Synthesis of quinoxalines fused with triterpenes, ursolic acid and betulin derivatives

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Oxidation of triterpenoids methyl ursonate, acetylbetulone, and allobetulone with atmospheric oxygen in the presence of Bu^{t}OK in Bu^{t}OH afforded the corresponding 2,3-diketo derivatives in 90—97% yields. These derivatives exist predominantly as tautomers containing the enolized keto group at the C(2) atom. Their reactions with *o*-phenylenediamine gave rise to the corresponding quinoxalines in 85—95% yields.

Key words: triterpenoids, ursolic acid, betulin, allobetulin, quinoxaline, pyrazine, ^{1}H and ^{13}C NMR spectroscopy, oxidation, molecular oxygen, α-diketones, *o*-phenylenediamine.

Many natural and synthetic biologically active molecules contain the pyrazine ring. In particular, steroid pyrazines, which have recently been isolated from the marine worm *Cephalodiscus gilchristi*, exhibit high antitumor activity.[1,2] Benzopyrazine (quinoxaline) derivatives based on steroids and structurally related isoprenoids were synthesized and their biological activities were examined in a number of studies.[1,3,4,5] In the present work, we developed an improved procedure for the preparation of 2,3-diketo derivatives of triterpenes and for the introduction of the fused quinoxaline (benzopyrazine) fragment into ursolic acid (**1**) and betulin (**2**), which belong to the most readily accessible natural triterpenoids.

Chemical conversions of the ring A of triterpenes of the α-amyrin and lupeol series have been extensively studied over many years. Procedures for the preparation of a large number of oxygen-containing derivatives have been well studied.[6—8] 3-Keto derivatives of ursolic acid and betulin (**3—5**) are the most suitable starting compounds for the introduction of the quinoxaline fragment.

Various steroid ketones can be converted into quinoxaline derivatives through the corresponding α-bromoketones.[9] However, we found that bromination[10] of compounds **3—5** (giving rise to 2-bromo derivatives) followed by treatment with *o*-phenylenediamine afforded only resinous products. It is known that 3-ketosteroids are oxidized with atmospheric oxygen in the presence of strong bases.[11] A procedure for the preparation of 2,3-diketotriterpenes, which has been described in detail, consists in passing oxygen through a warm (40 °C) solution of 3-ketone and Bu^{t}OK in Bu^{t}OH for 20—30 min giving rise to a mixture of diketone and a substantial amount of by-products. The formation of the latter is primarily associated with further oxidation of the diketone to the corresponding 2,3-*seco* derivative[7] accompanied by the rearrangement of 2,3-diketones to yield α-hydroxycarboxylic acids under the action of bases.[12] We found that oxidation of 3-keto derivatives at room temperature and the use of atmospheric oxygen instead of pure oxygen afforded 2,3-diketones **6—8** in virtually quantitative yields (90—97%). Oxidation of compound **4** was accompanied by hydrolysis of the ester group to form compound **7**.

The formation of 2,3-diketo derivatives **6—8** was confirmed by spectroscopic data, which also indicated that the enol tautomeric form predominated in chloroform solutions of these compounds at ~20 °C. Thus the NMR spectra of compounds **6—8** have signals characteristic of the enol form of α-diketone: $\delta_{H(1)}$ 6.3—6.4, δ_{OH} 5.9—6.0, $\delta_{C(1)}$ 128.2—129.0, $\delta_{C(2)}$ 143.5—143.8.

The conventional procedure for the synthesis of quinoxalines is based on the reactions of *o*-diaminoarenes with α-diketones.[13] However, triterpenic 2,3-diketones **6—8** appeared to be unstable on heating in alcoholic solutions and decomposed more rapidly than reacted with *o*-diaminoarenes to give pyrazine derivatives. Condensation of diketones **6—8** with *o*-phenylenediamine in the EtOH—PhH mixture in the presence of AcOH afforded quinoxaline derivatives **9—11**, respectively, in high yields (in the absence of the acid, resinification occurred). The structures of compounds **9—11** casted no doubts and were readily confirmed by the spectral data. It should be noted that we failed to make unambiguous assignment of the signals for the H and C atoms of the benzene ring of the quinoxaline fragment in the NMR spectra of these compounds. However, the chemical shifts of these atoms are observed in the range typical of

