.27 (C3), 57.17 (C18), 55.35 (C5), 53.16 (C22), 52.05 (O−CH$_3$), 47.88 (C9), 45.83 (C28), 42.16 (C14), 41.29 (C17), 40.15 (C8), 39.68 (C19), 39.59 (C20), 39.00 (C4), 38.91 (C1), 38.29 (C21), 37.02 (C10), 32.90 (C7), 28.25 (C23), 27.38 (C2), 26.05 (C15), 23.68 (C11), 23.49 (C27), 21.29 (C30), 20.37 (C16), 18.38 (C6), 17.89 (C29), 16.92 (C26), 15.83 (C25), 15.74 (C24).

Betulin core-derived picolinic azetidines **8** and **11** were isolated as a stable 1:1 mixture of rotamers and characterized together. Oleanane core-derived azetidine was isolated as a stable 2:1 mixture of rotamers, and characterization of both rotamers was found to be possible due to different integral intensities.

N-Picolinoyl Azetidine 8 Mixture of Rotamers.



8A

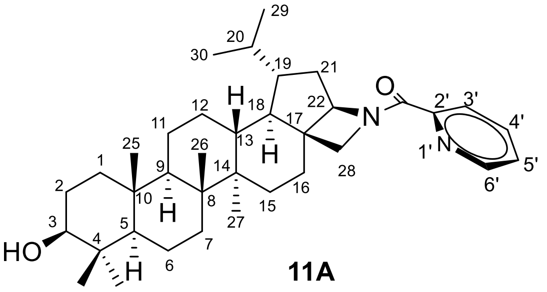


8B

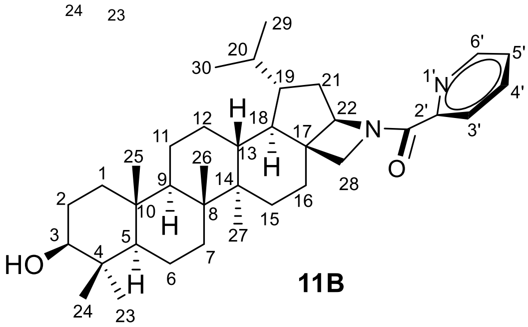
HRMS (ESI): *m/z* calc. for [C$_{36}$H$_{52}$N$_2$O$_2$ + H]$^+$ 545.4102; found 545.4123. ^{1}H NMR (500 MHz, CDCl$_3$) δ 8.63 (d, ^3J = 4.7 Hz, 1H, H−C(6′A), 8.54 (d, ^3J = 4.7 Hz, 1H, H−C(6′B), 8.10 (d, ^3J = 7.8 Hz, 1H, H−C(3′A)), 8.08 (d, ^3J = 7.8 Hz, 1H, H−C(3′B)), 7.81 (td, ^3J = 7.8 Hz, ^4J = 1.7 Hz, 1H, H−C(4′A)), 7.78 (td, ^3J = 7.8 Hz, ^4J = 1.7 Hz, 1H, H−C(4′B)), 7.35 (dd, ^3J = 7.7, 4.7 Hz, 1H, H−C(5′A)), 7.33 (dd, ^3J = 7.7, 4.7 Hz, 1H, H−C(5′B)), 4.95 (d, ^3J = 5.8 Hz, 1H, H−C(22B)), 4.84 (s, 1H, H$_a$-C(29A)), 4.81 (s, 1H, H$_a$-C(29B)), 4.70 (s, 1H, H$_b$-C(29A)), 4.67 (s, 1H, H$_b$-C(29B)), 4.60 (d, ^2J = 11.0 Hz, 1H, H$_a$-C(28A)), 4.45 (d, ^3J = 5.8 Hz, 1H, H−C(22A)), 4.16 (d, ^2J = 11.0 Hz, 1H, H$_b$-C(28A)), 4.09 (d, ^2J = 11.0 Hz, 1H, H$_a$-C(28B)), 3.75 (d, ^2J = 11.0 Hz, 1H, H$_b$-C(28B)), 3.22−3.16 (m, 2H, H−C(3A), H−C(3B)), 2.73−2.75 (m, 1H, H−C(19A)), 2.71−2.67 (m, 1H, H−C(19B)), 2.18 (dd, ^2J = 13.8 Hz, ^3J = 5.8 Hz, 1H, H$_a$-C(21A)), 1.98−1.85 (m, 3H, H$_a$-C(21B), H$_a$-C(16A), H$_a$-C (16)), 1.84−1.77 (m, 2H, H$_a$-C(12A), H$_a$-C(12B)), 1.77−1.47 (m, 22H, H$_b$-C(16A), H$_b$-C(16B), H$_3$−C(30A), H$_3$−C(30B), H$_b$-C(21A), H$_b$-C(21B), H$_a$-C(6A), H$_a$-C(6B), H$_2$−C(2A), H$_2$−C(2B), H−C(13A), H−C(13B), H$_a$-C(1A), H$_a$-C(1B), H−C(18A), H−C(18B)), 1.47−1.35 (m, 10H, H$_b$-C(6A), H$_b$-C(6B), H$_a$-C(11A), H$_a$-C(11B), H$_a$-C(15A), H$_a$-C(15B), H$_2$−C(7A), H$_2$−C(7B)), 1.29−1.17 (m, 8H, H$_b$-C(11A), H$_b$-C(11B), H$_b$-C(12A), H$_b$-C(12B), H$_b$-C(15A), H$_b$-C(15B), H−C(9A), H−C(9B)), 0.99 (s, 3H, H$_3$−C(27B)), 0.99 (s, 3H, H$_3$−C(27A)), 0.97 (s, 9H, H$_3$−C(23A), H$_3$−C(23B), H$_3$−C(26A)), 0.94 (s, 3H, H$_3$−C(26B)), 0.94−0.88 (m, 2H, H$_b$-C(1A), H$_b$-C(1B)), 0.83 (s, 6H, H$_3$−C(25A), H$_3$−C(25B)), 0.76 (s, 6H, H$_3$−C(24A), H$_3$−C(24B)), 0.71−0.64 (m, 2H, H−C(5A), H−C(5B). ^{13}C NMR (126 MHz, CDCl$_3$) δ 164.93 (N−C=O A), 163.97 (N−C=O B), 152.77 (C2′A), 152.19 (C2′B), 148.18 (C6′B), 148.14 (C6′A), 147.43 (C20A + C20B), 136.87 (C4′B), 136.84 (C4′A), 125.26 (C5′A), 125.20 (C5′B), 124.09 (C3′B), 124.04 (C3′A), 111.67 (C29A + C29B), 79.12 (C3), 79.08 (C3), 71.97 (C22A), 66.98 (C22B), 60.69

(C28A), 55.45 (C5), 55.41 (C5), 54.66 (C28B), 50.59 (C9A + C9B), 49.10 (C17A), 48.57 (C17B), 48.21 (C19A), 48.15 (C19B), 47.20 (C18), 46.98 (C18), 42.32 (C14), 42.25 (C14), 41.35 (C21B), 41.07 (C8), 41.03 (C8), 39.02 (C13B), 39.00 (C1A + C1B), 38.89 (C4A + C4B), 38.88 (C21A), 38.81 (C13A), 37.31 (C10A + C10B), 34.51 (C7), 34.44 (C7), 31.00 (C16A + C16B), 28.31 (C15A + C15B), 28.12 (C23A + C23B), 27.53 (C2), 27.51 (C2), 25.42 (C12), 24.98 (C12), 21.01 (C11), 20.98 (C11), 18.42 (C6), 18.41 (C6), 16.33 (C26A), 16.30 (C25A + C25B), 16.04 (C26B), 15.52 (C24), 15.50 (C24), 14.51 (C27), 14.48 (C27).

N-Picolinoyl Azetidine 11 Mixture of Rotamers.



