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### Abstract

An efficient and facile synthetic technique of a new  $\alpha$ , $\beta$ -unsaturated ketones of  $18\alpha$ H, $19\beta$ H-ursane type from betulin and a possibility of their further heterocyclization to C20 pyrazoline derivative are reported. The synthetic scheme involves aldol condensation of 18aH,19BH-urs-20(21)-ene 30-aldehyde with acetone as a key stage.



**Keywords:** Triterpenoids; aldehydes; aldol condensation;  $\alpha$ , $\beta$ -unsaturated ketone, pyrazoline

## Introduction

Pentacyclic triterpenoids are a group of secondary plant metabolites therapeutically promising due to their prevalence in nature, unique skeleton arrangements, and versatile biological activities, along with the absence of toxicity<sup>1-6</sup>. The interest indicated by medicinal chemists in triterpenic carbon scaffolds is caused by attractive opportunities of improving physicochemical, pharmacokinetic, and pharmacodynamic properties of triterpenoids through their simple structural transformations, modifications of functional groups or the introduction of new reaction centers<sup>7-10</sup>. Considering that triterpenic oxo-derivatives are favorable objects for various chemical modifications, including the so-called aldol condensation forming new carbon-carbon bonds<sup>11</sup>, triterpenic  $\alpha$ ,  $\beta$ -unsaturated ketones were synthesized by a simple reaction of some aromatic and heterocyclic aldehydes as carbonyl component with triterpenic 3-ketones as a methylene component<sup>7,12-16</sup>, while lupane 28-aldehyde was used as a carbonyl reactant in condensation with acetophenone<sup>17</sup>. The introduction of  $\alpha$ ,  $\beta$ -unsaturated oxo-fragment into triterpenic structures frequently enables to enhance synthetic<sup>18,19</sup> and biological<sup>20,21</sup> potentials of polycyclic triterpenoids. So, the transformations of the lupane  $\alpha$ ,  $\beta$ -unsaturated 3-ketones in reactions of reduction, oxidation, and cvclopropanation were investigated<sup>15,16</sup>. An additional structural modification of triterpenic skeleton proceeding with the creation of new reaction centers prospective for the realization of aldol condensation is regarded as a promising approach to expansion of the spectrum of triterpenic  $\alpha,\beta$ -unsaturated ketones. For example, saturated alicyclic systems of lupane triterpenoids with a five-membered ring E and trisubstituted double bond in the side chain can selectively be converted to a six-membered ring E with a methyl substituent at the double bond, subsequent oxidation of which leads to  $\alpha,\beta$ -unsaturated aldehyde<sup>22</sup>. The consistent conversion of betulin through allobetulin to heterobetulin is an efficient method for the synthesis of  $I8\alpha H$ ,19 $\beta$ H-ursane derivatives<sup>23,24</sup>. Herein, we describe a convenient synthetic route for the preparation of the  $18\alpha$ H,19 $\beta$ H-ursane  $\alpha$ , $\beta$ -unsaturated methyl ketones using the aldol condensation as a key stage of betulin's transformations. The possibility of further heterocyclization of the synthesized ketones with formation of corresponding C20 pyrazoline derivatives has also been demonstrated.

### **Results and Discussion**

The synthetic route to the  $18\alpha$ H, $19\beta$ H-ursane  $\alpha$ , $\beta$ -unsaturated methyl ketones consists of two stages: (1) synthesis of  $18\alpha$ H, $19\beta$ H-ursane aldehydes (Scheme 1), and (2) aldol condensation of triterpenic aldehyde with acetone (Scheme 2). Allobetulin **2** can be easily obtained by the Wagner–Meerwein rearrangement of betulin **1** under various acidic conditions<sup>7</sup>. The 3,28-dibenzoyl-heterobetulin **3** was prepared from allobetulin **2** by treatment with benzoyl chloride in refluxing toluene<sup>23</sup>.  $\alpha$ , $\beta$ -Unsaturated aldehyde **4** was obtained by oxidation of compound **3** with H<sub>2</sub>SeO<sub>3</sub> in 1,4-dioxane<sup>24</sup>. The NMR spectral data were obtained and compared with those reported<sup>23,24</sup> for the known compounds **3** and **4**. Here we additionally confirmed the structure of aldehyde **4** by X-ray diffraction analysis (Figure 1).