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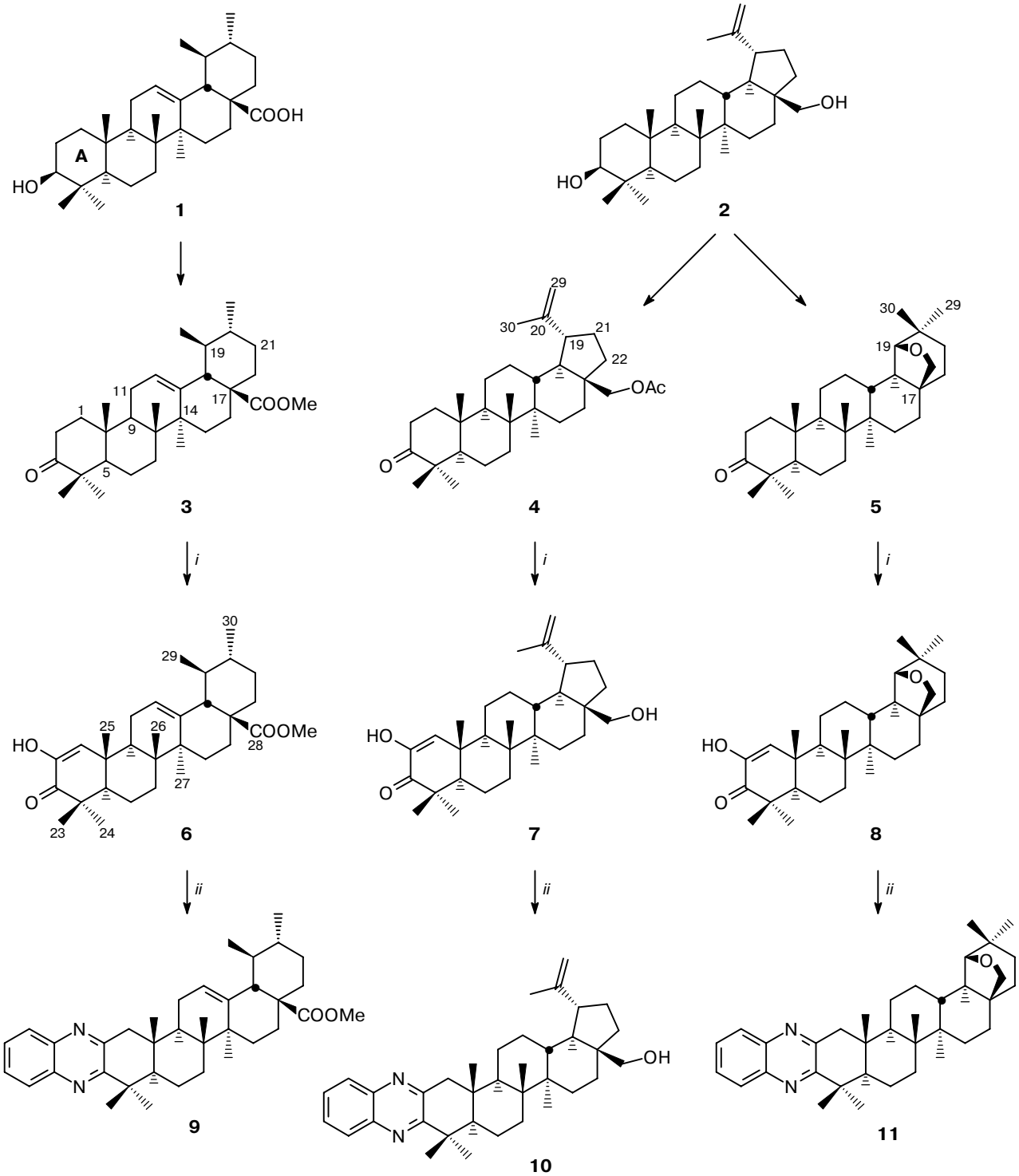
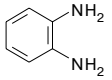
Scheme 1



Reagents and conditions: *i*. O_2 (air)—Bu^{t}OK—Bu^{t}OH, 2—3 h, ~20 °C, the yield was 90—97%;

ii.  EtOH—C_6H_6—AcOH, 5—6 h, reflux, the yield was 85—95%.

compounds of the quinoxaline series and the presence of the quinoxaline core is confirmed by the UV spectral data.