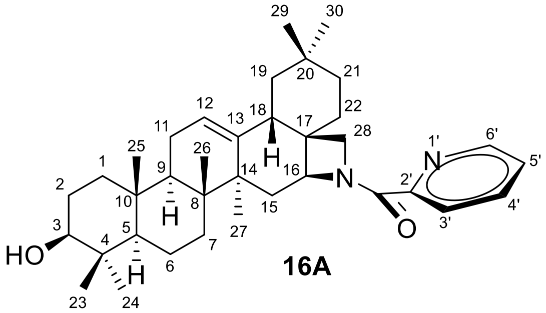
11A



11B

HRMS (ESI): *m*/*z* calc. for $[C_{36}H_{54}N_2O_2 + H]^+$ 547.4258; found 547.4254. ^{1}H NMR (500 MHz, CDCl$_3$) δ 8.60 (d, ^3J = 4.7 Hz, 1H, H−C(6′A)), 8.56 (d, ^3J = 4.7 Hz, 1H, H−C(6′B)), 8.10 (d, ^3J = 7.8 Hz, 1H, H−C(3′A)), 8.08 (d, ^3J = 7.8 Hz, 1H, H−C(3′B)), 7.80 (td, ^3J = 7.8 Hz, ^4J = 1.7 Hz, 1H, H−C(4′A)), 7.77 (td, ^3J = 7.8 Hz, ^4J = 1.7 Hz, 1H, H−C(4′B)) 7.35 (dd, ^3J = 7.7, 4.7 Hz, 1H, H−C(5′A)), 7.33 (dd, ^3J = 7.7, 4.7 Hz, 1H, H−C(5′B)), 4.86 (d, ^3J = 5.8 Hz, 1H, H−C(22B)), 4.54 (d, ^2J = 10.8 Hz, 1H, H$_a$-C(28A)), 4.36 (d, ^3J = 5.8 Hz, 1H, H−C(22A)), 4.12 (d, ^2J = 10.8 Hz, 1H, H$_b$-C(28A)), 4.02 (d, ^2J = 10.8 Hz, 1H, H$_a$-C(28B)), 3.70 (d, ^2J = 10.8 Hz, 1H, H$_b$-C(28B)), 3.22−3.16 (m, 2H, H−C(3A), H−C(3B)), 2.23−2.12 (m, 3H, H−C(20A), H−C(20B), H−C(18B)), 2.12−2.04 (m, 2H, H−C(18A, H$_a$-C(21A)), 1.94−1.82 (m, 5H, H$_a$-C(12A), H$_a$-C(12B), H$_b$-C(21A), H−C(16A, H−C(16B)), 1.80−1.74 (m, 1H, H$_a$-C(21B), 1.74−1.44 (m, 19H, H$_b$-C(16A), H$_b$-C(16B), H$_b$-C(21B), H$_a$-C(6A), H$_a$-C(6B), H$_a$-C(11A), H$_a$-C(11B), H$_2$−C(2A), H$_2$−C(2B), H$_a$-C(15A), H$_a$-C(15B), H$_b$-C(12A), H$_b$-C(12B), H−C(13A), H−C(13B), H$_a$-C(1A), H$_a$-C(1B)), 1.44−1.24 (m, 12H, H$_b$-C(6A), H$_b$-C(6B), H$_b$-C (11), H$_b$-C (11), H$_2$−C(7A), H$_2$−C(7B), H−C(19A), H−C(19B), H−C(9A), H−C(9B)), 1.23−1.15 (m, 2H, H$_b$-C(15A), H$_b$-C(15B)), 0.99−0.95 (m, 15H, H$_3$−C(23A), H$_3$−C(23B), H$_3$C(26A), H$_3$−C(27A), H$_3$−C(27B)), 0.94 (s, 3H, H$_3$−C(26B)), 0.94 −0.89 (m, 2H, H$_b$-C(1A), H$_b$-C(1B)), 0.89 (d, ^3J = 6.5 Hz, 3H, H$_3$−C(30B)), 0.84 (s, 6H, H$_3$−C(25A), H$_3$−C(25B)), 0.80 (d, ^3J = 6.5 Hz, 6H, H$_3$−C(30A), H$_3$−C(29B), 0.78−0.75 (m, 9H, H$_3$−C(29A), H$_3$−C(24A), H$_3$−C(24B)), 0.72−0.66 (m, 2H, H−C(5A), H−C(5B)). ^{13}C NMR (126 MHz, CDCl$_3$) δ 164.98 (N−C = O A), 163.97(N−C = O B), 152.90 (C2′A), 152.36 (C2′B), 148.24 (C6′B), 148.11 (C6′B), 136.83 (C4′B), 136.80 (C4′A), 125.19, (C5′A), 125.11 (C5′B), 124.03 (C3′B), 123.96 (C3′A), 79.13 (C3), 79.08 (C3), 71.48 (C22A), 66.48 (C22B), 60.65 (C28A), 55.38 (C5), 55.34 (C5), 54.64 (C28B), 50.12 (C9A + C9B), 49.42 (C17A), 48.93 (C17B), 45.94 (C19), 45.76 (C19), 45.60 (C18A), 45.45 (C18B), 42.60 (C14), 42.52 (C14), 41.07 (C8), 41.04 (C8), 39.00 (C13), 38.99 (C4A + C4B), 38.86 (C1), 38.85 (C1), 38.80 (C13), 37.25 (C10A + C10B), 34.60 (C7), 34.53 (C7), 32.98 (C21B), 31.14 (C16), 31.11 (C16), 30.59 (C21A), 28.13 (C23A + C23B), 28.09 (C15), 28.00 (C20A + C20B), 27.92 (C15), 27.52 (C2), 27.51 (C2), 26.04 (C12), 26.01 (C12), 23.13 (C30A), 23.05 (C30B), 20.91(C11), 20.88 (C11), 18.44 (C6), 18.42 (C6), 16.31 (C26A), 16.25 (C25), 16.22 (C25), 16.04 (C26B), 15.54 (C24), 15.52 (C24), 15.35 (C29A), 15.28 (C29B), 14.35 (C27), 14.32 (C27).

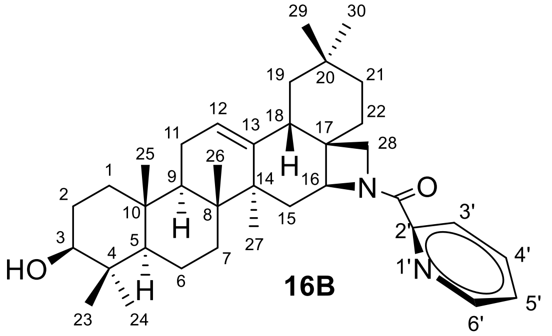
N-Picolinoyl Azetidine 16 Mixture of Rotamers: Rotamer A.



16A

HRMS (ESI): *m*/*z* calc. for $[C_{36}H_{52}N_2O_2 + H]^+$ 545.4102; found 545.4075. ^{1}H NMR (500 MHz, CDCl$_3$) δ 8.57 (d, *J* = 5.4 Hz, 1H, H−C(6′)), 8.09 (d, ^3J = 7.9 Hz, 1H, H−C(3′)), 7.79 (td, ^3J = 7.9 Hz, ^4J = 1.8 Hz, 1H, H−C(4′)), 7.37−7.30 (m, 1H, H−C(5′)), 5.50 (bs, 1H, H−C (12)), 4.46 (d, ^2J = 10.3 Hz, 1H, H$_a$-C (28)), 4.41 (t, ^3J = 7.4 Hz, 1H, H−C (16)), 4.22 (d, ^2J = 10.3 Hz, 1H, H$_b$-C (28)), 3.21 (dd, ^3J = 10.0, 4.5 Hz, 1H, H−C (3)), 2.55 (bs, 1H, H−C (18)), 2.06 (d, *J* = 7.6 Hz, 2H, H$_2$−C (15)), 2.05 −1.97 (m, 1H, H$_a$-C (11)), 1.97−1.78 (m, 3H, H$_a$-C (19), H$_b$-C (11), H$_a$-C (22)), 1.77−1.53 (m, 6H, H$_a$-C (6), H$_2$−C (2), H$_b$-C (22), H$_a$-C (1), H−C (9)), 1.53−1.22 (m, 5H, H$_b$-C (6), H$_2$−C (7), H$_2$−C (21)), 1.21−1.14 (m, 1H, H$_b$-C (19)), 1.13 (s, 3H, H$_3$−C (27)), 1.05−1.00 (m, 1H, H$_b$-C (1)), 0.99 (s, 3H, H$_3$−C (25)), 0.91 (s, 3H, H$_3$−C (29)), 0.90 (s, 3H, H$_3$−C (30)), 0.89 (s, 3H, H$_3$−C (25)), 0.81−0.77 (m, 4H, H$_3$−C (26), H−C (5)), 0.77 (s, 3H, H$_3$−C (24)).^{13}C NMR (126 MHz, CDCl$_3$) δ 165.40 (C=O), 152.46 (C2′), 148.10 (C6′), 140.95 (C13), 136.88 (C4′), 125.20 (C5′), 123.97 (C3′), 120.51 (C12), 79.15 (C3), 66.45 (C28), 64.60 (C16), 55.48 (C5), 47.33 (C9), 42.78 (C18), 42.39 (C14), 39.33 (C8), 38.93 (C4), 38.47 (C1), 37.46 (C10), 37.12 (C17), 36.35 (C21+ C19), 33.10 (C7), 31.48 (C30), 31.35 (C22), 30.65 (C20), 30.23 (C15), 28.78 (C29), 28.16 (C23), 27.32 (C2), 24.42 (C27) 23.50 (C11), 18.60 (C6), 16.35 (C26), 15.67 (C25), 15.59 (C24).

