INTRAMOLECULAR CYCLOADDITIONS WITH ISOBENZOFURANS XI[1] - SYNTHESIS OF ANNULATED INDOLES

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Abstract: Transition metal catalyzed decomposition of diazoester **4b** results in the formation of furo[3,4-b]indol **5**. This intermediate is trapped intramolecularly *in situ* to give **6**. Furo[3,4-b]indoles of type **10** can be prepared similarly, but *intra*molecular *Diels-Alder* reactions seem to be prevented for sterical reasons. Some quantum chemical calculations (AM1, PM3, *ab initio*, density functional studies) concerning the geometry and different reactivity of benzo[c]furans and furo[3,4-d]indoles are reported. The results are in agreement with observations.

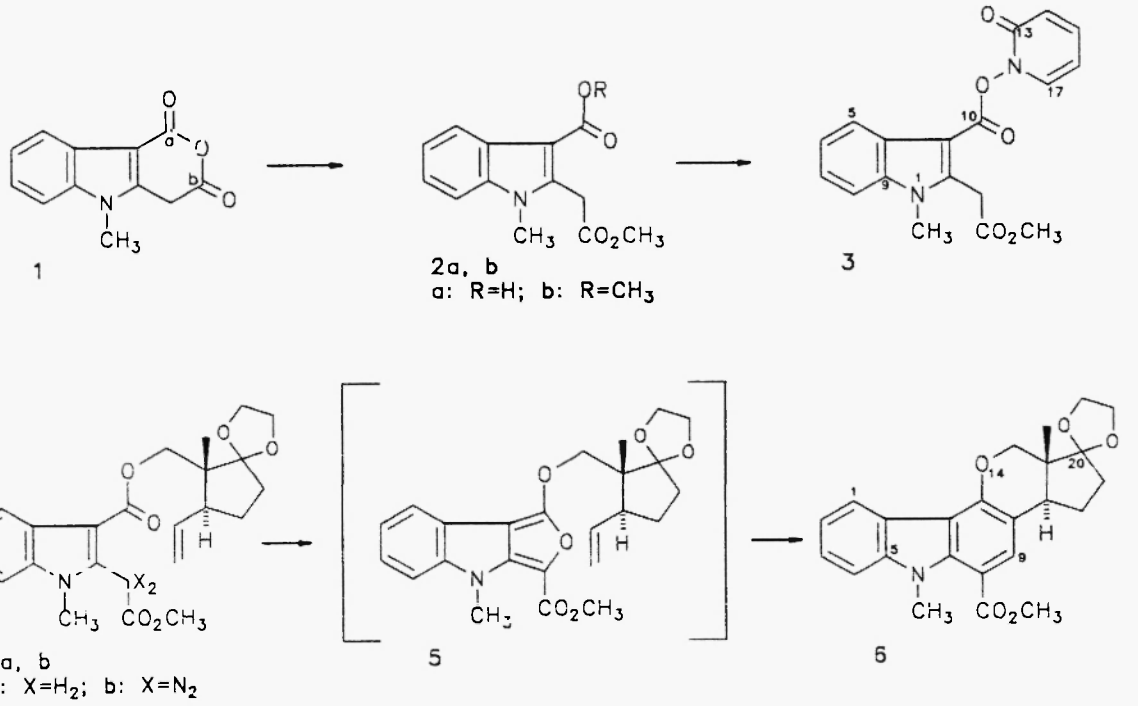
Introduction

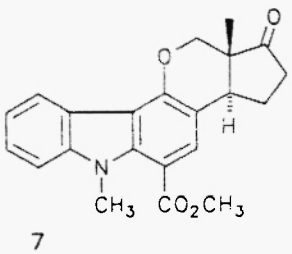
Benzo[c]furans (isobenzofurans) constitute a unique class of compounds inasmuch as these heterocycles may undergo cycloaddition reactions even with unactivated alkenes and alkynes to form complex polycyclic systems which are difficult to obtain by other synthetic strategies[2-5]. The extension of this methodology to thieno[2,3-c]furans[6] and furo[3,4- d]isoxazoles[7] was straightforward. In this paper the generation and reaction of furo[3,4-b]indoles is reported[8].

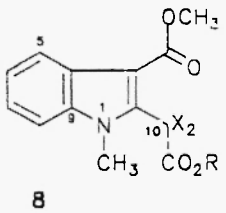
Preparative and Computational Results

Treatment of anhydride **1**[9] with methanol results in a regioselective ring opening[10] giving **2**[8j] which on reaction with N-hydroxypyridone/DCC yields the activated ester **3**[11]. This compound can be transformed quite easily to **4a**[12,13]. Diazo group transfer by the *Regitz* methodology[14] yields **4b**[15]. As was shown by *Hamaguchi* and *Ibata*[16] diazo esters of this type are versatile starting materials for the generation of c-annulated furans. Treatment of **4b** with $Cu(acacF_6)_2$[17] results in the formation of **6**[18]. Obviously in the first step a carbene (carbenoid)[19] is generated which after an intramolecular reaction with a carbonyl group yields a furo[3,4-b]indole (**5**). An intramolecular *Diels-Alder* reaction[20], subsequent ring opening of the resulting 1,4-oxido adduct[21] and elimination of water results in the observed product. The deprotection of the carbonyl group was accomplished with 2N HCl/MeOH giving the ketone **7**[22].
Interestingly enough, analogous reactions with diazoesters **8c** and **8e** did *not* result in the formation of the corresponding cycloadducts. This was demonstrated as follows. Regioselective saponification of **2b**[23] with KOH/MeOH yields monoester **8a**[24]. The esterification to **8b** was accomplished with O-propenylurea using the methodology of *Vowinkel*[25,26]. Diazo group transfer yields **8c**[27] which on decomposition with $Cu(acacF_6)_2$ results - besides other products[28] - in