To summarize, we developed a simple and efficient procedure for the preparation of 2,3-diketones **6—8**, which makes this type of triterpenic compounds readily accessible and opens up possibilities for the synthesis of a wide range of polycyclic molecules in which the ring A of triterpenoids is fused to different heterocyclic fragments.

Table 1. ^{1}H and ^{13}C NMR spectral data for compounds **3**, **6**, and **9**

Atom No.	**3**[a]		**6**[b]		**9**[c]	
	$\delta_C{}^i$	$\delta_H{}^i$ (J/Hz)	$\delta_C{}^i$	$\delta_H{}^i$ (J/Hz)	$\delta_C{}^i$	$\delta_H{}^i$ (J/Hz)
1	39.16	[1.40] 1.86 (ddd, J = 13.2, 7.3, 3.7)	128.17	6.32 (s, 2 H)	49.46	2.65 and 3.24 (AB system J_{AB} = 16.5)
2	34.01	2.33 (ddd, J = 15.8, 7.0, 3.7) 2.50 (ddd, J = 15.8, 11.0, 7.3)	143.52	—	151.83	—
3	217.43	—	200.89	—	160.79	—
4	47.23	—	43.70	—	40.13	—
5	55.16	[1.26]	53.68	[1.56]	53.39	[1.54]
6	19.46	[1.43] (2 H)	18.51	[1.48] (2 H)	20.16	[1.55, 1.68]
7	32.36	[1.33, 1.48]	32.63	[1.37]	32.19	[1.44, 1.60]
8	39.34	—	39.98	—	39.24	—
9	46.65	[1.55]	42.78	[1.79]	45.25	[1.76]
10	36.54	—	38.11	—	36.63	—
11	23.31	[1.90, 1.94]	23.12	[2.02, 2.10]	23.18	[2.07, 2.15]
12	125.20	5.23 (dd, J = 3.6, 3.6)	124.73	5.26 (dd, J = 3.7, 3.7)	125.30	5.33 (dd, J = 3.7, 3.7)
13	138.16	—	138.48	—	138.01	—
14	41.99	—	42.23	—	42.01	—
15	27.89	[1.05, 1.74]	27.76	[1.04, 1.73]	27.82	[1.12, 1.81]
16	24.07	[1.64, 1.97]	23.96	[1.65, 1.97]	24.07	[1.69, 1.99]
17	47.98	—	47.95	—	47.96	—
18	52.83	2.21 (dd, J = 11.4, 1.3)	52.79	2.22 (d, J = 11.2)	52.84	2.27 (d, J = 11.1)
19	38.92	[1.30]	38.76	[1.30]	38.94	[1.34]
20	38.72	[0.96]	38.66	[0.97]	38.69	[0.98]
21	30.50	[1.26, 1.45]	30.44	[1.26, 1.45]	30.48	[1.28, 1.47]
22	36.45	[1.55, 1.63]	36.37	[1.55, 1.63]	36.41	[1.58, 1.61]
23	26.43	1.04 (s)	27.05	1.17 (s)	32.15	1.42 (s)
24	21.33	1.00 (s)	21.65	1.07 (s)	25.15	1.40 (s)
25	15.04	1.01 (s)	19.53	1.19 (s)	15.55	0.90 (s)
26	16.73	0.76 (s)	17.27	0.78 (s)	16.52	0.83 (s)
27	23.37	1.04 (s)	23.34	1.04 (s)	23.35	1.12 (s)
28	177.80	—	177.81	—	177.74	—
29	16.87	0.82 (d, J = 6.2)	16.82	0.81 (d, J = 6.5)	16.89	0.88 (d, J = 6.3)
30	20.99	0.90 (d, J = 6.1)	20.98	0.90 (d, J = 6.2)	20.98	0.93 (d, J = 5.9)
					Signals of the quinoxaline fragment	
					127.95 (d)[d]	7.90—7.95 (m), 7.95—8.00 (m)
					128.25 (d)[d]	7.57—7.62 (m)
					128.54 (d)[d]	7.57—7.62 (m)
					128.63 (d)[d]	7.90—7.95 (m), 7.95—8.00 (m)
					140.70 (s)[d]	
					141.94 (s)[d]	

Notes. The chemical shifts of the hydrogen atoms given in brackets were taken from the two-dimensional $^{13}C—^{1}H$ correlation spectra at the direct spin-spin coupling constants ($^{1}J_{CH}$ = 135 Hz) and are given relative to Me_4Si.