N-Picolinoyl Azetidine 16 Mixture of Rotamers: Rotamer B.



16B

HRMS (ESI): m/z calc. for $[C_{36}H_{52}N_2O_2 + H]^+$ 545.4102; found 545.4075. ^{1}H NMR (500 MHz, CDCl$_3$) δ 8.57 (d, J = 5.4 Hz, 1H, H−C(6′)), 8.05 (d, ^3J = 7.9 Hz, 1H, H−C(3′)), 7.79 (td, ^3J = 7.9 Hz, ^4J = 1.8 Hz, 1H, H−C(4′)), 7.37−7.30 (m, 1H, H−C(5′)), 5.48 (bs, 1H, H−C (12)), 4.84 (t, ^3J = 7.4 Hz, 1H, H−C (16)), 3.86 (ABq, Δδ AB = 0.05 Hz, ^2J = 10.2 Hz, 2H, H$_2$−C (28)),3.21 (dd, ^3J = 10.0, 4.5 Hz, 1H, H−C (3)), 2.43 (bs, 1H, H−C (18)), 2.05 −1.97 (m, 1H, H$_a$-C (11)), 1.97−1.78 (m, 5H, H$_2$−C (15)), H$_a$-C (19), H$_b$-C (11), H$_a$-C (22)), 1.77−1.53 (m, 6H, H$_a$-C (6), H$_2$−C (2), H$_b$-C (22), H$_a$-C (1), H−C (9)), 1.53−1.22 (m, 5H, H$_b$-C (6), H$_2$−C (7), H$_2$−C (21)), 1.21−1.14 (m, 1H, H$_b$-C (19)), 1.09 (s, 3H, H$_3$−C (26)), 1.05−1.00 (m, 1H, H$_b$-C (1)), 0.96 (s, 3H, H$_3$−C (25)), 0.91 (s, 3H, H$_3$−C (29)), 0.90 (s, 3H, H$_3$−C (30)), 0.86 (s, 3H, H$_3$−C (25)), 0.81−0.77 (m, 1H, H−C (5)), 0.76 (s, 3H, H$_3$−C (24)), 0.71 (s, 3H, H$_3$C-26)). ^{13}C NMR (126 MHz, CDCl3) δ 166.01 (C═O) 152.46 (C2′), 148.17 (C6′), 140.80 (C13), 136.88 (C4′), 125.30 (C5′), 124.11 (C3′), 120.61 (C12), 79.10 (C3), 68.95 (C16), 60.07 (C28), 55.61 (C5), 47.36 (C9), 43.28 (C18), 42.39 (C14), 39.19 (C8), 38.89 (C4), 38.47 (C1), 37.43 (C10), 36.73 (C17), 36.45 (C19), 36.25 (C21), 33.00 (C7), 31.81 (C15), 31.57 (C22), 31.48 (C30), 30.65 (C20), 28.78 (C29), 28.14 (C23), 27.33 (C2), 24.65 (C27), 23.44 (C11), 18.55 (C6), 16.51 (C26), 15.65 (C25), 15.58 (C24).

General Procedure III for Directing Group Cleavage. To a suspension of arylated picolinic amide (0.15 mmol, 1 equiv) in THF/H$_2$O 1:1 (5 mL), aqueous 12 M HCl (0.24 mL) was added dropwise, and the reaction mixture was stirred for 10 min at room temperature. Then zinc dust (146 mg, 2.25 mmol, 15 equiv) was added portion wise and the resulting reaction mixture was stirred at room temperature for 4 h. Then the reaction mixture was filtered through Celite pad (H = 50 mm, d = 15 mm) and filtrate was washed with 2 M NaOH aqueous solution (25 mL) and the mixture was extracted with DCM (3 × 25 mL). The combined organic phase was dried over anhydrous Na$_2$SO$_4$, filtered, and evaporated under reduced pressure. The residue was purified by silica column chromatography (DCM-MeOH 100:1−20:1) to yield an amine as a white amorphous solid.

*(22S)-22-(4-Methoxyphenyl)-3β-hydroxy-lup-20(29)en-28-amine (**24**).* According to GP III, compound **24** was prepared from **6a** (100 mg, 0.153 mmol, 1 equiv), zinc dust (150 mg, 2.297 mmol, 15 equiv), and 12 M HCl (0.33 mL). Yield 78 mg, 90%. HRMS (ESI): m/z calc. for $[C_{37}H_{57}NO_2 + H]^+$ 548.4462; found 548.4467. ^{1}H NMR (500 MHz, CDCl$_3$) δ 7.24−7.20 (m, 2H, H−C(2′), H−C(6′)), 6.88−6.79 (m, 2H, H−C(3′) + H−C(5′)), 4.75 (d, ^4J = 2.5 Hz, 1H, H$_a$-C (29)), 4.61 (s, 1H, H$_b$-C (29)), 3.78 (s, 3H, H$_3$C−O), 3.17 (dd, ^3J = 11.3, 4.9 Hz, 1H), 2.77−2.63 (m, 3H, H$_2$−C (28), H−C (22)), 2.57−2.43 (m, 2H, H−C (19), H$_a$-C (21)), 1.95 (dt, ^2J = 13.0, ^3J = 3.3 Hz, 1H, H$_a$-C (16)), 1.81 (td, ^3J = 12.0, 4.0 Hz, 1H, H−C (13)), 1.79 (dd, ^3J = 12.0, 10.9 Hz, 1H, H−C (18)), 1.72 (s, 3H, H$_3$−C (30)), 1.71−1.62 (m, 2H, H$_a$-C (12), H$_a$-C (1)), 1.62−1.48 (m, 3H, H$_2$−C (2), H$_a$-C (6)), 1.47−1.33 (m, 6H, H$_b$-C (6), H$_a$-C (11), H$_a$-C (15), H$_2$−C (7), H$_b$-C (21)), 1.33−1.17 (m, 3H, H$_b$-C (11), H$_b$-C (16), H−C (9)), 1.12−1.06 (m, 2H, H$_b$-C (12), H$_b$-C (15)), 1.03 (s, 3H, H$_3$−C (27)), 0.99 (s, 3H, H$_3$−C (26)), 0.96 (s, 3H, H$_3$−C (23)), 0.90−0.86 (m, 1H, H$_b$-C (1)), 0.82 (s, 3H, H$_3$−C (25)), 0.75 (s, 3H, H$_3$−C (24)), 0.72−0.65 (m, 1H, H−C (5)). ^{13}C NMR (126 MHz, CDCl3) δ 158.43 (C4′), 150.34 (C20), 132.63 (C1′), 128.58 (C2′ + C6′), 114.10 (C3′ + C5′), 110.17 (C29), 78.99 (C3), 55.49 (C5), 55.35 (CH$_3$−O), 54.04 (C22), 50.67 (C9), 50.57 (C18), 50.17 (C17), 46.16 (C19), 42.57 (C14), 40.97 (C8), 38.99 (C4), 38.87 (C1), 38.51 (C28), 37.56 (C13), 37.30 (C10), 34.70 (C21), 34.32 (C7), 29.14 (C16), 28.12 (C23), 27.54 (C2), 27.51 (C15), 25.12 (C12), 21.05 (C11), 19.12 (C30), 18.42 (C6), 16.26 (C25), 16.13 (C26), 15.49 (C24), 15.18 (C27)