*Reagents and conditions: a*, HCOOH, reflux; b, PhCOCl, toluene, reflux; *c*, H<sub>2</sub>SeO<sub>3</sub>, 1,4-dioxane, reflux; *d*, C<sub>2</sub>H<sub>5</sub>OH, KOH, reflux

**Scheme 1.** Synthesis of  $18\alpha$ H,  $19\beta$ H-ursane aldehydes **4** and **5** from allobetulin.



**Figure 1.** Molecular structure of compound **4** with atoms represented as thermal vibration ellipsoids, with 50% probability.

According to the literature<sup>14</sup>, alkaline hydrolysis of 3,28-diacylderivatives of 30-nitril-, or 30-carboxy-, or 30-carbomethoxy-, or 30-hydroxyheterobetulin leds to the formation of the tetrahydrofuran cycle bonded to ring E via the C17 and C21 carbon atoms. When  $\alpha$ , $\beta$ -unsaturated aldehyde **4** was boiled in an alcoholic solution of KOH, the 21 $\beta$ ,28-epoxy aldehyde **5** was also formed. The presence of 21 $\beta$ ,28-epoxy-moiety in the structure

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of the synthesized compound **5** was confirmed by detecting AB system of two doublets for the H28 protons (3.26 and 4.08 ppm) and doublet for H21 proton (4.48 ppm) in the <sup>1</sup>H NMR spectrum, and signals of C21 and C28 atoms at 73.94 and 65.39 ppm in the <sup>13</sup>C NMR spectrum, respectively. The conversion of betulin **1** to  $18\alpha$ H,19 $\beta$ H-ursane aldehydes **4** and **5** opens up attractive prospects in a wide range of their synthetic applications.



*Reagents and conditions: a*, NaOH, (CH<sub>3</sub>)<sub>2</sub>CO, r.t.; *b*, NaH, (CH<sub>3</sub>)<sub>2</sub>CO, r.t.; *c* CH<sub>3</sub>ONa, (CH<sub>3</sub>)<sub>2</sub>CO, C<sub>6</sub>H<sub>6</sub>, reflux; *d* NH<sub>2</sub>NHCOCH<sub>3</sub>, CH<sub>3</sub>COOH; reflux



Since compound **4** does not contain any proton at the  $\alpha$ -carbon position to the aldehyde group and can be used only as a carbonyl reactant, we had selected acetone as a compound with active methyl group for the condensation reaction. In the condensation process of aldehyde **4** with acetone, the conditions of base catalysis typical of the aldol reaction were tested<sup>25</sup>. The reaction of aldehyde **4** in acetone using NaOH or NaH at room temperature afforded  $\alpha$ , $\beta$ -unsaturated ketone **6** as a single product in reasonable yields of 30% or 57%, respectively (Scheme 2). The attempts to force the aldol condensation of aldehyde **4** using NaOH or KOH during boiling gave rise to hydrolysis of 3,28-dibenzoyl groups with the formation of aldehyde **5**, which under these conditions was inert. We were able to obtain  $\alpha$ , $\beta$ -unsaturated methyl ketone **7** in an extremely low yield (5%) when using MeONa as a base catalyst, while the main product of the reaction was 21 $\beta$ ,28 $\beta$ -epoxy aldehyde **5**. The <sup>1</sup>H NMR spectrum of the triterpenic  $\alpha$ , $\beta$ -unsaturated methyl ketones **6** and **7** showed CH<sub>3</sub>-33 protons of the methyl ketone moieties as singlet signal at 2.24-2.26 ppm, and two characteristic peaks in the downfield area at 5.98-6.04 and 6.72-7.02 ppm which can be assigned to the protons of the double bond C30–C31, the coupling constant of which at 16 Hz indicates their *trans* relative position and, hence, the *E*configuration of the double bond. The signals of the aromatic and the olefinic carbons (125.4-150.5 ppm) and the carbonyl group at 198.7-199.0 ppm were observed in the <sup>13</sup>C NMR spectrum of compounds **6** and **7**.



Figure 2. The key HMBC and NOESY correlations of compound 7.