[a] C = 110 mg mL^{-1}; the methoxy group: δ_C 51.27, δ_H 3.57.

[b] C = 110 mg mL^{-1}; the OH group: δ_H 5.9 ($W_{1/2}$ = 95 Hz); the methoxy group: δ_C 51.27, δ_H 3.57.

[b] C = 110 mg mL^{-1}; the OH group: δ_H 5: δ_C 51.33, δ_H 3.57.

[c] C = 250 mg mL^{-1}; the methoxy group: δ_C 51.27, δ_H 3.57.

[b] C = 110 mg mL^{-1}; the OH group: δ_H 5: δ_C 51.23, δ_H 3.60.

[d] The multiplicities of the signals in the spectra using off-resonance irradiation of protons.

Experimental

All solvents, *viz.*, *tert*-butyl methyl ether, acetone, ethyl acetate, benzene, and ethanol, were freshly distilled prior to use. TLC was carried out on Silufol plates with a Silpearl silica gel layer fixed on an aluminum foil. The components were visualized by spraying the plates with concentrated H_2SO_4 followed by heating to 100—150 °C. Column chromatography was performed on KSK silica gel (Russia; 0.10—0.20 mm), which was dried in air and activated by heating at 140 °C for 5 h. The IR spectra were measured on a Specord M-80 spectrophotometer for solutions in $CHCl_3$ (*c* 1%) or in KBr pellets (*c* 0.25%). The UV spectra were recorded on a Specord UV-VIS

Table 2. ^1H and ^{13}C NMR spectral data for compounds **4**, **7**, and **10**

Atom No.	**4**[a]		**7**[b]		**10**[c]	
	$\delta_C{}^i$	$\delta_H{}^i$ (*J*/Hz)	$\delta_C{}^i$	$\delta_H{}^i$ (*J*/Hz)	$\delta_C{}^i$	$\delta_H{}^i$ (*J*/Hz)
1	39.51	[1.35, 1.86]	128.65	6.40 (s)	49.68	2.57 and 3.27 (AB system, J_{AB} = 16.4)
2	33.99	[2.37, 2.45]	143.82	—	152.10	—
3	217.57	—	201.04	—	160.87	—
4	47.19	—	43.86	—	40.30	—
5	54.92	[1.28]	53.87	[1.56]	53.42	[1.56]
6	19.52	[1.45]	18.60	[1.48, 1.51]	20.23	[1.65, 1.69]
7	33.43	[1.41]	33.77	[1.43, 1.45]	33.17	[1.55]
8	40.76	—	41.64	—	40.71	—
9	49.67	[1.35]	45.51	[1.58]	48.37	[1.59]
10	36.77	—	38.48	—	36.93	—
11	21.22	[1.30, 1.41]	20.96	[1.31, 1.58]	21.33	[1.64, 1.67]
12	25.16	[1.04, 1.64]	24.97	[1.06, 1.59]	25.14	[1.68, 1.76]
13	37.62	[1.68]	37.28	[1.67]	37.36	[1.72]
14	42.67	—	42.91	—	42.71	—
15	26.99	[1.04, 1.67]	26.85	[1.04, 1.68]	26.99	[1.13, 1.75]
16	29.65	[1.23, 1.83]	29.01	[1.19, 1.94]	29.06	[1.21, 1.98]
17	46.23	—	47.65	—	47.72	—
18	48.68	[1.59]	48.53	[1.56]	48.60	[1.65]
19	47.56	[2.42]	47.62	2.37 (ddd, *J* = 11.0, 11.0, 5.9)	47.65	2.39 (ddd, *J* = 10.8, 10.8, 5.8)
20	149.91	—	150.05	—	150.11	—
21	29.53	[1.38, 1.95]	29.61	[1.40, 1.95]	29.74	[1.98, 1.43]
22	34.43	[1.06, 1.76]	33.82	[1.01, 1.85]	33.87	[1.06, 1.89]
23	26.48	1.04 (s)	26.96	1.18 (s)	32.02	1.41 (s)
24	20.91	1.00 (s)	21.45	1.08 (s)	25.01	1.40 (s)
25	15.75	0.91 (s)	19.99	1.10 (s)	16.06	0.82 (s)
26	15.74	1.05 (s)	16.33	1.07 (s)	15.48	1.10 (s)
27	14.58	0.96 (s)	14.53	0.96 (s)	14.64	1.04 (s)
28	62.63	3.84 and 4.24 (AB system, J_{AB} = 11.0)	60.40	3.33 and 3.77 (AB system, J_{AB} = 10.8)	60.33	3.80 and 3.35 (AB system, J_{AB} = 11.0)
29	109.76	4.57 (s) 4.67 (s)	109.74	4.59 (dq, *J* = 2.3, 1.4) 4.68 (d, *J* = 2.3)	109.68	4.61 (s) 4.70 (s)
30	19.02	1.66 (s)	18.93	1.67 (s)	19.05	1.70 (s)
					Signals of the quinoxaline fragment	
					127.97 (d)[d]	7.90—7.95 (m), 7.96—8.00 (m)
					128.33 (d)[d]	7.59—7.63 (m)
					128.60 (d)[d]	7.59—7.63 (m)
					128.69 (d)[d]	7.90—7.95 (m), 7.96—8.00 (m)
					140.80 (s)[d]	
					142.02 (s)[d]	