*(22S)-22-(4-Carboxyphenyl)-3β-hydroxy-lup-20(29)en-28-amine (**26**).* According to GP III, compound **26** was prepared from **25** (60 mg, 0.097 mmol, 1 equiv), zinc dust (94 mg, 1.455 mmol, 15 equiv), and 12 M HCl (0.24 mL). Yield 42 mg, 84%. HRMS (ESI): m/z calc. for $[C_{37}H_{55}NO_3 + H]^+$ 562.4255; found 562.4236. ^{1}H NMR (500 MHz, DMSO) δ 7.86 (d, ^3J = 8.0 Hz, 2H, H−C(3″), H−C(5″)), 7.43 (d, ^3J = 8.0 Hz, 2H, H−C(3″), H−C(5″)), 4.73 (s, 1H, H$_a$-C (29)), 4.60 (s, 1H, H$_b$-C (29)), 4.28 (s, 1H, OH), 3.03 (d, ^2J = 14.0 Hz, 1H, H$_a$-C (28)), 3.00−2.93 (m, 2H, H−C (3), H−C (22)), 2.59 (d, ^2J = 14.0 Hz, 1H, H$_b$-C (28)), 2.55−2.50 (m, 1H, H−C (19)), 2.31−2.22 (m, 1H, H$_a$-C (21)), 1.91−1.79 (m, 2H, H−C (18), H$_a$-C (16)), 1.71 (s, 3H, H−C (30)), 1.67−1.52 (m, 5H, H$_a$-C (12), H$_2$−C (15), H−C (13), H$_a$-C (1)), 1.50−1.34 (m, 7H, H$_2$−C (6), H$_a$-C (11), H$_2$−C (2), H$_2$−C (7)), 1.33−1.18 (m, 3H, H$_b$-C (11), H$_b$-C (16), H−C (9)), 1.13−1.06 (m, 4H, H$_3$−C (26), H$_b$-C (21)), 1.04 (s, 3H, H$_3$−C (27)), 1.02−0.97 (m, 1H, H$_b$-C (12)), 0.87 (s, 3H, H$_3$−C (23)), 0.84−0.81 (m, 1H, H$_b$-C (1)), 0.80 (s, 3H, H$_3$−C (25)), 0.68−0.62 (m, 4H, H$_3$−C (24), H−C (5)). ^{13}C NMR (126 MHz, DMSO) δ 167.58 (COOH), 149.96 (C20), 148.20 (C4″), 129.34 (C3″ + C5″), 127.85 (C2″ + C6″), 116.19 (C1″), 109.79 (C29), 76.77 (C3), 54.83 (C5), 50.71 (C18), 50.34 (C17), 49.72 (C9), 48.12 (C22), 46.39 (C19), 42.74 (C14), 40.78 (C8), 38.53 (C4), 38.27 (C1), 37.73 (C28), 36.71 (C10), 36.06 (C13), 33.74 (C7), 32.85 (C15), 32.06 (C21), 29.15 (C16), 28.12 (C23), 27.16 (C2), 24.95 (C12), 20.33 (C11), 19.31 (C30), 17.92 (C6), 16.00 (C25), 15.82 (C26), 15.80 (C24), 14.98 (C27).

*(22S)-22-(4-Carboxyphenyl)-3β-hydroxy-28-picolinamido-lup-20(29)en (**25′**) and (16R)-16-(4-Carboxyphenyl)-3β-hydroxy-28-picolinamido-lup-20(29)en (**25′**).* To a solution of compound **7f** (80 mg, 0.117 mmol, 1 equiv) in EtOH (4 mL), NaOH (20 mg, 0.500 mmol, 4.3 equiv) was added. Reaction was stirred for 16 h at 80 °C, the reaction was quenched by addition of ion-exchange resin (Dowex 50WX8, 50−100 mesh, H−form) until pH 7, filtered, and evaporated in vacuum. The residue was purified by column chromatography on silica with Hex/EtOAc + (30%→50% EtOAc). Yield (67 mg, 86%, 9:1). HRMS (ESI): m/z calc. for $[C_{43}H_{58}N_2O_4 + H]^+$ 667.4469; found 667.4454.

*(22S)-22-(4-Carboxyphenyl)-3β-hydroxy-28-picolinamido-lup-20(29)ene (**25**).* ^{1}H NMR (500 MHz, CDCl$_3$) δ 8.13 (dd, 1H, ^3J = 4.5 Hz, ^4J = 1.5 Hz, H−C(6′)), 8.02 (d, ^3J = 8.1 Hz, 2H, H−C(3″), H−C(5″)), 7.98 (d, ^3J = 7.7 Hz, 1H, H−C(3′)), 7.68 (td, ^3J = 7.7 Hz, ^4J = 1.5 Hz, 1H, H−C(4′)), 7.45 (d, ^3J = 8.1 Hz, 2H, H−C(2″), H−C(6″)), 7.22 (dd, ^3J = 7.7, 4.5 Hz, 1H, H−C(5′)),), 6.90 (dd, ^3J = 8.8, 3.4 Hz, 1H, H−N), 4.82 (d, ^4J = 2.2 Hz, 1H, H$_a$-C (29)), 4.69 (s, 1H, H$_b$-C (29)), 4.07 (dd, ^2J = 14.3, ^3J = 8.8 Hz, 1H, H$_a$-C (28)), 3.21 (dd, ^3J = 11.4, 4.8 Hz, 1H, H−C (3)), 3.10 (dd, ^2J = 14.3, ^3J = 3.4 Hz, 1H, H$_b$-C (28)), 3.00 (dd, ^3J = 9.9, 9.6 Hz, 1H, H−C (22)), 2.75 (ddd, ^2J = 13.7 Hz, ^3J = 11.2, 9.9 Hz, 1H H$_a$-C (21)), 2.67 (ddd, ^3J = 11.2, 10.6, 5.1 Hz, 1H, H−C (19)), 2.02 (td, ^3J = 11.9, 3.5 Hz, 1H, H−C (13)), 1.95 (dd, ^3J = 11.9, 11.0 Hz, 1H, H−C (18)), 1.89 (ddd, ^2J = 13.1 Hz, ^3J = 6.7, 3.5 Hz, 1H, H$_a$-C (16)), 1.77 (s, 3H, H−C (30)), 1.77−1.65 (m, 4H, H$_a$-C (12), H$_a$-C (7), H$_a$-C (1), H$_a$-C (15)), 1.65−1.23 (m, 10H, H$_2$−C (2), H$_2$−C (6), H$_2$−C (11), H$_b$-C (16) H$_b$-C (7), H$_b$-C (21), H−C (9)), 1.14 (s, 3H, H$_3$−C (26), H−C (9)), 1.13−1.08 (m, 1H, H$_{b-}$C (12)), 1.07−1.02 (m, 4H, H$_3$−C (27), H$_b$-C (15)), 0.96 (s, 3H,H$_3$−C (23)), 0.95−0.88 (m, 1H, H$_b$-C (1)), 0.84 (s, 3H, H$_3$−C (25)), 0.76 (s, H$_3$−C (24)), 0.73−0.66 (m, 1H, H−C (5)). ^{13}C NMR (126 MHz, CDCl$_3$) δ 170.52 (COOH), 164.11 (N−C=O), 149.61 (C20), 149.45 (C2′), 147.58 (C6′), 146.99 (C1″), 137.12 (C4′), 130.85 (C3″ + C5″), 128.00 (C4″), 127.50 (C2″ + C6″), 125.95 (C5′), 121.87 (C3′), 110.74 (C29), 79.27 (C3), 55.52 (C5), 54.92 (C22), 51.00 (C17), 50.86 (C18), 50.65 (C9), 46.16 (C19), 42.70 (C14), 41.02 (C8), 39.01 (C4), 38.89 (C1), 37.70 (C13), 37.34 (C10), 36.00 (C28), 34.13 (C7), 33.89 (C21), 30.31 (C16), 28.12 (C23), 27.53 (C2), 27.39 (C15), 25.22 (C2), 20.98 (C11), 19.39 (C30), 18.37 (C6), 16.22 (C25), 16.05 (C26), 15.50 (C24), 15.17 (C27).