The structural features of ring E of compound **7** were finally elucidated by the analysis of the HMBC and NOESY data (Figure 2). The location of the oxo-group at C-32 ( $\delta$  199.0 ppm) and the C30–C31 double bond were determined by the HMBC correlations between H30 ( $\delta$  6.72 ppm) and H31 ( $\delta$  5.98 ppm) olefinic protons with oxygenated quaternary carbon atom at 199.04 ppm. A cross-peak C30/H21 ( $\delta$  150.46/4.00 ppm) appeared to be the key HMBC cross-peak confirming the 17 $\beta$ ,21 $\beta$ -orientation of the tetrahydrofuran cycle bonded to ring E. The 2D 1H—1H (NOESY) NMR spectrum showed cross-peaks H20/H30 ( $\delta$  1.83/6.72 ppm), H20/H31 ( $\delta$  1.83/5.98 ppm), H21/H30 ( $\delta$  4.00/6.72 ppm), H21/H31 ( $\delta$  4.00/5.98 ppm), H30/H<sub>3</sub>29 ( $\delta$  6.72/1.00 ppm). The NOESY correlations between H20/H<sub>3</sub>29 ( $\delta$  1.83/1.00 ppm) and H20/H21 ( $\delta$  1.83/4.00 ppm) confirmed the  $\alpha$ -orientation of H20 and H21 protons.

The synthetic suitability of  $\alpha$ , $\beta$ -unsaturated methyl ketone **6** for heterocyclization was shown. To obtain the ursane pyrazoline derivative **8**, compound **6** was refluxed with hydrazine acetate in acetic acid for 4 h. In the <sup>1</sup>H NMR spectrum of the synthesized pyrazoline **8**, the two dd signals at 2.63 and 3.15 ppm were identified as H<sub>2</sub>4' protons, the signal at 4.48 ppm as H5' proton, two singlets that appeared at 2.01 and 2.17 ppm were assigned to the methyl groups, the one at the C3' and the other one – belonging to the *N*-acetyl function. In the <sup>13</sup>C NMR spectrum of compound **8**, the characteristic signals of the pyrazoline ring were registered at 46.38 (C4'), 58.79 (C5'), 155.00 (C3') ppm, and 167.84 ppm (N-COCH<sub>3</sub>). The 2D NMR data of compound **8** showed the product to be a 5'(*S*) isomer (Figure 3).





The key HMBC data for the pyrazolyne cycle were cross-peaks C20/H5′ ( $\delta$  148.82/4.48 ppm), C20/H4′ ( $\delta$  148.82/2.63 ppm and  $\delta$  148.82/3.15 ppm), C3′/H5′ ( $\delta$  155.00/4.48 ppm), C3′/H4′ ( $\delta$  155.00/2.63 ppm and 155.00/3.15 ppm), C3′/H<sub>3</sub>6′ ( $\delta$  155.00/2.01 ppm), and C20/H19 ( $\delta$  148.82/2.25 ppm). The NOESY techniques were then used to determine the relative figuration of C5′. The NOESY correlations between H19/H5′ ( $\delta$  2.25/4.48 ppm) demonstrated the  $\beta$ -orientation of H5′ proton.

# Conclusions

The aldol condensation of  $18\alpha$ H, $19\beta$ H-ursane  $\alpha$ , $\beta$ -unsaturated aldehydes with acetone makes the synthesis of  $\alpha$ , $\beta$ -unsaturated ketones of  $18\alpha$ H, $19\beta$ H-urs-20(21)-ene type based on easily accessible pentacyclic triterpenoid betulin possible. The  $\alpha$ , $\beta$ -unsaturated ketones synthesized were evinced as being able to be a promising platform to produce  $18\alpha$ H, $19\beta$ H-ursane heterocycles, particularly pyrazolines.