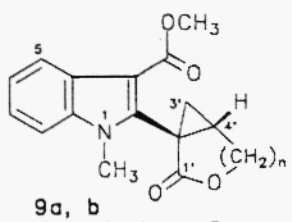
the formation of a small amount of the cyclopropane derivative **9a**[29]. Similarly the esterification of **8a** with O-butenylurea yields **8d**[30] which after diazo group transfer (to **8e**)[31] and subsequent decomposition with $Cu(acacF_6)_2$ - again besides a number of other products[28] - gives **9b**[32].

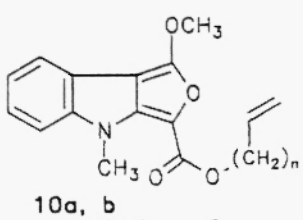


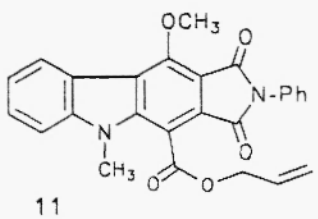




8	X	R
a	H	H
b	H	-$CH_2CH=CH_2$
c	N	-$CH_2CH=CH_2$
d	H	-$(CH_2)_2CH=CH_2$
e	N	-$(CH_2)_2CH=CH_2$



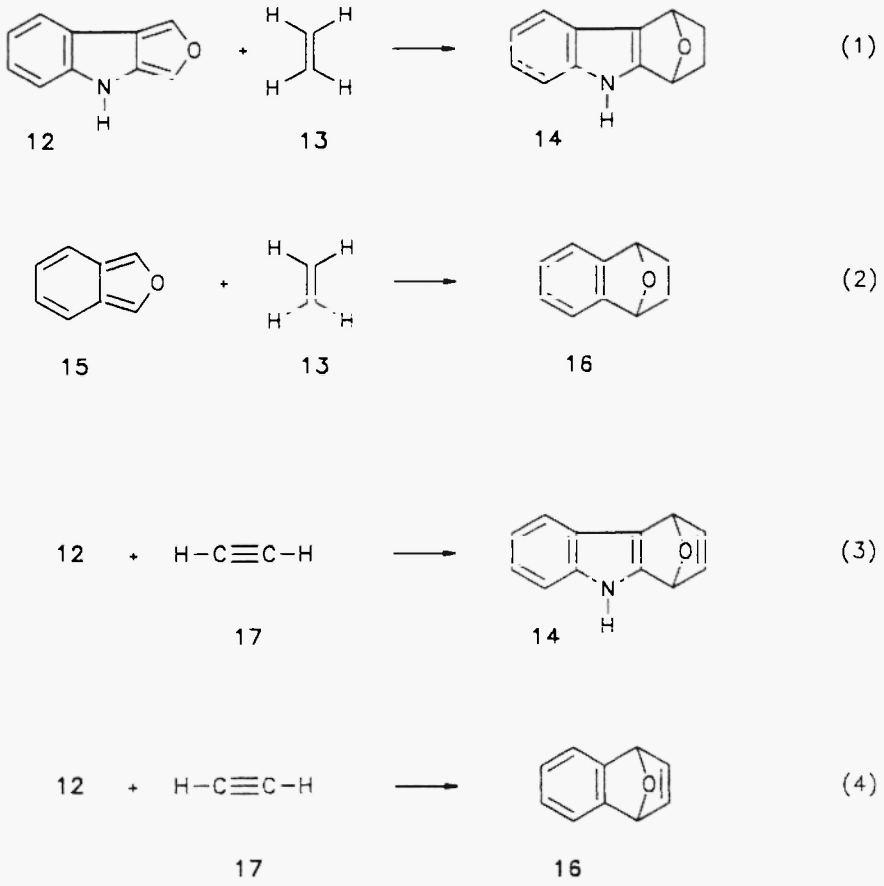




Scheme 1

Decomposition of **8c** in the presence of N-phenylmaleimide results in the formation of **11**[33] in 62% yield (from **8b**). This experiment demonstrates that furo[3,4-b]indoles of type **10** are indeed formed, but obviously *intra*molecular cycloaddition reactions are prevented. Model calculations reveal that a prerequisite for this type of reaction seems to be a *planar* arrangement of the carbonyl group and the indole ring. According to these calculations such an arrangement seems to be difficult to achieve.