*(16R)-16-(4-Carboxyphenyl)-3β-hydroxy-28-picolinamido-lup-20(29)ene (**25′**).* ^{1}H NMR (500 MHz, CDCl$_3$) δ 8.15 (d, 1H, ^3J = 4.7 Hz, H−C(6′)), 8.02 (d, ^3J = 8.1 Hz, 2H, H−C(3″), H−C(5″)), 7.98 (d, ^3J = 7.7 Hz, 1H, H−C(3′)), 7.70 (td, ^3J = 7.7 Hz, ^4J = 1.7 Hz, 1H, H−C(4′)), 7.43 (d, ^3J = 8.1 Hz, 2H, H−C(2″), H−C(6″)), 7.23 (dd, ^3J = 7.7, 4.7 Hz, 1H, H−C(5′)),), 7.01 (dd, ^3J = 9.1, 3.4 Hz, 1H, H−N), 4.76 (d, ^4J = 2.2 Hz, 1H, H$_a$-C (29)), 4.64 (s, 1H, H$_b$-C (29)), 3.71−3.61 (m, 1H, H$_a$-C (28)), 3.48 (dd, ^2J = 14.6 Hz, ^3J = 3.4 Hz, 1H, H$_b$-C (28)), 3.21 (dd, ^3J = 11.3, 4.8 Hz, 1H, H−C (3)), 3.00 (dd, ^3J = 13.1, 3.4 Hz, 1H, H−C (16)), 2.69 (td, ^3J = 11.0, 4.4 Hz, 1H, H−C (19)), 2.50 (dd, ^2J = 13.3 Hz, ^3J = 13.1 Hz, 1H, H$_a$-C (15)), 2.11−1.99 (m, 1H, H$_a$-C (21)), 1.93 (dd, ^3J = 11.9, 11.0 Hz, 1H, H−C (18)), 1.83 (td, ^3J = 11.9, 3.7 Hz, 1H, H−C (13)), 1.76 (s, 3H, H−C (30)), 1.76−1.59 (m, 5H, H$_a$-C (12), H$_a$-C (22), H$_a$-C (1), H$_2$−C (2)), 1.58−1.43 (m, 6H, H$_2$−C (6), H$_a$-C (11), H$_b$-C (22), H$_2$−C (7)), 1.43- 1.23 (m, 4H, H$_b$-C (11), H$_b$-C (21), H$_b$-C (15), H−C (9)), 1.21 (s, 3H, H$_3$−C (26)), 1.16−1.09 (m, 4H, H$_{b-}$C (12), H$_3$−C (27)), 0.98 (s, 3H,H$_3$−C (23)), 0.97−0.90 (m, 1H, H$_b$-C (1)), 0.88 (s, 3H, H$_3$−C (25)), 0.79 (s, 3H, H$_3$−C (24)), 0.74−0.69 (m, 1H, H−C (5)). ^{13}C NMR (126 MHz, CDCl$_3$) δ 170.42 (O−C=O), 164.14 (N−C=O), 150.39 (C20), 150.16 (C1″), 149.54 (C2′), 147.67 (C6′), 137.12 (C4′), 130.67 (C3″ + C5″), 127.95 (C2″ + C6″), 127.39 (C4″), 125.95 (C5′), 121.82 (C3′), 109.88 (C29), 79.14 (C3), 55.49 (C5), 51.55 (C17), 51.43 (C18), 50.62 (C9), 48.94 (C16), 46.87 (C19), 43.40 (C14), 41.46 (C8), 39.04 (C4), 38.93 (C1), 37.38 (C10), 37.11 (C13), 36.31 (C28), 35.07 (C22), 34.53 (C7), 32.16 (C15), 30.06 (C21), 28.15 (C23), 27.55 (C2), 25.65 (C12), 21.05 (C11), 20.21 (C30), 18.43 (C6), 16.45 (C25), 16.37 (C26), 15.62 (C24), 15.54 (C27).

General Procedure IV for Synthesis of Unprotected Azetidines. To a solution of N-acyl azetidine **8**, **11**, or **16** (0.12 mmol, 1 equiv) in anhydrous THF (1.5 mL), LiAlH$_4$ (13 mg, 0.36 mmol, 3 equiv) was added in one portion at 0 °C. The resulting reaction mixture was stirred under a nitrogen atmosphere at 0 °C for 1 h. The reaction mixture was warmed up to room temperature, and after 3 h, it was cooled back to 0 °C and slowly quenched sequentially with MeOH (0.5 mL) and water (0.5 mL). The reaction mixture was diluted with DCM (15 mL) and washed with 10% NaOH aqueous solution (10 mL). The organic phase was then washed with water (1 × 10 mL), brine (1 × 10 mL), and dried over anhydrous Na$_2$SO$_4$. After filtration, the filtrate was concentrated in vacuo, and the crude mixture was purified by silica column chromatography (DCM-MeOH 100:1→25:1) to yield an unprotected amine as a white amorphous solid.

Azetidine 12. HRMS (ESI): m/z calc. for [C$_{30}$H$_{49}$NO + H]$^+$ 440.3887; found 440.3876. ^{1}H NMR (500 MHz, CDCl$_3$) δ 4.87 (s, 1H, H$_a$-C (29)), 4.69 (s, 1H, H$_b$-C (29)), 3.65 (d, ^3J = 5.2 Hz, 1H, H−C (22)), 3.61 (d, ^2J = 9.3 Hz, 1H, H$_a$-C (28)), 3.17 (dd, ^3J = 11.2, 4.8 Hz, 1H, H−C (3)), 3.14 (d, ^2J = 9.3 Hz, 1H, H$_b$-C (28)), 2.90 (ddd, ^3J = 10.3, 8.9, 8.5 Hz, 1H, H−C (19)), 2.01 (ddd, ^2J = 12.5 Hz, 3.7, 3.4 Hz, 1H, H$_a$-C (16)), 1.83−1.75 (m, 1H, H$_a$-C (12)), 1.69 (s, 3H, H$_3$−C (30)), 1.68−1.48 (m, 7H, H$_a$-C (6), H$_2$−C (2), H$_a$-C (21), H$_b$-C (16), H−C (13), H$_a$-C (1)), 1.47−1.18 (m, 9H, H$_b$-C (6), H$_2$−C (11), H$_b$-C (21), H$_a$-C (15), H$_2$−C (7), H−C (18), H−C (9)), 1.17 −1.09 (m, 2H, H$_b$-C (12), H$_b$-C (15)), 0.95 (s, 3H, H$_3$−C (23)), 0.94 (s, 3H, H$_3$−C (26)), 0.90−0.86 (m, 4H, H$_3$−C (27), H$_b$-C (1)), 0.81 (s, 3H, H$_3$−C (25)), 0.74 (s, 3H, H$_3$−C (24)), 0.66 (d, ^3J = 9.8 Hz, 1H, H−C (5)). ^{13}C NMR (126 MHz, CDCl$_3$) δ 148.22 (C20), 111.23 (C29), 79.02 (C3), 64.37 (C22), 55.43 (C5), 52.45 (C28), 52.20 (C17), 50.59 (C9), 49.15 (C19), 47.79 (C18), 42.08 (C14), 41.01 (C8), 39.00 (C4), 38.89 (C1), 38.17 (C13), 37.30 (C10), 34.47 (C7), 31.61 (C16), 28.14 (C23), 27.99 (C15), 27.55 (C2), 27.05 (C21), 25.12 (C12), 21.01 (C11), 18.88 (C30),18.42 (C6), 16.30 (C25), 16.07 (C26), 15.52 (C24), 14.38 (C27).