Notes. The chemical shifts of the hydrogen atoms given in brackets were taken from the two-dimensional $^{13}C—^1H$ correlation spectra at the direct spin-spin coupling constants ($^1J_{CH}$ = 135 Hz) and are given relative to Me_4Si.

[a] *C* = 80 mg mL; the acetate group: δ_C 20.83 and 171.33, δ_H 2.04.

[b] *C* = 90 mg mL; the OH group: δ_H 5.90 br.s.

[c] *C* = 85 mg mL.

[d] The multiplicities of the signals in the spectra using off-resonance irradiation of protons.

spectrophotometer in 95% EtOH. The optical rotations were measured on a Polamat A polarimeter for solutions in $CHCl_3$, c = 4—11. The melting points were determined on a Kofler stage. Microanalyses were carried out on Hewlett Packard 185 and Carlo Erba 1106 analyzers. The mass spectra were obtained on a Finnigan MAT-8200 mass spectrometer (EI, 70 eV). The NMR spectra were recorded (in $CDCl_3$) on a Bruker AM-400 spectrometer (400.13 MHz for ^1H and 100.61 MHz for ^{13}C)

Table 3. ^1H and ^{13}C NMR spectral data for compounds **5**, **8**, and **11**

Atom No.	**5**[a]		**8**[b]		**11**[c]	
	$\delta_C{}^i$	$\delta_H{}^i$ (J/Hz)	$\delta_C{}^i$	$\delta_H{}^i$ (J/Hz)	$\delta_C{}^i$	$\delta_H{}^i$ (J/Hz)
1	39.67	[1.39] 1.90 (ddd, J = 12.7; 7.4; 4.9)	129.01	6.44 (s)	49.85	2.60 and 3.31 (AB system, J_{AB} = 16.4)
2	33.93	αH: 2.39 (ddd, J = 15.6; 7.8; 4.5) βH: 2.46 (ddd, J = 16.0; 9.4; 7.6)	143.83	—	151.99	—
3	217.89	—	201.14	—	160.80	—
4	47.14	—	43.89	—	40.22	—
5	54.85	[1.32]	54.05	[?]	53.47	[1.54]
6	19.47	[1.44]	18.54	[1.50] 2H	20.07	[1.58, 1.66]
7	33.03	[1.37, 1.44]	33.39	[1.41, 1.50]	32.78	[1.47, 1.54]
8	40.61	—	41.31	—	40.29	—
9	50.26	[1.39]	46.06	[1.63]	48.95	[1.59]
10	36.81	—	38.55	—	36.91	—
11	21.37	[1.32, 1.46]	21.09	[1.37, 1.67]	21.36	[1.35, 1.72]
12	26.08	[1.30, 1.44]	26.06	[1.30, 1.38]	26.05	[1.30, 1.42]
13	34.12	[1.45]	34.11	[1.49]	34.12	[1.50]
14	40.39	—	40.87	—	40.61	—
15	26.28	[0.90, 1.09,	26.15	[1.10, 1.55]	26.24	[1.14 1.57]
16	26.28	1.52, 1.64]	26.06	[0.94, 1.71]	26.28	[1.68, 1.76]
17	41.31	—	41.31	—	41.29	—
18	46.64	[1.44]	46.56	[1.46]	46.57	[1.49]
19	87.75	3.52 (s)	87.80	3.51 (s)	87.70	3.54 (s)
20	36.12	—	36.09	—	36.09	—
21	32.55	[1.18, 1.47]	32.52	[1.20, 1.49]	32.53	[1.19, 1.48]
22	36.58	[1.26, 1.38]	36.53	[1.27, 1.39]	36.55	[1.27, 1.39]
23	26.60	1.04 (s)	26.96	1.17 (s)	31.98	1.40 (s)
24	20.84	0.99 (s)	21.42	1.07 (s)	24.91	1.38 (s)
25	16.17	0.91 (s)	20.38	1.11 (s)	16.33	0.82 (s)
26	15.37	0.97 (s)	16.03	1.00 (s)	15.20	1.03 (s)