# **Experimental Section**

**General.** All the reactions were conducted in air atmosphere. All the commercial reagents and solvents were used as received, without further purification. Column chromatography was performed using Macherey-Nagel 60 Silica (0.063-0.2 mm) as an adsorbent. Sorbfil plates used for thin layer chromatography (TLC) were at first visualized under UV light (254 nm), then treated with 5% solution of H<sub>2</sub>SO<sub>4</sub>. Melting points were determined on an OptiMelt MPA100 device at the heating rate of 1°C/min. IR spectra of the compounds dissolved in CHCl<sub>3</sub> were recorded on a Bruker 66/S IFS Fourier spectrometer. The <sup>1</sup>H, <sup>13</sup>C and 2D NMR spectra of compounds dissolved in CDCl<sub>3</sub> were recorded on a Bruker AVANCE II spectrometer at 400 MHz and 100 MHz, respectively, with chemical shift values expressed in parts per million (ppm), relative to TMS. Optical rotation was measured on a Perkin-Elmer 341 polarimeter using sodium D for CHCl<sub>3</sub> solutions at 589 nm. The initial compound in our experiments, allobetulin **2**, was prepared from betulin **1** by the known procedure<sup>1</sup>. For the known compounds **3**, **4** first described in the 1960s<sup>2,3</sup>, we herein submit updated findings of NMR spectroscopy and X-ray diffraction analysis.

**Dibenzoylheterobetulin (3β,28-dibenzoyloxy-I8αH,19βH-urs-20(21)-ene) (3)**. Allobetulin **2** (4 g, 9.0 mmol) was added to a mixture of dry toluene (1 mL) with benzoyl chloride (4 mL, 3.2 equivalents); the mixture was refluxed for 16 h. The solution was then cooled to rt, H<sub>2</sub>O (20 mL) was added, and the mixture was let stand overnight. The mixture was extracted with chloroform. The extract was subjected to silica gel column chromatography (CC) (eluent: light petroleum–ethyl acetate 25:1) to yield pure dibenzoylheterobetulin **3** as a white crystalline solid. Yield: 50%, mp 229.2 °C, lit.<sup>23</sup> 234-235 °C;  $[\alpha]^{22}_{D}$  +20.0 (*c* 0.5, CHCl<sub>3</sub>), lit.<sup>23</sup>  $[\alpha]_{D}$  +35 (*c* 1.7). IR (solution in CH<sub>3</sub>OH, cm-1): 1717 (OCOPh), 1451 (C=C). <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>):  $\delta_{H}$  7.94-7.99 (4H, m, Ph), 7.45-7.49 (2H, m, Ph), 7.34-7.386 (4H, m, Ph), 5.22 (H, d, *J* 6.8, Hz, 21-H), 4.67 (H, dd, *J* 11.2, 5.1, Hz, 3-H), 4.51 (H, d, *J* 10.8 Hz, 28-H), 4.04 (H, d, *J* 10.8 Hz, 28-H), 1.60 (3H, s, 30-CH<sub>3</sub>), 0.99 (3H, d, *J* 7.8, 29-CH<sub>3</sub>), 0.86, 0.87, 0.94, 0.96, 1.04 (15H, 5s, 5CH<sub>3</sub>). <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>):  $\delta_{C}$  166.18, 165.77, 139.74, 132.20, 132.14, 130.60, 130.28, 129.03 (2C), 129.00 (2C), 127.82 (2C), 127.79 (2C), 117.55, 81.11, 61.89, 55.05, 49.91, 48.35, 41.82, 40.72, 38.26, 38.03, 37.74, 37.31, 36.63, 35.73, 35.12, 33.63, 30.27, 27.63, 27.12, 26.41, 23.28, 22.45, 21.08, 21.00, 17.72, 16.29, 15.84, 15.65, 14.55; Anal. Calcd. for C<sub>44</sub>H<sub>58</sub>O<sub>4</sub>: C, 81.19; H, 8.98. Found: C, 81.89; H, 9.12.