Generally speaking furo[3,4-b]indoles are *less* reactive than the corresponding benzo[c]furans[2e]. This observation can be rationalized quite easily by thermochemical arguments. Using quantum chemical methods (AM1, PM3[34,35]; *ab initio* methods (RHF/6-31G*, MP2/6-31G*//6-31G*)[37,38], density functional methods (BLYP/6-31G*)[41-43]) the exothermicity of the model



Scheme 2

reactions (1)-(4) are calculated. These data (Table 1) show that - irrespective of the computational methods - (1) and (3) are *less* exothermic than (2) and (4), resp. Similar calculations in

other series (furo[3,4-d]isoxazoles)[44] point into the same direction.

Table 1: Calculated Reaction Enthalpies ($\Delta\Delta H_f$) and Reaction Energies (ΔE) for (1) and (2) (Semiempirical and *ab initio* Values, in kcal/mol)

method	$\Delta\Delta H_f(1)^a(\Delta E(1))^b$	$\Delta\Delta H_f(2)(\Delta E(2))$	$\Delta\Delta\Delta H(\Delta\Delta E^c)$
AM1	22.2	34.8	12.6
PM3	22.0	32.5	10.5
6-31G*	22.4	36.9	14.5
MP2/6-31G*//6-31G*	33.5	44.3	10.8
BLYP/6-31G*	12.1	21.5	9.3

[a] $\Delta\Delta H_f(1) = \Delta H_f(\mathbf{14}) - (\Delta H_f(\mathbf{12}) + \Delta H_f(\mathbf{13}))$(semiempirical values)
[b] $\Delta E(1) = E(\mathbf{14}) - (E(\mathbf{12}) + E(\mathbf{13}))$(*ab initio* and DFT values)
[c] $\Delta\Delta\Delta H = \Delta\Delta H_f(2) - \Delta\Delta H_f(1); \Delta\Delta E = \Delta E(2) - \Delta E(1)$

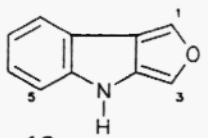
Table 2: Calculated Reaction Enthalpies ($\Delta\Delta H_f$) and Reaction Energies (ΔE) for (3) and (4) (Semiempirical and *ab initio* Values, in kcal/mol)

method	$\Delta\Delta H_f(3)^a(\Delta E(3))^b$	$\Delta\Delta H_f(4)(\Delta E(4))$	$\Delta\Delta\Delta H(\Delta\Delta E^c)$
AM1	15.7	28.9	13.2
PM3	17.6	28.3	10.7
6-31G*	19.1	37.2	18.1
MP2/6-31G*//6-31G*	29.1	42.7	13.6
BLYP/6-31G*	27.6	15.3	12.3

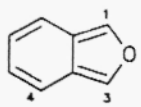
[a] $\Delta\Delta H_f(3) = \Delta H_f(\mathbf{18}) - (\Delta H_f(\mathbf{12}) + \Delta H_f(\mathbf{17}))$(semiempirical values)
[b] $\Delta E(3) = E(\mathbf{18}) - (E(\mathbf{12}) + E(\mathbf{17}))$(*ab initio* and DFT values)
[c] $\Delta\Delta\Delta H = \Delta\Delta H_f(4) - \Delta\Delta H_f(3); \Delta\Delta E = \Delta E(4) - \Delta E(3)$

Although a considerable amount of reliable DFT studies - even for molecules with unusual bonds[45] - are available[40,41] the detailed structures of **12** and **15** are not known with certainty. In Table 3 some geometrical data for these compounds are presented. The values for **15** are in sufficient agreement with *ab initio* data on the RHF/4-31g* level[2e,46]. This again underlines the validity of this method for computational studies in the field of organic molecules.

Table 3: Calculated Bond Lengths for **12** and **15** (DFT Results[a], in Å)



12



15

bond	length	bond	length	bond	length
1-8b	1.379	4a-5	1.404	1-7a	1.387
1-2	1.381	5-6	1.407	1-2	1.376
2-3	1.397	6-7	1.412	3a-7a	1.469
3-3a	1.373	7-8	1.406	3a-4	1.434
3a-8b	1.453	8-8a	1.406	4-5	1.382
3a-4	1.396	4a-8a	1.439	5-6	1.443
4-4a	1.407	8a-8b	1.458		