Azetidine 13. HRMS (ESI): m/z calc. for [C$_{30}$H$_{51}$NO + H]$^+$ 442.4043; found 442.4033. ^{1}H NMR (500 MHz, CDCl$_3$) δ 3.60 −3.54 (m, 2H, H−C (22), H$_a$-C (28)), 3.19 (dd, ^3J = 11.6, 4.8 Hz, 1H, H−C (3)), 3.12 (d, ^2J = 8.9 Hz, 1H, H$_b$-C (28)), 2.34−2.25 (m, 1H, H−C (19)), 2.24−2.16 (m, 1H, H−C (20)), 2.04−1.97 (m, 1H, H$_a$-C (16)), 1.89−1.83 (m, 1H, H$_a$-C (12)), 1.72−1.43 (m, 9H, H$_a$-C (1), H$_a$-C (6), H$_a$-C (11), H$_2$−C (2), H$_b$-C (16), H$_2$−C (21), H−C (13)), 1.43−1.19 (m, 8H, H$_b$-C (6), H$_b$-C (11), H$_b$-C (12), H$_a$-C (15), H$_2$−C (7), H−C (18), H−C (9)), 1.14−1.08 (m, 1H, H$_b$-C (15)), 0.97 (s, 3H, H−C (23)), 0.95−0.90 (m, 7H, H$_3$−C (30), H$_3$−C (27), H$_b$-C (1)), 0.89 (s, 3H, H$_3$−C (26)), 0.82 (s, 3H, H$_3$−C (25)), 0.78 (d, ^3J = 6.8 Hz, 3H, H$_3$−C (29)), 0.76 (s, 3H, H$_3$−C (24)), 0.68 (d, J = 10.3 Hz, 1H, H−C (5)). ^{13}C NMR (126 MHz, CDCl$_3$) δ 79.03 (C3), 63.70 (C22), 55.36 (C5), 52.47 (C17), 52.43 (C28), 50.12 (C9), 46.60 (C18), 46.40 (C19), 42.35 (C14), 41.00 (C8), 38.99 (C4), 38.85 (C1), 38.07 (C13), 37.23 (C10), 35.19 (C21), 34.55 (C7), 31.78 (C16), 28.25 (C23), 28.13 (C20), 27.79 (C15), 27.52 (C2), 26.12 (C12), 23.23 (C30), 20.91 (C11), 18.43 (C6), 16.21 (C25), 16.06 (C26), 15.54 (C24), 15.28 (C29), 14.22 (C27).

Azetidine 17 HRMS (ESI). m/z calc. for $[C_{30}H_{49}NO + H]^+$ 440.3887; found 440.3868. ^{1}H NMR (500 MHz, $CDCl_3$) δ 5.47 (t, $^3J = 3.5$ Hz, 1H, H−C (12)), 3.81 (t, $^3J = 8.3$ Hz, 1H, H−C (16)), 3.46 (d, $^2J = 8.4$ Hz, 1H, H_a-C (28)), 3.37 (d, $^2J = 8.4$ Hz, 1H, H_b-C (28)), 3.22 (dd, $^3J = 10.9$, 4.6 Hz, 1H, H−C (3)), 2.65 (bs, 1H, H−C (18)), 2.08−1.99 (m, 1H, H_a-C (11)), 1.92−1.74 (m, 4H, H_a-C (19), H_b-C (11), H_a-C (15), H_a-C (22)), 1.69−1.54 (m, 7H, H_a-C (6), H_2−C (2), H_b-C (15), H_b-C (22), H_a-C (1), H−C (9)), 1.48−1.35 (m, 3H, H_b-C (6), H_2−C (7)), 1.26−1.16 (m, 2H, H_b-C (19), H_a-C (21)), 1.14−1.05 (m, 1H, H_b-C (21)), 1.04−1.00 (m, 1H, H_b-C (1)), 1.00 (s, 3H, H_3−C (27)), 0.99 (s, 3H, H_3−C (23)), 0.91 (s, 3H, H_3−C (25)), 0.88 (s, 3H, H_3−C (29)), 0.87 (s, 3H, H_3−C (30)), 0.84 (s, 3H, H_3−C (26)), 0.79 (s, 3H, H_3−C (24)), 0.78−0.74 (m, 1H, H−C (5)).^{13}C NMR (126 MHz, $CDCl_3$) δ 141.05 (C13), 119.63 (C12), 79.17 (C3), 61.15 (C16), 58.34 (C28), 55.60 (C5), 47.16 (C9), 42.67 (C18), 42.06 (C14), 39.57 (C8), 39.19 (C17), 38.93 (C4), 38.38 (C1), 37.48 (C10), 36.09 (C22), 34.65 (C19), 33.59 (C30), 33.43 (C15), 33.24 (C7), 31.91 (C21), 30.65 (C20), 28.18 (C23), 28.09 (C29), 27.33 (C2), 23.52 (C11), 23.21 (C27), 18.74 (C6), 16.58 (C26), 15.62 (C25 + C24).

Synthesis of Azetidinium Picrate 18. Picric acid (1.6 mg, 0.0068 mmol, 1 equiv) was added in one portion to a solution of azetidine **17** (3.0 mg, 0.0068 mmol, 1 equiv) in MeOH (0.5 mL). After 5 min, the solvent was evaporated to dryness under reduced pressure to yield pure product as a yellow amorphous solid (4.6 mg, 100%). Obtained solid was slowly recrystallized from MeOH to obtain the crystalline form of azetidinium picrate **18**.

Azetidinium Picrate 18. ^{1}H NMR (500 MHz, $CDCl_3$) δ 9.09 (s, 1H, H−N), 8.97 (s, 2H, H−C_{Ar}), 8.23 (s, 1H, H−N), 5.55 (t, $^3J = 3.5$ Hz, 1H, H−C (12)), 4.49−4.42 (m, 1H, H−C (16)), 3.98−3.87 (m, 2H, H_2−C (28)), 3.20 (dd, $^3J = 10.9$, 4.6 Hz, 1H, H−C (3)), 2.66 (bs, 1H, H−C (18)), 2.10−1.97 (m, 3H, H_a-C (11), H_a-C (19), H_a-C (15)), 1.91−1.82 (m, 2H, H_a-C (21), H_b-C (11)), 1.79−1.71 (m, 2H, H_b-C (15), H_b-C (21)), 1.66−1.54 (m, 5H, H_a-C (6), H_2−C (2), H_a-C (1), H−C (9)), 1.40−1.17 (m, 5H, H_b-C (6), H_2−C (7), H_b-C (19), H_a-C (22)), 1.06−1.01 (m, 1H, H_b-C (22)), 0.99 (s, 6H, H_3−C (23), H_3−C (27)), 0.99−0.94 (m, 1H, H_b-C (1)), 0.90 (s, 3H, H_3−C (30)), 0.87 (s, 6H, H_3−C (29), H_3−C (25)), 0.78 (s, 3H, H_3−C (24)), 0.75−0.70 (m, 1H, H−C (5)), 0.62 (s, 3H, H_3−C (26)). ^{13}C NMR (126 MHz, $CDCl_3$) δ 160.16 (C1′), 140.87 (C2′ + C6′), 137.63 (C13), 131.17 (C4′), 126.85 (C3′ + C5′), 121.91 (C12), 79.05 (C3), 64.89 (C16), 57.52 (C28), 55.50 (C5), 46.81 (C9), 42.38 (C14), 41.05 (C18), 39.16 (C8), 38.91 (C17), 38.83 (C4), 38.29 (C1), 37.42 (C10), 35.82 (C22), 33.92 (C19), 33.44 (C30), 33.09 (C7), 30.57 (C21), 30.43 (C20), 28.50 (C15), 28.16 (C23), 27.67 (C29), 27.21 (C2), 23.43 (C11), 22.79 (C27), 18.56 (C6), 16.30 (C26), 15.59 (C24 + C25).

General Procedure V for C−H Deuteration Experiments. A solution of picolinic amide (20 mg, 0.0366 mmol, 1 equiv), CsOAc (7 mg, 0.0366 mmol, 1 equiv) and $Pd(OAc)_2$ (3 mg, 0.0146 mmol, 0.4 equiv) in CD_3COOD (1 mL) was stirred at 80 °C for 16h. Reaction mixture was concentrated in vacuo, and the obtained residue was purified by silica column chromatography (Hexanes-EtOAc 10:1 → 5:1) to yield the desired deuterated product as a white amorphous solid.