**3β,28-Dibenzoyloxy-I8αH,19βH-urs-20(21)-en-30-al (4).** 7 Mmol of SeO<sub>2</sub> were added to a solution of 4 mmol **3** in 1,4-dioxane (20 mL). The reaction mixture was refluxed for 4 h, then washed with H<sub>2</sub>O (50 mL) and extracted with ethylacetate (50 mL x 2). The organic layer was separated and dried over anhydrous MgSO<sub>4</sub> and then the solvent was evaporated. The residue was subjected to silica gel CC. The elution of the residue with a mixture of light petroleum–ethylacetate (7:1) gave a white solid. Yield: 73%, mp 249.0 °C, lit.<sup>24</sup> 247-251 °C;  $[\alpha]^{22}_{D}$  +24,3 (*c* 0.56, CHCl<sub>3</sub>), lit.<sup>24</sup>  $[\alpha]_{D}$  +24 (*c* 0.9, CHCl<sub>3</sub>). IR (solution in CH<sub>3</sub>OH, cm-1): 1717 (COOPh), 1682 (HC=O). <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>):  $\delta_{H}$  9.40 (H, s, 30-CH), 7.99-8.05 (4H, m, Ph), 7.52-7.58 (2H, m, Ph), 7.41-7.46 (4H, m, Ph), 6.72 (H, dd, *J* 7.0, 1.9 Hz, 21-CH), 4.75 (H, dd, *J* 10.8, 5.0 Hz, 3-CH), 4.58 (H, d, *J* 11.2 Hz, 28-CH), 3.87 (H, d, *J* 11.2 Hz, 28-CH), 1.09 (3H, d, *J* 6.4 Hz, 29-CH<sub>3</sub>), 0.94, 0.95, 1.02, 1.06, 1.11, (15H, 5c, 5CH<sub>3</sub>). <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>):  $\delta_{C}$  192.84, 165.81, 165.77, 147.78, 146.67, 132.46, 132.15, 130.57, 129.82, 129.02 (2C), 128.99 (2C), 127.91 (2C), 127.79 (2C), 81.05, 61.15, 55.06, 49.87, 47.79, 41.77, 40.70, 38.13, 38.03, 37.74 (2C), 36.63, 36.12, 33.60, 30.34, 28.77, 27.63, 26.80, 26.31, 23.27, 23.12, 20.90, 17.70, 16.28, 15.81, 15.59, 14.53; Anal. Calcd. for C<sub>44</sub>H<sub>56</sub>O<sub>5</sub>: C, 79.48; H, 8.49. Found: C, 79.73; H, 8.64.

**21β,28-Epoxy-3-hydroxy-18αH,19βH-urs-20(21)-en-30-al (5).** A solution of **4** (1.3 mmol) in alcoholic KOH (30 mL, 3%) was refluxed for 2 h. The course of the reaction was monitored by TLC. The solvent was evaporated, and the residue was then treated with H<sub>2</sub>O (30 mL). The product was extracted with ethylacetate (30 mL x 2). The organic layer was separated, washed with H<sub>2</sub>O, and dried over anhydrous MgSO<sub>4</sub>. The solvent was evaporated, and the residue was subjected to silica gel CC (eluent: light petroleum–ethylacetate 5:1). Yield: 90%; mp 233.5 °C;  $[\alpha]^{22}_{D}$  +43.6 (*c* 0.52, CHCl<sub>3</sub>). IR (solution in CH<sub>3</sub>OH, cm-1): 3391 (OH), 1705 (HC=O). <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>):  $\delta_{H}$  9.56 (H, s, 30-H), 4.48 (H, d, *J* 6.2 Hz, 21-H), 4.08 (H, d, *J* 8.3 Hz, 28-H), 3.26 (H, d, *J* 8.3 Hz, 28-H), 3.13 (1H, dd, *J* 5.1, 11.2 Hz, 3-H), 0.95 (3H, d, *J* 8.0 Hz, 29-CH<sub>3</sub>), 0.91 (9H, s, 3CH<sub>3</sub>), 0.71, 0.79, 0.80, (9H, 3s, 3CH<sub>3</sub>). <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>):  $\delta_{c}$  202.81, 78.96, 74.02, 73.94, 65.39, 55.40, 50.22, 49.14, 45.27, 44.28, 42.29, 41.81, 41.01, 38.85, 37.14, 34.31, 32.52, 29.50, 27.98 (2C), 27.95, 27.65, 27.43, 25.81, 21.42, 18.29, 16.25, 15.94, 15.33, 14.25; Anal. Calcd. for C<sub>30</sub>H<sub>48</sub>O<sub>3</sub>: C, 78.90; H, 10.59. Found: C, 79.05; H, 10.64.