[a] $BLYP/6-31G^*//6-31G^*$

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10. The course of this reaction cannot be explained by simple electrostatic arguments. AM1 calulations reveal that $q_\pi(a) < q_\pi(b)$.
11. 11a. Method: L.A.Paquette, *J.Am.Chem.Soc.* **1965**, *87*, 5186, footnote 27. - 11b. **3**: IR(KBr): $\tilde{\nu}$ = 3080 cm^{-1}, 2950, 1740 (C=O), 1665 (C=O), 1590; UV(CH_3CN): λ_{max} (lg ϵ) = 214 nm (4.710), 235 (4.486), 293 (4.392), 303 (sh, 4.353), 325 (sh, 3.583); ^1H NMR (200 MHz, $CDCl_3$): δ = 3.71 ppm (s, 3H, CO_2CH_3*), 3.76 (s, 3H, NCH_3*), 4.39 (s, 2H, $CH_2CO_2CH_3$), 6.22 (ddd, J_1 = 1.7 Hz, J_2 = 6.6 Hz, J_3 = 7.1 Hz, 1H, H-16), 6.77 (ddd, J_1 = 0.5 Hz, J_2 = 1.7 Hz, J_3 = 9.3 Hz, 1H, H-14), 7.26-7.43 (m, 3H, H-6, H-7, H-8), 7.40 (ddd, J_1 = 2.0 Hz, J_2 = 6.6 Hz, J_3 = 9.3 Hz, 1H, H-15), 7.50 (ddd, J_1 = 0.5 Hz, J_2 = 2.0 Hz, J_3 = 7.1 Hz, 1H, H-17), 8.12-8.20 (m, 1H, H-5); ^{13}C NMR (50 MHz, $CDCl_3$): δ = 30.44 (q, NCH_3) ppm, 31.70 (t, Ar-CH_2CO_2R), 52.59 (q, CO_2CH_3), 100.87 (s, C-3), 104.90 (d, C-16), 110.27 (d, C-8), 122.02 (d, C-6*), 122.92 (d, C-7*), 122.95 (d, C-14*), 123.59 (d, C-5), 125.77 (s, C-4), 136.55 (d, C-15**), 137.20 (s, C- 9**), 139.33 (d, C-17), 143.03 (s, C-2**), 157.81 (s, C-13), 161.70 (s, C-10), 169.09 (s, -CH_2CO_2R); MS (70 eV): m/z (%) = 340 (2, M^+), 230 (100), 214 (11), 202 (83), 198 (28), 186 (48), 169 (19), 142 (23), 128 (12), 115 (31); $C_{18}H_{16}N_2O_5$: Calc. 340.1059 Found 340.1059 (MS).
12. *Trans*-7-ethenyl-6-methyl-1,4-dioxaspiro[4.4]nonane-6-methanol was prepared from the corresponding carboxylic ester by reduction with $LiAlH_4$ (98% colorless liquid; IR(KBr): $\tilde{\nu}$ = 3480 cm^{-1}, 3080, 2960, 2880, 1640). For details see K.Hildebrandt, Dissertation,University of Kiel 1988.
13. **4a**: 52% fine . lles with mp 116-117 °C; IR(KBr): $\tilde{\nu}$ = 3050 cm^{-1}, 2951, 1738, 1687, 1544; UV(CH_3CN): λ_{max} (lg ϵ)= 217 nm (4.541), 228 (4.357), 248 (3.961), 288 (4.134); ^1H NMR (300 MHz, $CDCl_3$): δ = 1.19 ppm (s, 3H, H-21), 1.63-1.74 (m, 1H, H-18a), 1.81-2.05 (m, 3H, H-18b, H-19a, H-19b), 2.61-2.69 (m, 1H, H- 17), 3.72 (s, 3H, NCH_3), 3.73 (s, 3H, CO_2CH_3), 3.81-3.91 (m, 4H, OCH_2CH_2O), 4.16 (d, J = 11.1 Hz, 1H, H-15a)*, 4.42 (d, J = 11.1 Hz, 1H, H-15b)*, 4,48 (s, 2H, H-8), 5.04 (ddd, J_1 = 0.7 Hz, J_2 = 2.0 Hz, J_3 = 10.2 Hz, 1H, H-9b), 5.06 (ddd, J_1 = 0.9 Hz, J_2 = 2.0 Hz, J_3 = 16.8 Hz, 1H, H-9a), 5.80 (ddd, J_1 = 8.4 Hz, J_2 = 10.2 Hz, J_3 = 16.8 Hz, 1H, H-10), 7.27-7.36 (m, 3H, H-6, H-7, H-8), 8.35 (ddd, J_1 = 0.9 Hz, J_2 = 3.3 Hz, J_3 = 6.0 Hz, 1H, H-5); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 14.24 ppm (q, C-21), 24.88 (t, C-18), 29.91 (q, NCH_3), 31.33 (t, C-8), 33.72 (t, C-19), 48.01 (d, C-17), 48.81 (s, C-16), 52.29

(q, CO_2CH_3), 64.55 (t, OCH_2CH_2O), 65.00 (t, OCH_2CH_2O), 66.99 (t, C-15), 105.60 (s, C-12), 109.27 (d, C-4), 116.27 (t, C-9), 118.75 (s, C-20), 121.82 (d, C-1)*, 122.12 (d, C-2)*, 122.62 (d, C-3)*, 126.13 (s, C- 13), 136.71 (s, C-5), 138.49 (d, C-10), 140.18 (s, C-7), 165.96 (s, C-11), 169.62 (s, CO_2CH_3); $C_{24}H_{29}NO_6$: Calc. 427.1995 Found 427.1994 (MS).