27	13.29	0.88 (s)	13.17	0.89 (s)	13.33	0.94 (s)
28	71.10	3.44 and 3.77 (AB system, J_{AB} = 7.8)	71.07	3.42 and 3.74 (AB system, J_{AB} = 7.7)	71.06	3.42 and 3.76 (AB system, J_{AB} = 7.7)
29	24.40	0.76 (s)	24.38	0.77 (s)	24.39	0.79 (s)
30	28.65	0.89 (s)	28.62	0.90 (s)	28.63	0.91 (s)
					Signals of the quinoxaline fragment	
					127.92 (d)[d]	7.89—7.93 (m), 7.95—7.99 (m)
					128.29 (d)[d]	7.58—7.62 (m)
					128.57 (d)[d]	7.58—7.62 (m)
					128.64 (d)[d]	7.89—7.93 (m), 7.95—7.99 (m)
					140.72 (s)[d]	
					141.96 (s)[d]	

Notes. The chemical shifts of the hydrogen atoms given in brackets were taken from the two-dimensional $^{13}C—^1H$ correlation spectra at the direct spin-spin coupling constants ($^1J_{CH}$ = 135 Hz) and are given relative to Me_4Si; the signal for the H(5) atom is not observed in the two-dimensional spectrum due to the low intensity of the corresponding cross-peak.

[a] C = 77 mg mL.

[b] C = 50 mg mL; the OH group: δ_H 5.97 br.s.

[c] C = 150 mg mL.

[d] The multiplicities of the signals in the spectra using off-resonance irradiation of protons.

at 25—28 °C with the solvent signal δ_C = 76.90 and residual signal for the proton in $CHCl_3$ δ_H = 7.24 as the internal standards. The assignment of the signals was made using the ^{13}C NMR spectra, which were recorded with *J* modulation (proton-noise-decoupled spectra, the opposite phases for the signals of the atoms with the odd and even numbers of the attached protons, tuning to the constant *J* = 135 Hz), and based on the two-dimensional spectra, *viz.*, 1) homonuclear $^1H—^1H$ correlation, 2) heteronuclear $^{13}C—^1H$ correlation at the direct spin-spin coupling constants (*J* = 135 Hz), and 3) heteronuclear $^{13}C—^1H$ correlation at the long-range spin-spin coupling constants (*J* = 10 Hz) using the data published previously for natural and synthetic derivatives of the ursane, oleanane, and betulin series.[14] The NMR spectra are given in Tables 1—3.

The starting compounds were prepared as follows.

Ursolic acid (**1**) was isolated from an extract of fruits of sea buckthorn *Hippophae rhamnoides* L. (Elaeagnaceae) according to a procedure reported previously[15] and purified by crystallization from 95% aqueous EtOH to obtain the product with m.p. 276—279 °C (according to the ^1H NMR spectral data, a solvate with one EtOH molecule) and $[\alpha]^{22}$ +59.8 (*c* 2.24, Py) (lit. data:[16] m.p. 278—280 °C (MeOH) and $[\alpha]_D$+76.8 (*c* 0.6)).