*(16S,22R)-2,2,16,22-Tetradeutero-3-oxo-17-quinolin-8-ylcarbamoyl-28-norlup-20(29)ene (**2a′**).* Yield 15 mg, 74%. HRMS (ESI): m/z calc. for $[C_{36}H_{54}D_2N_2O_2 + H]^+$ 585.4353; found 585.4357. ^{1}H NMR (500 MHz, $CDCl_3$) δ 10.16 (s, 1H, H−N), 8.81 (dd, $^3J = 4.2$ Hz, $^4J = 1.7$ Hz, 1H, H−C(2′)), 8.77 (d, $^3J = 7.6$ Hz, 1H, H−C(7′)), 8.16 (dd, $^3J = 8.2$ Hz, $^4J = 1.8$ Hz, 1H, H−C(4′)), 7.53 (dd, $^3J = 7.9$, 7.6 Hz, 1H, H−C(6′)), 7.50−7.42 (m, 2H, H−C(5′), H−C(3′)), 4.80 (s, 1H, H_a-C (29)), 4.63 (s, 1H, H_b-C (29)), 3.27 (td, $^3J = 11.2$, 4.6 Hz, 1H, H−C (19)), 2.73 (td, $^3J = 12.4$, 3.5 Hz, 1H, H−C (13)), 2.05 (dt, $^2J = 13.9$ Hz, $^3J = 11.2$ Hz, 1H, H_a-C (21)), 1.89 (d, $^2J = 13.4$ Hz, 1H, H_a-C (1)), 1.87−1.78 (m, 1H, H_a-C (12)), 1.75−1.68 (m, 5H, H_3−C (30), H−C (16), H−C (18)), 1.66−1.55 (m, 2H, H_a-C (15), H−C (22)), 1.54−1.21 (m, 11H, H_2−C (6), H_2−C (11), H_b-C (15), H_b-C (21), H_2−C (7), H_b-C (1), H−C (9), H−C (5)), 1.07−1.04 (m, 1H, H_b-C (12)), 1.04 (s, 3H, H_3−C (23)), 1.03 (s, 3H, H_3−C (27)), 0.99 (s, 3H, H_3−C (24)), 0.95 (s, 3H, H_3−C (26)), 0.90 (s, 3H, H_3−C (25)). ^{13}C NMR (126 MHz, $CDCl_3$) δ 218.43 (C3), 175.24 (O=C-NH), 151.00 (C20), 148.29 (C2′), 138.78 (C8a′), 136.46 (C4′), 135.13 (C8′), 128.10 (C4a′), 127.60 (C6′), 121.67 (C3′), 121.02 (C5′), 116.15 (C7′), 109.65 (C29), 57.34 (C17), 55.19 (C5), 50.19 (C18 + C9), 47.46 (C4), 46.72 (C19), 42.77 (C14), 40.83 (C8), 39.66 (C1), 38.25 (t, $^1J = 19.3$ Hz, C (22)), 37.84 (C13), 37.04 (C10), 33.86 (quint, $^1J = 18.2$ Hz, (C2)), 33.78 (C7), 33.67 (t, $^1J = 17.9$ Hz, (C16)), 30.91 (C21), 29.70 (C15), 26.65 (C23), 25.83 (C12), 21.63 (C11), 21.08 (C24), 19.74 (C30), 19.66 (C6), 16.10 (C27), 14.73 (C26 + C25).

*(16S)-2,2,16-Trideutero-3-oxo-17-quinolin-8-ylcarbamoyl-28-norolean-12(13)ene (**2c′**).* Yield 10 mg, 50%. HRMS (ESI): m/z calc. for $[C_{39}H_{49}D_3N_2O_2 + H]^+$ 584.4290; found 584.4283. ^{1}H NMR (500 MHz, $CDCl_3$) δ 10.38 (s, 1H, H−N), 8.85 (d, $^3J = 7.4$ Hz, 1H, H−C(7′)), 8.80 (dd, $^3J = 4.2$ Hz, $^4J = 1.7$ Hz, 1H, H−C(2′)), 8.15 (dd, $^3J = 8.3$ Hz, $^4J = 1.7$ Hz, 1H, H−C(4′)), 7.56−7.41 (m, 3H, H−C(6′), H−C(5′), H−C(3′)), 5.73 (t, $^3J = 3.7$ Hz, 1H, H−C (12)), 3.00 (dd, $^3J = 13.1$, 4.4 Hz, 1H, H−C (18)), 2.20−2.11 (m, 1H, H−C (16)), 2.01−1.93 (m, 2H, H_2−C (11)), 1.89−1.79 (m, 3H, H_a-C (21), H_a-C (1), H_a-C (19)), 1.78−1.69 (m, 1H, H_a-C (15)), 1.65 (t, $^3J = 8.8$ Hz, 1H, H−C (9)), 1.49−1.23 (m, 10H, H_2−C (6), H_2−C (7), H_2−C (22), H_b-C (21), H_b-C (1), H_b-C (19), H−C (5)), 1.22 (s, 3H, H_3−C (27)), 1.14 (dd, $^2J = 12.5$ Hz, $^3J = 7.9$ Hz, 1H, H_b-C (15)), 1.04 (s, 3H, H_3−C (23), 0.98 (s, 3H, H_3−C (29)), 0.96 (s, 3H, H_3−C (30)), 0.95 (s, 3H, H_3−C (24)), 0.85 (s, 3H, H_3−C (26)), 0.54 (s, 3H, H_3−C (25)). ^{13}C NMR (126 MHz, $CDCl_3$) δ 217.98 (C3), 177.10 (C28), 147.97 (C2′), 143.38 (C8a′), 139.16 (C13), 136.37 (C4′), 135.07 (C8′), 128.12 (C4a′), 127.70 (C6′), 124.01 (C12), 121.58 (C3′), 121.27 (C5′), 116.51 (C7′), 55.43 (C5), 48.27 (C17), 47.56 (C4), 47.04 (C9), 46.90 (C19), 42.41 (C18), 42.12 (C14), 39.57 (C8), 39.21 (C1), 36.75 (C10), 34.45 (C22), 33.70 (quint, $^1J = 18.0$ Hz, (C2)), 33.24 (C21), 33.10 (C30), 32.10 (C7), 30.95 (C20), 27.72 (C15), 26.49 (C23), 26.01 (C27), 23.83 (C29), 23.75 (C11), 23.65 (t, $^1J = 17.1$ Hz, (C16)), 21.47 (C24), 19.60 (C6), 16.36 (C26), 15.17 (C25).

*(16S)-2,2,16-Trideutero-3-oxo-17-quinolin-8-ylcarbamoyl-28-norurs-12 (13),21(22)diene (**2d′**).* Yield 4 mg, 20%. HRMS (ESI): m/z calc. for $[C_{39}H_{47}D_3N_2O_2 + H]^+$ 582.4133; found 582.4135. ^{1}H NMR (500 MHz, $CDCl_3$) δ 9.40 (d, $^3J = 5.3$ Hz, 1H, H−C(2′)), 8.90 (d, $^3J = 7.9$ Hz, 1H, H−C(7′)), 8.34 (d, $^3J = 8.2$ Hz, 1H, H−C(4′)), 7.54−7.48 (m, 2H, H−C(3′), H−C(6′)), 7.39 (d, $^3J = 7.9$ Hz, 1H, H−C(5′)), 6.36 (dd, $^3J = 8.0$, 2.2 Hz, 1H, H−C (21)), 5.92 (dd, $^3J = 8.0$ Hz, $^4J = 1.9$ Hz, 1H, H−C (22)), 5.36 (t, $^3J = 4.0$ Hz, 1H, H−C

(12)), 2.87 (dd, ^2J = 13.7 Hz, ^3J = 10.5 Hz, 1H, H_a-C (15)), 2.40 (dddd, ^3J = 8.3, 7.1, 2.2 Hz, ^4J = 1.9 Hz, 1H, H−C (20)), 2.28 (d, ^3J = 11.4 Hz, 1H, H−C (18)), 2.09−2.02 (m, 1H, H_a-C (11)), 1.96−1.88 (m, 2H, H_b-C (11), H_a-C (1)), 1.77 (dd, ^3J = 10.5, 4.3 Hz, 1H, H−C (16)), 1.57−1.41 (m, 7H, H_2−C (6), H_2−C (7), H_b-C (1), H−C (19), H−C (9)), 1.38−1.34 (m, 1H, H−C (5)), 1.34 (d, ^3J = 7.1 Hz, 3H, H_3−C (30)), 1.16 (s, 3H, H_3−C (26)),1.11 −1.08 (m, 1H, H_b-C (15), 1.11 (s, 3H, H_3−C (23)), 1.10 (s, 3H, H_3−C (27)), 1.09 (s, 3H, H_3−C (25)), 1.07 (s, 3H, H_3−C (24)), 0.90 (d, ^3J = 6.5 Hz, 3H, H_3−C (29)). ^{13}C NMR (126 MHz, $CDCl_3$) δ 219.33 (C3), 187.68 (C28), 148.41 (C2′), 148.08, (C8a′), 147.23 (C8), 140.01 (C4′), 136.98 (C13), 130.48 (C4a′), 129.95 (C6′), 127.22 (C12), 123.23 (C7′), 121.03 (C3′), 120.25 (C5′), 115.25 (C21), 104.92 (C22), 56.45 (C18), 55.60 (C5), 50.69 (C17), 47.55 (C4), 47.17 (C9), 42.26 (C14), 40.47 (C20), 40.15 (C8), 39.82 (C19), 39.56 (C1), 36.87 (C10), 33.63 (quint, ^1J = 18.0 Hz, (C2)), 33.16 (C7), 30.37 (t, ^1J = 15.6 Hz, (C16)), 26.85 (C23), 25.61 (C15), 23.94 (C11), 23.80 (C27), 21.60 (C24), 19.94 (C30), 19.78 (C6), 17.62 (C26), 17.05 (C25), 15.87 (C29).