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15. **4b**: 95 % yellow oil; IR (KBr): $\tilde{\nu}$ = 3051 cm^{-1}, 2930, 2123 (CN_2), 1709 , 1692, 1535; ^1H NMR (300 MHz, $CDCl_3$): δ = 1.20 ppm (s, 3H, H-21), 1.58-1.74 (m, 1H, H-18a), 1.81-2.05 (m, 3H, H-18b, H-19a, H-19b), 2.61-2.70 (m, 1H, H- 17), 3.74 (s, 3H, NCH_3), 3.85 (s, 3H, CO_2CH_3), 3.83-3.88 (m, 4H, OCH_2CH_2O), 4.22 (br d, 1H, H-15a)*, 4.46 (br d, 1H, H-15b)*, 5.04 (ddd, J_1 = 0.7 Hz, J_2 = 2.0 Hz, J_3 = 10.2 Hz, 1H, H-9b), 5.06 (ddd, J_1 = 1.0 Hz, J_2 = 2.0 Hz, J_3 = 17.0 Hz, 1H, H-9a), 5.80 (ddd, J_1 = 8.6 Hz, J_2 = 10.2 Hz, J_3 = 17.0 Hz, 1H, H-10), 7.27-7.36 (m, 3H, H-6, H- 7, H-8), 8.35 (ddd, J_1 = 1.0 Hz, J_2 = 2.9 Hz, J_3 = 6.4 Hz, 1H, H-5); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 14.28 ppm (q, C-21), 24.97 (t, C- 18), 31.14 (q, NCH_3), 33.79 (t, C-19), 48.12 (d, C-17), 48.89 (s, C-16), 52.29 (q, CO_2CH_3), 56.46 (br s, C-8), 64.57 (t, OCH_2CH_2O), 65.03(t, OCH_2CH_2O), 67.46 (t, C-15), 106.38 (s, C-12), 109.81 (d, C-4), 116.30 (t, C-9), 118.80 (s, C-20), 122.17 (d, C-3)*, 122.62 (d, C-2)*, 123.56 (d, C-1)*, 125.88 (s, C-13), 130.79 (s, C-7), 137.78 (d, C-5), 138.51 (s, C-10), 164.86 (s, C-11), 165.06 (br s, CO_2CH_3);

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18. **6**: 58 % colorless needles with mp 132-133 °C; ^1H NMR (300 MHz, $CDCl_3$): δ = 0.88 ppm (d, J = 0.8 Hz, 3H, H-21), 1.73 (dddd, J_1 = 6.3 Hz, J_2 = 11.3 Hz, J_3 = 11.8 Hz, J_4 = 12.3 Hz, 1H, H-18a), 2.11 (ddd, J_1 = 6.3 Hz, J_2 = 9.8 Hz, J_3 = 14.5 Hz, 1H, H-19b), 2.27 (ddd, J_1 = 3.0 Hz, J_2 = 11.3 Hz, J_3 = 14.5 Hz, 1H, H-19a), 2.31 (dddd, J_1 = 3.0 Hz, J_2 = 7.3 Hz, J_3 = 9.8 Hz, J_4 = 11.8 Hz, 1H, H-18b), 3.33 (ddd, J_1 = 1.4 Hz, J_2 = 7.3 Hz, J_3 = 12.3 Hz, 1H, H-17), 3.81-3.91 (m, 4H, OCH_2CH_2O), 3.87 (s, 3H, NCH_3), 3.96 (s, 3H, CO_2CH_3), 4.41 (d, J = 9.7 Hz, 1H, H-15a), 4.64 (qd, J_1 = 0.8 Hz, J_2 = 9.7 Hz, 1H, H-15b), 7.24 (ddd, J_1 = 1.4 Hz, J_2 = 6.8 Hz, J_3 = 7.8 Hz, 1H, H-2), 7.40 (ddd, J_1 = 0.7 Hz, J_2 = 1.4 Hz, J_3 = 8.3 Hz, 1H, H-4), 7.45 (ddd, J_1 = 1.3 Hz, J_2 = 6.8 Hz, J_3 = 8.3 Hz, 1H, H-3), 7.57 (d, J = 1.4 Hz, 1H, H-9), 8.35 (ddd, J_1 = 0.7 Hz, J_2 = 1.3 Hz, J_3 = 7.8 Hz, 1H, H-1); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 13.01 ppm (q, C-21), 22.71 (t, C-18), 33.94 (q, NCH_3), 35.67 (t, C-19), 41.71 (d, C-17), 44.09 (s, C-16), 51.82 (q, CO_2CH_3), 64.63 (t, OCH_2CH_2O), 65.32 (t, OCH_2CH_2O), 75.22 (t, C-15), 106.72 (s, C-8), 108.72 (d, C-4), 112.62 (s, C-12), 115.90 (s, C-10), 118.61 (s, C-20), 119.72 (d, C-2), 121.80 (s, C-13), 122.93 (d, C-1), 125.31 (d, C-3), 127.47 (d, C-9), 140.80 (s, C-7), 142.18 (s, C-5), 152.90 (s, C-11), 167.62 (s, CO_2CH_3); $C_{24}H_{25}NO_5$: Calc. 407.1733 Found 407.1730 (MS).

19. See, e.g., M.Orchin, F.Kaplan, R.S.Macomber, R.M.Wilson, H.Zimmer, *The Vocabulary of Organic Chemistry*, Wiley, New York 1980.
20. See e.g., J.L.Charlton, M.M.Alauddin, *Tetrahedron* **1987**, *43*, 2873.

21. As was observed in the 11-oxasteroid series in some cases the ring opening reaction of the primary cycloadduct can be prevented if only *minute* amounts of transition metal catalysts are used: K.Hildebrandt, Dissertation, University of Kiel 1988.

