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The 1,3-Carbalkoxy Shift. An Unusual Photorearrangement

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Abstract: *Irradiation of the 2-oxoindeno[1,7-bc]furan-6-carbonitrile* **1** *in protic solvents with light of 254 nm induces a 1,3-carbalkoxy shift Supported by X-ray analyses of* **2** *and* **3a** *it could be shown that the resulting 3,7-dioxo-3H-1,3a-ethano-isobenzofuran-9-carbonitriles* **2** *and* **3** *are distinguished by the sterical arrangement of the substituents at C-atom 9 In MeOH 9α-carbonitrile* **2** *and in t-BuOH 9β-carbonitrile* **3** *is the main product In contrast to t-BuOH the primary reaction in MeOH is overlapped by typical ketone photochemistry of the newly formed 7-oxo group Lack of any photoreaction of* **1** *in aprotic solvents indicates an ionic mechanism rather than the involvement of free radicals All new compounds were fully characterized by* ^1H *and* ^{13}C *NMR and the assignments supported by NOE and* ^1H*-detected one-bond and multiple-bond* $^1H,^{13}C$*-COSY*

INTRODUCTION

In literature there are only two examples concerning photorearrangements of cyclic conjugated carbonitriles Proceeding from their π,π^* singlet excited state cyclohexene-1-carbonitriles yield as major products the corresponding bicyclo[3 1 0]-1-carbonitriles[1] and 2-cyanonorbornene gives bicyclo[4.1 0]hept-2-ene-1-carbonitrile[2] In both cases the 1,3-migration of a σ-bond is involved This carbon-to-carbon migration finds its analogue in the photorearrangement of 2-diphenylmethylenefenchane which has been interpreted as a photochemical Wagner-Meerwein rearrangement[3], a process which in ground-state chemistry is characteristic of an electron-deficient carbon Nevertheless, based on the fact that the reactions were performed in the aprotic solvent hexane, a rationale involving free-radical intermediates was proposed for the photorearrangements of the conjugated carbonitriles mentioned above[1] On the other hand, free-radical chemistry may become admixed with ionic chemistry when photoreactions of that type are performed in protic solvents[4] The therefrom arising mechanistic question concerns the comparison of concomitant homolytic and heterolytic cleavage *vs* a sequential mechanism wherein electron transfer occurs within an initially formed radical pair We now report on a novel 1,3-carbalkoxy shift exhibiting a solvent dependence which could furnish a valuable contribution to this problem

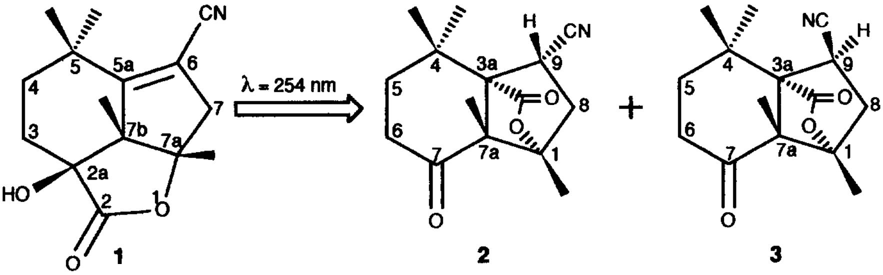
RESULTS

The 2-oxoindeno[1,7-bc]furan-6-carbonitrile **1** was prepared by reaction of 4-oxo-β-ionone with 2 eq NaCN in MeOH and subsequent acid catalyzed hydrolysis of the resulting imine[5]. Compared with other compounds which contain the same chromophore the absorption maximum of the tricyclic **1** exhibits a remarkable bathochromic shift with an absorption coefficient ε_{max} in the order of magnitude of cyclohexene-1-carbonitrile (Tab 1)

Table 1. UV-Absorption of Conjugated Carbonitriles

Compound	λ_{max} /nm (EtOH)	log ε_{max}
Acrylonitrile	215	1 69
Methacrylonitrile	215	2 83
Cyclohexene-1-carbonitrile	212	4 05
Compound **1**	223	4 10

Irradiation of **1** with 254 nm light in protic solvents induced a hitherto unknown photochemical 1,3-carbalkoxy shift (Scheme 1), whereas in the aprotic solvent 1,4-dioxane no reaction occurred (Tab 2) Furthermore, **1** dissolved in 2-propanone remained unchanged when the solution was irradiated with light of 313 nm Thus, the ketone was not able to photosensitize the 1,3-carbalkoxy shift