*(16S,22R)-16,22-Dideutero-3β-hydroxy-28-picolinamido-lup-20(29)ene (**19**).* Yield 6 mg, 30%. HRMS (ESI): *m/z* calc. for $[C_{36}H_{54}D_2N_2O_2 + H]^+$ 549.4384; found 549.4364. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.54 (d, ^3J = 4.8 Hz, 1H, H−C(6′), 8.21 (d, ^3J = 7.8 Hz, 1H, H−C(3′)), 8.03 (t, ^3J = 6.5 Hz, 1H, H−N), 7.84 (td, ^3J = 7.8 Hz, ^4J = 1.7 Hz, 1H, H−C(4′), 7.41 (dd, ^3J = 7.8, 4.8 Hz, 1H, H−C(5′)), 4.72 (d, ^4J = 2.3 Hz, 1H, H_a-C (29)), 4.60 (s, 1H, H_b-C (29)), 3.71 (dd, ^2J = 13.8 Hz, ^3J = 6.5 Hz, 1H, H_a-C (28)), 3.24 (dd, ^2J = 13.8 Hz, ^3J = 6.5 Hz, 1H, H_b-C (28)), 3.18 (dd, ^3J = 11.3, 4.8 Hz, 1H, H−C (3)), 2.55 (td, ^3J = 11.2, 5.6 Hz, 1H, H−C (19)), 2.12 (dt, ^2J = 13.0 Hz, 11.3 Hz, 1H, H_a-C (21)), 1.90 (dd, ^2J = 13.7 Hz, ^3J = 13.5 Hz, 1H, H_a-C (15)), 1.83 (td, ^3J = 12.0, 3.4 Hz, 1H, H−C (13)), 1.70 (s, 3H, H_3−C (30)), 1.69−1.47 (m, 5H, H_a-C (16), H_a-C (12), H_2−C (2), H_a-C (1)), 1.47−1.36 (m, 6H, H_b-C (6), H_a-C (11), H_b-C (21), H_2−C (7), H−C (18)), 1.34−1.22 (m, 3H, H_b-C (11), H−C (16), H−C (9)), 1.14−1.03 (m, 6H, H_3−C (26), H_b-C (12), H_b-C (15), H−C (22)), 0.99 (s, 3H, H_3−C (27)), 0.97 (s, 3H, H_3−C (23)), 0.93−0.86 (m, 1H, H_b-C (1)), 0.84 (s, 3H, H_3−C (25)), 0.76 (s, 3H, H_3−C (25)), 0.72−0.66 (m, 1H, H−C (5)). ^{13}C NMR (126 MHz, $CDCl_3$) δ 164.71 (N−C═O), 150.43 (C20), 150.17 (C2′), 148.14 (C6′), 137.51 (C4′), 126.17 (C5′), 122.37 (C3′), 109.92 (C29), 79.13 (C3), 55.47 (C5), 50.56 (C9), 49.17 (C18), 47.57 (C19), 47.18 (C17), 42.88 (C14), 41.08 (C8), 39.01 (C4), 38.86 (C1), 37.48 (C13), 37.43 (C28), 37.31 (C10), 35.91 (t, ^1J = 14.3 Hz, C22), 34.30 (C7), 30.20 (t, ^1J = 18.4 Hz, C16), 29.88 (C21), 28.13 (C23), 27.56 (C2), 27.32 (C15), 25.37 (C12), 20.98 (C11), 19.46 (C30), 18.43 (C6), 16.24 (C25), 16.20 (C26), 15.51 (C24), 14.96 (C27).

*(16S,22R)-12,16,22-Trideutero-3β-28-picolinamido-olean-12(13)-ene (**20**).* Yield 7 mg, 35%. HRMS (ESI): *m/z* calc. for $[C_{36}H_{53}D_3N_2O_2 + H]^+$ 550.4446; found 550.4422. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.54 (d, ^3J = 4.8 Hz, 1H, H−C(6′), 8.20 (d, ^3J = 7.8 Hz, 1H, H−C(3′)), 8.10 (dd, ^3J = 7.5, 5.6 Hz, 1H, H−N), 7.83 (td, ^3J = 7.8 Hz, ^4J = 1.7 Hz, 1H, H−C(4′), 7.41 (dd, ^3J = 7.8, 4.8 Hz, 1H, H−C(5′)), 3.74 (dd, ^2J = 13.7 Hz, ^3J = 7.5 Hz, 1H, H_a-C (28)), 3.22 (dd, ^3J = 10.9, 4.8 Hz, 1H, H−C (3)), 2.97 (dd, ^2J = 13.7 Hz, ^3J = 5.6 Hz, 1H, H_b-C (28)), 2.08 (dd, ^3J = 13.5, 4.5 Hz, 1H, H−C (18)), 2.00−1.83 (m, 4H, H_2−C (11), H−C (16), H_a-C (15)), 1.75 (dd, ^2J = 13.6 Hz, ^3J = 13.5 Hz, 1H, H_a-C (19)), 1.68−1.47 (m, 7H, H_a-C (6), H_2−C (2), H_a-C (7), H−C (22), H_a-C (1), H−C (9)), 1.46−1.36 (m, 2H, H_b-C (6), H_b-C (7)), 1.32−1.25 (m, 1H, H_a-C (21)), 1.22−1.18 (m, 1H, H_b-C (21)), 1.18 (s, 3H, H_3−C (27)), 1.14−1.09 (m, 1H, H_b-C (19)), 1.09 (s, 3H, H_3−C (26)), 1.04 −1.00 (m, 1H, H_b-C (15)), 0.99 (s, 3H, H_3−C (23)), 0.99−0.96 (m, 1H, H_a-C (1)), (s, 3H, H_3−C (25)), 0.89 (s, 3H, H_3−C (30)), 0.88 (s, 3H, H_3−C (29)), 0.79 (s, 3H, H_3−C (24)), 0.77−0.72 (m, 1H, H−C (5)). ^{13}C NMR (126 MHz, $CDCl_3$) δ 164.39 (C = O), 150.29 (C2′), 148.13 (C6′), 143.97 (C13), 137.46 (C4′), 126.09 (C5′), 122.81 (t, ^1J = 23.3 Hz, C12), 122.39 (C3′), 79.17 (C3), 55.35 (C5), 47.80 (C9), 47.41 (C28), 46.70 (C19), 44.67 (C18), 41.88 (C14), 40.04 (C8), 38.93 (C4), 38.78 (C1), 37.09 (C10), 36.83 (C17), 34.15 (C21), 33.34, (C30), 32.60 (C7), 31.69 (t, ^1J = 16.6 Hz, C22), 31.08 (C20), 28.24 (C13), 27.39 (C2), 26.24 (C27), 25.99 (C15), 23.77 (C11), 23.70 (C29), 22.14 (t, ^1J = 18.0 Hz, C16), 18.47 (C6), 16.86 (C26), 15.73 (C24), 15.67 (C25).

ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge at https://pubs.acs.org/doi/10.1021/acsomega.5c01632.

Single crystal X-ray analysis data for compounds **3c** (CIF)

Single crystal X-ray analysis data for compounds **6a** (CIF)

Single crystal X-ray analysis data for compounds **6b** (CIF)

Single crystal X-ray analysis data for compounds **18** (CIF)

NMR spectral data for all compounds, description of deuteration experiments on compounds **2a, 2c, 2d** and description of radical trap experiments (PDF)

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Notes

The authors declare no competing financial interest.

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