22. **7**: 32 % fine needles; ^1H NMR (300 MHz, $CDCl_3$): δ = 0.98 ppm (d, J = 0.8 Hz, 3H, H-21), 2.04 (dddd, J_1 = 8.9 Hz, J_2 = 9.0 Hz, J_3 = 12.2 Hz, J_4 = 12.3 Hz, 1H, H-18a), 2.46 (ddd, J_1 =

8.6 Hz, J_2 = 8.9 Hz, J_3 = 19.3 Hz, 1H, H-19b), 2.61 (dddd, J_1 = 1.0 Hz, J_2 = 6.2 Hz, J_3 = 8.6 Hz, J_4 = 12.2 Hz, 1H, H-18b), 2.74 (ddd, J_1 = 1.0 Hz, J_2 = 9.0 Hz, J_3 = 19.3 Hz, 1H, H-19a), 3.29 (ddd, J_1 = 1.2 Hz, J_2 = 6.2 Hz, J_3 = 12.3 Hz, 1H, H-17), 3.90 (s, 3H, NCH_3), 3.99 (s, 3H, CO_2CH_3), 4.52 (qd, J_1 = 0.8 Hz, J_2 = 10.4 Hz, 1H, H-15b), 4.66 (d, J = 10.4 Hz, 1H, H- 15a), 7.27 (ddd, J_1 = 1.2 Hz, J_2 = 6.8 Hz, J_3 = 7.8 Hz, 1H, H-2), 7.42 (ddd, J_1 = 0.9 Hz, J_2 = 1.2 Hz, J_3 = 8.2 Hz, 1H, H-4), 7.48 (ddd, J_1 = 1.3 Hz, J_2 = 6.8 Hz, J_3 = 8.2 Hz, 1H, H-3), 7.64 (d, J = 1.2 Hz, 1H, H-9), 8.32 (ddd, J_1 = 0.9 Hz, J_2 = 1.3 Hz, J_3 = 7.8 Hz, 1H, H-1); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 13.18 ppm (q, C-21), 21.77 (t, C-18), 33.92 (q, NCH_3), 36.67 (t, C-19), 42.33 (d, C-17), 46.40 (s, C-16), 51.91 (q, CO_2CH_3), 75.07 (t, C-15), 107.47 (s, C-8), 108.84 (d, C-4), 113.03 (s, C-12), 113.68 (s, C-10), 120.04 (d, C-2), 121.60 (s, C- 13), 123.13 (d, C-1), 125.71 (d, C-3), 126.89 (d, C-9), 141.11 (s, C-7), 142.28 (s, C-5), 152.88 (s, C-11), 167.49 (s, CO_2CH_3), 215.58 (s, C-20); $C_{22}H_{21}NO_4$: Calc. 363.1471 Found 363.1470 (MS).

23. Prepared as reported[9b] (71% (69%)[9b], mp 100 °C (100-101 °C)[9b]).

24. **8a**: 92% colorless crystals with mp 180-183 °C (dec.); IR (KBr): $\tilde{\nu}$ = 3500-2800 cm^{-1}, 1734, 1659, 1541; ^{1}H NMR (90 MHz, $CDCl_3$): δ = 3.74 ppm (s, 3H, NCH_3), 3.95 (s, 3H, CO_2CH_3), 4.23 (s, 2H, Ar-CH_2CO_2H), 7.17-7.43 (m, 3H, Ar-H), 7.93-8.17 (m, 1H, Ar-H), 9.3-10.2 (br s, 1H, COOH).

25. E.Vowinkel, *Chem.Ber.* **1967**, *100*, 16.

26. **8b**: 89% colorless needles with mp 78-80 °C; IR(KBr): $\tilde{\nu}$ = 2944 cm^{-1}, 1720, 1688, 1543; UV(CH_3CN): λ_{max} (lg ϵ)= 216 nm (4.607), 229 (sh, 4.438), 250 (sh, 3.976), 287 (4.160); ^{1}H NMR (300 MHz, $CDCl_3$): δ = 3.72 ppm (s, 3H, NCH_3), 3.92 (s, 3H, CO_2CH_3), 4.43 (s, 2H, CH_2CO_2R), 4.63 (ddd, J_1 = 1.4 Hz, J_2 = 1.4 Hz, J_3 = 5.7 Hz, 1H, H-13), 5.22 (tdd, J_1 = 1.4 Hz, J_2 = 1.4 Hz, J_3 = 10.4 Hz, 1H, H-15a), 5.29 (tdd, J_1 = 1.4 Hz, J_2 = 1.4 Hz, J_3 = 17.2 Hz, 1H, H-15b), 5.90 (tdd, J_1 = 5.7 Hz, J_2 = 10.4 Hz, J_3 = 17.2 Hz, 1H, H-14), 7.22-7.35 (m, 3H, H-6, H-7, H-8), 8.13 (ddd, J_1 = 0.8 Hz, J_2 = 2.6 Hz, J_3 = 6.7 Hz, 1H, H-5); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 29.89 ppm (q, NCH_3), 31.55 (t, C-10), 50.75 (q, CO_2CH_3), 65.78 (t, C-13), 105.37 (s, C-3), 109.41 (d, C-8), 118.37 (t, C-15), 121.80 (d, C-5)*, 121.88 (d, C-6)*, 122.68 (d, C-7)*, 126.16 (s, C-4), 131.78 (d, C-14), 136.79 (s, C-9), 140.02 (s, C-2), 165.94 (s, CO_2CH_3), 168.75 (s, C-11); $C_{16}H_{17}NO_4$: Calc. 287.1158 Found 287.1156 (MS).