Ursolic acid was methylated to obtain methyl ursolate with m.p. 171—173 °C (CH_3CN) and $[\alpha]^{19}$ +47.7 (*c* 8.25, $CHCl_3$) (lit. data:[17] m.p. 172—173 °C).

Methyl ursolate was further oxidized with the Johnson reagent in acetic acid at room temperature to produce methyl ursonate **3** with m.p. 191—193 °C (EtOH) and $[\alpha]^{24}$ +87.8 (*c* 0.5, $CHCl_3$) (lit. data:[18] m.p. 192—193 °C).

Betulin (**2**) was isolated from an extract of birch bark and purified according to a procedure reported previously.[19] The monoacetyl derivative of betulin was prepared by the reaction with an equimolar amount of Ac_2O in pyridine at the temperature from —12 to 17 °C[7] and the resulting product was oxidized with the Johnson reagent to form 3-keto derivative **4** with m.p. 117—119 °C and $[\alpha]^{22}$ +38.0 (*c* 1.35, $CHCl_3$) (lit. data:[7] $[\alpha]_D$ +36.5, m.p. 114—118 °C).

The acid-catalyzed rearrangement of betulin (**2**) afforded allobetulin with m.p. 262—264 °C and $[\alpha]^{22}$ +48 (*c* 0.2, $CHCl_3$) (lit. data:[8] m.p. 260—261 °C, $[\alpha]_D^{15}$ +48.25),[8] which was then oxidized with the Johnson reagent to yield 3-keto derivative (allobetulone) **5** with m.p. 229—231 °C and $[\alpha]^{22}$ +86 (*c* 1.0, $CHCl_3$) (lit. data:[8] $[\alpha]_D$ +84.40, m.p. 230—231 °C).

Synthesis of diketones 6—8. A solution of 3-keto derivative **3—5** (0.20—0.45 mmol) and Bu^tOK (0.56 g, 5.0 mmol, Aldrich) in Bu^tOH (5 mL) was vigorously stirred at 22—27 °C for 2.5—3 h with the provision of efficient access of air to the reaction mixture. Then the reaction mixture was diluted with $MeOBu^t$ (20 mL) and neutralized with 1*M* HCl (20 mL) on cooling to 0 °C. The organic layer was separated, washed successively with water (2×20 mL) and a saturated solution of NaCl (10 mL), dried with Na_2SO_4, and concentrated *in vacuo*. 2,3-Diketones **6—8** were obtained in 90—97% yields.

Methyl 2-hydroxy-3-oxoursa-1,12-dien-28-oate (6). A colorless glassy substance, $[\alpha]_{578}^{21}$ +93.6 (*c* 10.7); IR ($CHCl_3$), ν/cm^{-1}: 3600 (O—H), 3450 (O—H, enol of α-diketone), 1707 (C=O, ester), 1660 (C=O, enol of α-diketone), 1635 (C=COH, enol of α-diketone). UV (EtOH), λ_{max}/nm (ε): 270 (5460). High-resolution MS: found *m/z* = 482.3399; for $C_{31}H_{46}O_4$, calculated $[M]^+$ = 482.3396. MS, *m/z* (I_{rel} (%)): 482 $[M]^+$ (45), 262 (75), 203 (100), 189 (49), 119 (43).

2,28-Dihydroxylupa-1,20(29)-dien-3-one (7). A colorless glassy substance, $[\alpha]_{578}^{21}$ +52 (*c* 8.5) (*cf.* lit. data:[7] $[\alpha]_D$ +61). IR ($CHCl_3$), ν/cm^{-1}: 3630 (O—H), 3480 (O—H, enol of α-diketone), 1660 (C=O, enol of α-diketone), 1640 (C=COH, enol of α-diketone), 880 (=CH_2). UV (EtOH), λ_{max}/nm (ε): 271 (7030). High-resolution MS: found *m/z* = 454.3440; for $C_{30}H_{46}O_3$, calculated $[M]^+$ = 454.3447. MS, *m/z* ($I_{rel.}$ (%)): 454 $[M]^+$ (63), 424 (49), 189 (59), 177 (100), 154 (65), 153 (65), 147 (40), 123 (49), 121 (56), 109 (53), 107 (59), 105 (51), 95 (78), 93 (51), 69 (52), 67 (41), 55 (52), 28 (90).