**3**β,28-Dibenzoyloxy-30-(2-oxopropylidene)-18αH,19βH-urs-20(21)-ene (6). Method A. Solution (0.1 mL) of NaOH (10%) in water was added to a solution of **4** (1.5 mmol) in acetone (4 ml); the reaction mixture was then stirred for 6 h at rt. After addition of 10% HCl, the reaction mixture was extracted with ethylacetate (30 mL x 2). The organic layer was separated, washed with H<sub>2</sub>O, and dried over anhydrous MgSO<sub>4</sub>. The solvent was evaporated, and the residue was subjected to silica gel CC (eluent: light petroleum–ethylacetate 5:1). Yield: 30%; mp 236.8 °C;  $[\alpha]_D^{21}$  +19.6 (*c* 0.5, CHCl<sub>3</sub>). IR (solution in CH<sub>3</sub>OH, cm-1): 1716 (OCOPh), 1667 (C=O), 1591,

1451 (C=C). <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>):  $\delta_{H}$  7.97-8.04 (4H, m, Ph), 7.51-7.56 (2H, m, Ph), 7.40-7.44 (4H, m, Ph), 7.02 (H, d, *J* 16.3 Hz, 30-CH), 6.14 (H, dd, *J* 2.3, 7.4 Hz, 21-CH), 6.04 (H, d, *J* 16.3 Hz, 31-CH), 4.74 (H, dd, *J* 5.0, 10.8 Hz, 3-CH), 4.56 (H, d, *J* 8.2 Hz, 28-CH<sub>2</sub>), 3.88 (H, d, *J* 8.2 Hz, 28-CH<sub>2</sub>), 2.26 (3H, s, 33-CH<sub>3</sub>), 1.09 (3H, d, *J* 7.3 Hz, 29-CH<sub>3</sub>), 0.93, 0.94, 1.01, 1.04, 1.10 (15H, 5s, 5CH<sub>3</sub>). <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>):  $\delta_{C}$  198.73, 166.45, 166.28, 145.31, 142.59, 135.43, 132.90, 132.67, 131.04, 130.39, 129.51 (2C), 129.47 (2C), 128.38 (2C), 128.29 (2C), 125.41, 81.54, 61.89, 55.53, 50.37, 49.00, 42.27, 41.18, 38.64, 38.51, 38.23, 37.94, 37.12, 36.94, 34.06, 31.05, 30.66, 28.12, 27.23, 27.08, 26.81, 24.54, 23.75, 21.44, 18.18, 16.78, 16.32, 16.09, 15.03; Anal. Calcd. for C<sub>47</sub>H<sub>60</sub>O<sub>5</sub>: C, 80.07; H, 8.58. Found: C, 79.84; H, 8.87.

**Method B.** NaH (1.5 mmol) was added to a solution of **4** (1.5 mmol) in acetone (4 mL). The mixture was stirred for 15 min at rt. After addition of 10% HCl, the reaction mixture was extracted with ethylacetate (30 mL x 2). The organic layer was separated, washed with  $H_2O$ , and dried over anhydrous MgSO<sub>4</sub>. The solvent was evaporated, and the residue was subjected to silica gel CC (eluent: light petroleum–ethylacetate 5:1). Yield: 57%.

**21**β,28-Epoxy-3β-hydroxy-30-(2-oxopropylidene)-18αH,19βH,20αH-ursane (7). Acetone (5 mL) was added to a solution of mixture of aldehyde **4** (0.2 mmol) and sodium methoxide (1.0 mmol) in anhydrous benzene (10 mL). The reaction mixture was stirred for 3 h under boiling, and then washed with 10% solution of HCl. The product was extracted with ethylacetate (30 mL x 2). The organic layer was separated, washed with H<sub>2</sub>O, and dried over anhydrous MgSO4. The solvent was evaporated, and the residue was subjected to silica gel CC (eluent: light petroleum–ethylacetate 5:1). Yield: 5%; mp 198.53 °C;  $[\alpha]_D^{21}$  +4.74 (*c* 0.95, CHCl<sub>3</sub>). IR (solution in CH<sub>3</sub>OH, cm-1): 3427 (OH), 1668 (C=O). <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>):  $\delta_{\rm H}$  6.72 (H, dd, *J* 9.0, 16.2 Hz, 30-CH), 5.98 (H, d, *J* 16.2 Hz, 31-CH), 4.17 (H, d, *J* 8.2 Hz, 28-CH<sub>2</sub>), 4.00 (H, dd, *J* 1.2, 5.6 Hz, 21-CH), 3.35 (H, d, *J* 8.2 Hz, 28-CH<sub>2</sub>), 3.18 (H, dd, *J* 5.0, 11.0 Hz, 3-CH), 2.24 (3H, s, 33-CH<sub>3</sub>), 1.00 (3H, d, *J* 5.5 Hz, 29-CH<sub>3</sub>), 0.96 (6H, s, 2CH<sub>3</sub>), 0.75, 0.84, 0.97 (9H, 3s, 3CH<sub>3</sub>). <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>):  $\delta_{\rm C}$  199.04, 150.46, 131.68, 78.96, 77.32, 73.86, 56.93, 55.34, 50.14, 49.46, 45.16, 44.55, 42.33, 41.95, 40.99, 38.86, 38.81, 37.11, 34.31, 33.64, 32.54, 29.52, 27.99, 27.81, 27.41, 26.40, 24.28, 21.46, 18.29, 16.29, 15.97, 15.37, 14.27; Anal. Calcd. for C<sub>33</sub>H<sub>52</sub>O<sub>3</sub>: C, 79.79; H, 10.55. Found: C, 79.99; H, 10.31.