27. **8c**: IR (KBr): $\tilde{\nu}$ = 2946 cm^{-1}, 2123 (CN_2), 1705, 1694 , 1537; UV(CH_3CN): λ_{max} (lg ϵ)= 212 nm (4.290), 238 (4.217), 295 (3.900), 385 (2.346); ^{1}H NMR (300 MHz, $CDCl_3$): δ = 3.73 ppm (s, 3H, NCH_3), 3.97 (s, 3H, CO_2CH_3), 4.74-4.76 (br m, 2H, H-13), 5.27-5.37 (br m, 2H, H-15), 5.95 (br m, 1H, H-14), 7.26-7.42 (m, 3H, H-6, H-7, H-8), 8.17-8.20 (m, 1H, H-5); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 31.21 ppm (q, NCH_3), 51.14 (q, CO_2CH_3), 56.47 (br s, CN_2, C-10), 65.91 (t, C-13), 106.04 (s, C-3), 109.88 (d, C-8), 118.58 (t, C-15), 122.21 (d, C-7)*, 122.48 (d, C-6)*, 123.60 (d, C-5)*, 125.98 (s, C-4), 130.46 (s, C-9), 131.90 (d, C-14), 137.78 (s, C-2), 164.32 (s, C-11), 164.79 (s, CO_2CH_3).

28. O.Peters, W.Friedrichsen, unpublished results.

29. **9a**: 35% colorless needles with mp 149-150 °C; IR(KBr): $\tilde{\nu}$ = 3100 cm^{-1}, 2961, 1772, 1686, 1541; UV (CH_3CN): λ_{max} (lg ϵ) = 216 nm (4.606), 232 (4.486), 250 (sh, 3.881), 290 (4.199), 299 (sh, 4.077); ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.67 ppm (dd, J_1 = 4.8 Hz, J_2 = 7.5 Hz, 1H, H-3'a), 1.69 (dd, J_1 = 4.8 Hz, J_2 = 5.5 Hz, 1H, H-3'b), 2.67 (dddd, J_1 = 0.6 Hz, J_2 = 4.7 Hz, J_3 = 5.5 Hz, J_4 = 7.5 Hz, 1H, H-4'), 3.93 (s, 3H, NCH_3), 3.94 (s, 3H, CO_2CH_3), 4.38 (dd, J_1 =

0.6 Hz, J_2 = 8.9 Hz, 1H, H-5'b), 4.84 (dd, J_1 = 4.7 Hz, J_2 = 8.9 Hz, 1H, H-5'a), 7.26 (ddd, J_1 = 1.7 Hz, J_2 = 6.7 Hz, J_3 = 7.4 Hz, 1H, H-6), 7.31 (ddd, J_1 = 1.5 Hz, J_2 = 6.7 Hz, J_3 = 7.8 Hz, 1H, H-7), 7.36 (ddd, J_1 = 0.9 Hz, J_2 = 1.7 Hz, J_3 = 7.8 Hz, 1H, H-8), 8.10 (ddd, J_1 = 0.9 Hz, J_2 = 1.5 Hz, J_3 = 7.4 Hz, 1H, H-5); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 20.09 ppm (t, C-3'), 24.96 (s, C-2'), 26.80 (d, C-4'), 30.82 (q, NCH_3), 50.97 (q, CO_2CH_3), 68.97 (t, C-5'), 107.32 (s, C-3), 109.67 (d, C-8), 121.95 (d, C-6)*, 122.18 (d, C-7)*, 123.31 (d, C-5)*, 125.78 (s, C-4), 136.87 (s, C-9), 138.92 (s, C-2), 165.23 (s, CO_2CH_3), 174.09 (s, CO_2R, C- 1').

30. **8d**: 90% colorless needles with mp 44-48 °C; IR (KBr): $\tilde{\nu}$ = 2950 cm^{-1}, 1722, 1691; UV (CH_3CN): λ_{max} (lg ϵ) = 216 nm (4.666), 228 (4.549), 247 (sh, 4.065), 287 (4.220), 297 (sh, 4.081); ^{1}H NMR (300 MHz, $CDCl_3$): δ = 2.37 ppm (ddtd, J_1 = 1.5 Hz, J_2 = 1.6 Hz, J_3 = 6.6 Hz, J_4 = 6.7 Hz, 2H, H-14), 3.72 (s, 3H, NCH_3), 3.93 (s, 3H, CO_2CH_3), 4.18 (t, J = 6.7 Hz, 2H, H-13), 4.41 (s, 2H, H-10), 5.03 (tdd, J_1 = 1.5 Hz, J_2 = 1.8 Hz, J_3 = 10.3 Hz, 1H, H- 16a), 5.05 (tdd, J_1 = 1.6 Hz, J_2 = 1.8 Hz, J_3 = 17.2 Hz, 1H, H-16b), 5.73 (tdd, J_1 = 6.6 Hz, J_2 = 10.3 Hz, J_3 = 17.2 Hz, 1H, H-15), 7.23-7.36 (m, 3H, H-6, H-7, H-8), 8.10-8.16 (m, 1H, H-5); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 29.85 ppm (q, NCH_3), 31.55 (t, C-10), 32.97 (t, C-14), 50.71 (q, CO_2CH_3), 64.21 (t, C-13), 105.24 (s, C-3), 109.40 (d, C-8), 117.26 (t, C-16), 121.74 (d, C-6)*, 121.82 (d, C-7)*, 122.61 (d, C-5)*, 126.16 (s, C-4), 133.68 (d, C-15), 136.75 (s, C-9), 140.16 (s, C-2), 165.91 (s, CO_2CH_3), 168.99 (s, C-11).