2-Hydroxy-19β,28-epoxylupa-1,20(29)-dien-3-one (8). White crystals, m.p. 231.5—233 °C (from $CHCl_3$—MeOH); $[\alpha]_{578}^{21}$ +85 (*c* 4.3). IR ($CHCl_3$), ν/cm^{-1}: 3450 (O—H, enol of α-diketone), 1664 (C=O, enol of α-diketone), 1642 (C=COH, enol of α-diketone). UV (EtOH), λ_{max}/nm (ε): 271 (6700). High-resolution MS: found *m/z* = 454.3454; for $C_{30}H_{46}O_3$, calculated $[M]^+$ = 454.3447. MS, *m/z* (I_{rel} (%)): 454 $[M]^+$ (100), 215 (86), 177 (49), 154 (78), 153 (52), 149 (44), 137 (42), 135 (64), 124 (43), 123 (47), 121 (45), 109 (50), 107 (56), 95 (79), 93 (44), 81 (86), 69 (64), 67 (44), 55 (59), 43 (50), 41 (41).

Synthesis of quinoxalines 9—11. Several drops of glacial AcOH were added to a solution of diketone **6—8** (1.20 mmol) and *o*-phenylenediamine (1.21 mmol) in a mixture of 95% EtOH (5 mL) and C_6H_6 (3 mL). The resulting mixture was refluxed with stirring for 5—7 h. Then the solvent was distilled off *in vacuo*, the resulting brown mixture was chromatographed on SiO_2 (C_6H_6—EtOAc), and the corresponding derivatives **9—11** were isolated in 85—95% yields.

Methyl quinoxalino[2,3-*b*]urs-12-en-28-oate (9). White crystals, m.p. 234—237 °C (from MePh—MeOH). $[\alpha]_{578}^{21}$ +75 (*c* 6.9). Found (%): C, 80.3; H, 9.3; N, 5.0. $C_{37}H_{50}N_2O_2$. Calculated (%): C, 80.10; H, 9.08; N, 5.05. IR (KBr), ν/cm^{-1}: 1725 (C=O). UV (EtOH), λ_{max}/nm (ε): 239 (31800), 322 (10800). High-resolution MS: found *m/z* = 554.3874; for $C_{37}H_{50}N_2O_2$, calculated $[M]^+$ = 554.3872. MS, *m/z* (I_{rel} (%)): 554 $[M]^+$ (56), 539 (67), 293 (41), 262 (88), 203 (100), 133 (81).

Quinoxalino[2,3-*b*]-28-hydroxy-20(29)-lupene (10). White crystals, m.p. 299—303 °C (from hexane), $[\alpha]_{578}^{21}$ +54 (*c* 6.6). Found (%): C, 82.0; H, 9.1; N, 5.1. $C_{36}H_{50}N_2O$. Calculated (%): C, 82.08; H, 9.57; N, 5.32. IR ($CHCl_3$), ν/cm^{-1}: 3625 (O—H), 1640 (C=C), 885 (=CH_2). UV (EtOH), λ_{max}/nm (ε): 238 (32550), 322 (11300). High-resolution MS: found *m/z* = 526.3994; for $C_{36}H_{50}N_2O$, calculated $[M]^+$ = 526.3923. MS, *m/z* (I_{rel} (%)): 526 $[M]^+$ (57), 510 (100), 496 (35), 495 (57), 222 (37), 208 (31), 27 (30).

Quinoxalino[2,3-*b*]-19b,28-epoxy-20(29)-lupene (11). White crystals, m.p. 272—293 °C (with decomp., from PhMe—hexane), $[\alpha]_{578}^{21}$ +70 (*c* 10.1). Found (%): C, 81.8; H, 9.5; N, 5.3. $C_{36}H_{50}N_2O$. Calculated (%): C, 82.08; H, 9.57; N, 5.32. UV (EtOH), λ_{max}/nm (ε): 239 (34600), 322 (11500). High-resolution MS: found *m/z* = 526.3924; for $C_{36}H_{50}N_2O$, calculated $[M]^+$ = 526.3923. MS, *m/z* (I_{rel} (%)): 526 $[M]^+$ (97), 510 (100), 305 (50).

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