20-(1´-Acetyl-3´-methyl-4´,5´-dihydro-1H-pyrazol-5´(S)-yl)-3β,28-dibenzoyloxy-30-nor-18αH,19βH-urs-

**20(21)-ene (8).** Compound **6** (0.1 mmol) was dissolved in 5 mL of acetic acid, and then hydrazine acetate (0.5 mmol) was added. The mixture was refluxed and monitored by TLC until starting material completely disappeared (4 h). The product was extracted with ethylacetate (20 mL x 2). The organic layer was separated, washed with H<sub>2</sub>O, and dried over anhydrous MgSO<sub>4</sub>. The solvent was evaporated, and the residue was subjected to silica gel CC (eluent: light petroleum–ethylacetate 5:1). Yield: 61%; mp 273.3 °C;  $[\alpha]_{D}^{21}$  +22.6 (c 0.5, CHCl<sub>3</sub>). IR (solution in CH<sub>3</sub>OH, cm-1): 1714 (OCOPh), 1658 (C=N), 1452 (C=C). <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>):  $\delta_{H}$  0.91, 0.93, 1.10 (9H, 3s, 3CH<sub>3</sub>), 0.99 (6H, s, 2CH<sub>3</sub>), 1.01 (3H, d, *J* 6.8 Hz, 29-CH<sub>3</sub>), 2.01 (3H, s, 3'-CH<sub>3</sub>), 2.17 (1'-COCH<sub>3</sub>), 2.63 (1H, dd, *J* 5.3, 18.9 Hz, H-4'), 3.15 (1H, dd, *J* 11.7, 18.9 Hz, H-4'), 4.23 (1H, d, *J* 11.1 Hz, H-28), 4.48 (1H, dd, *J* 5.5, 11.7 Hz, H-5'), 4.64 (1H, d, *J* 11.1 Hz, H-28), 4.72 (1H, dd, *J* 5.4, 10.8 Hz, H-3), 5.44 (H, dd, *J* 1.6, 7.2 Hz, H-21); 7.37-7.43 (4H, m, Ph); 7.48-7.55 (2H, m, Ph), 7.95-8.04 (4H, m, Ph). <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>):  $\delta_{C}$  167.84, 166.30, 166.04, 155.00, 145.82, 132.64, 132.43, 131.07, 129.71, 129.51 (2C), 129.46 (2C), 128.28 (2C), 128.20 (2C), 118.04, 81.65, 61.83, 58.79, 55.55, 50.37, 49.05, 46.38, 42.21, 41.21, 38.56, 38.52, 38.45, 38.22, 37.10, 35.58, 35.14, 34.08, 30.83, 28.12, 27.58, 26.87, 23.77, 23.20, 21.52, 21.41, 18.20, 16.77, 16.31, 16.10, 15.97, 14.92; Anal. Calcd. for C<sub>49</sub>H<sub>64</sub>N<sub>2</sub>O<sub>5</sub>: C, 77.33; H, 8.48; N, 3.68. Found: C, 77.61; H, 8.82; N, 3.44.

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#### **Supplementary Material**

X-ray studies and crystal structure determination. <sup>1</sup>H, <sup>13</sup>C NMR and 2D spectra.

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