31. **8e**: 91% yellow oil; IR (KBr): $\tilde{\nu}$ = 2952, 2123, 1688; UV (CH_3CN): λ_{max} (lg ϵ) = 212 nm (4.587), 238 (4.494), 295 (4.192); ^{1}H NMR (300 MHz, $CDCl_3$): δ = 2.36-2.54 ppm (br m, 2H, H-14), 3.73 (s, 3H, NCH_3), 3.97 (s, 3H, CO_2CH_3), 4.24-4.38 (br m, 2H, H- 13), 5.03-5.21 (br m, 2H, H-16), 5.70 (br m, 1H, H-15), 7.25- 7.42 (m, 3H, H-6, H-7, H-8), 8.17-8.20 (m, 1H, H-5); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 31.26 ppm (q, NCH_3), 33.35 (t, C-14), 51.15 (q, CO_2CH_3), 56.49 (br s, C-10), 64.40 (t, C-13), 106.04 (s, C-3), 109.91 (d, C-8), 117.51 (t, C-16), 122.23 (d, C-6)*, 122.47 (d, C-7)*, 123.61 (d, C-5)*, 126.05 (s, C-4), 133.62 (d, C-15), 135.68 (s, C-9), 137.82 (s, C-2), 164.62 (s, CO_2CH_3), 164.84 (s, C-11).

32. **9b**: 4.2% fine needles with mp 200-202 °C; IR(KBr): $\tilde{\nu}$ = 3044 cm^{-1}, 2942, 1723, 1687, 1531; UV (CH_3CN): λ_{max} (lg ϵ) = 217 nm (4.686), 230 (4.475), 250 (sh, 3.927), 290 (4.189), 297 (sh, 4.097); ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.46 ppm (dd, J_1 = 5.5 Hz, J_2 = 8.5 Hz, 1H, H-4'a), 2.10 (dddd, J_1 = 1.5 Hz, J_2 = 2.3 Hz, J_3 = 3.6 Hz, J_4 = 14.0 Hz, 1H, H-6'b), 2.16 (dd, J_1 = 5.5 Hz, J_2 = 5.9 Hz, 1H, H-4'b), 2.15-2.27 (m, 1H, H-5'), 2.84 (dddd, J_1 = 2.8 Hz, J_2 = 6.1 Hz, J_3 = 13.3 Hz, J_4 = 14.0 Hz, 1H, H-6'a), 3.83 (s, 3H, NCH_3), 3.93 (s, 3H, CO_2CH_3), 4.27 (ddd, J_1 = 3.6 Hz, J_2 = 11.9 Hz, J_3 = 13.3 Hz, 1H, H-7'b), 4.46 (dddd, J_1 = 1.4 Hz, J_2 = 1.5 Hz, J_3 = 6.1 Hz, J_4 = 11.9 Hz, 1H, H-7'a), 7.21-7.35 (m, 3H, H-6, H-7, H-8), 8.09-8.12 (m, 1H, H-5); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 17.22 ppm (t, C-4'), 20.76 (t, C-6'),22.43 (s, C-3'), 25.42 (d, C-5'), 30.84 (q, NCH_3), 50.96 (q, CO_2CH_3), 65.37 (t, C-7'), 105.78 (s, C-3), 109.57 (d, C-8), 122.02 (d, C-7)*, 122.10 (d, C-6)*, 123.04 (d, C-5)*, 125.93 (s, C-4), 136.62 (s, C-9), 144.33 (s, C-2), 165.35 (s, CO_2CH_3), 169.62 (s, CO_2R, C-2'); $C_{17}H_{17}NO_4$: Calc. 299.1158 Found 287.1157 (MS).

33. **11**: Yellow prisms with mp 176-180 °C; IR (KBr): $\tilde{\nu}$ = 3049, 1755, 1728, 1712, 1620; UV (CH_3CN): λ_{max} (lg ϵ) = 201 nm (4.551), 214 (4.452), 250 (sh, 4.385), 259 (4.471), 288 (4.788), 380 (3.893); ^{1}H NMR (90 MHz, $CDCl_3$): δ = 3.78 ppm (s, 3H, NCH_3), 4.41 (s, 3H, Ar- OCH_3), 4.93-5.10 (m, 2H, CO_2CH_2R), 5.20-5.60 (m, 2H, $CH{=}CH_2$), 5.90-6.43 (m, 1H, $CH{=}CH_2$), 7.17-

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