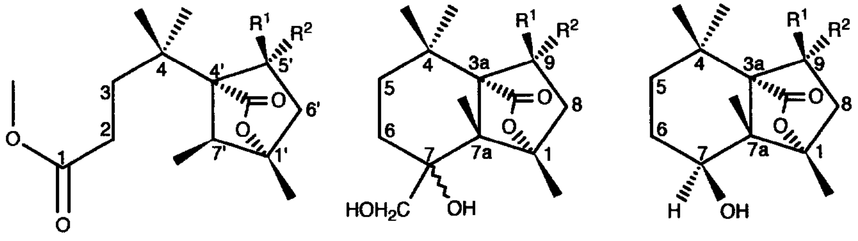


Scheme 1
Photochemical 1,3-carbalkoxy shift

Table 2. Solvent Dependent Yields of **2** and **3**

Solvent	**2** %	**3** %
1,4-dioxane	0.0	0.0
MeOH	65.5[6]	4.9[6]
t.-BuOH	5.7	64.9

With increasing concentrations the photochemically formed ketones **2** and **3** competed with **1** in the light absorption. This led in methanolic solution to further reactions which are characteristic for ketone photochemistry and which overlapped the original photorearrangement of **1**. In contrast to the irradiation in MeOH, in t.-BuOH no secondary reactions were observed. Main reaction of the photoexcited ketones **2** and **3** was the Norrish type I cleavage of their C(7)-C(7a) bond and addition of MeOH to the intermediate ketenes, hereby forming the methyl esters **2a** and **3a**. Minor products in this reaction mixture were the MeOH adduct **2b** and the 7-hydroxy compound **2c** (Fig. 1). After having performed the photorearrangement of **1** in t.-BuOH, the main product **3** was isolated and again irradiated in MeOH yielding the corresponding photoproducts **3a-c** with a stereochemistry on C(9) analogous to **3** (Fig. 1).



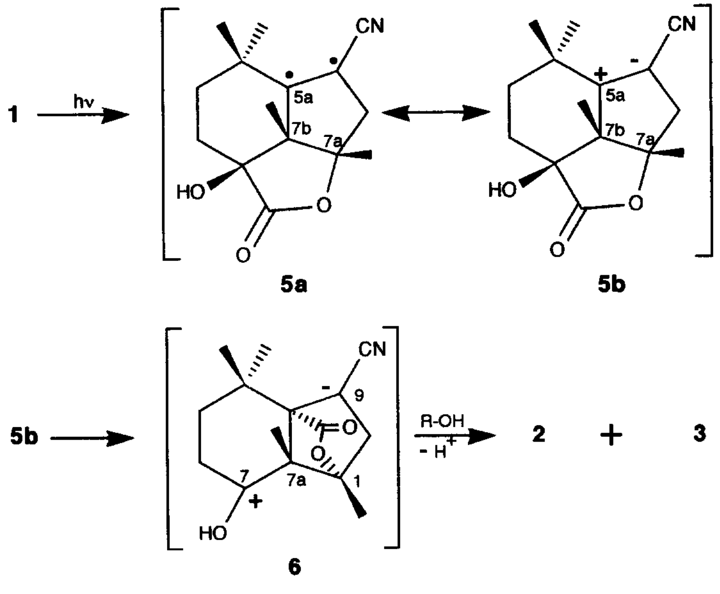
2a,3a **2b,3b** **2c,3c**

Figure 1 Products of the ketone photochemistry
2a-c: R^1=H, R^2=CN. **3a-c** R^1=CN; R^2=H

The structures of the compounds **2**, **3**, **2a-c**, and **3a-c** were elucidated by means of spectroscopic methods (^1H, ^{13}C NMR, NOE, MS, IR) supported by single-crystal X-ray diffraction analyses of the photoproducts **2** and **3a**. In **2b** and **3b** the sterical arrangement of CH_2OH and OH on C(7) could not be unambiguously assigned. But the $\delta(OCH_2)$-values in the corresponding ^{13}C-NMR spectra indicate an identical stereochemistry for the substituents on C(7) of **2b** and **3b**.

DISCUSSION

In contrast to the known photorearrangements of cyclic conjugated carbonitriles where free-radical intermediates are assumed[1,2], we have evidence that ionic chemistry is involved in the photoreaction of **1**. The carbalkoxy migration to C(5a) strongly suggests that this carbon has become electron deficient on excitation and that ionic resonance structure **5b** is a major contributor to the reactive excited state (Scheme 2) Furthermore, the lack of any photoreaction of **1** in the aprotic solvent 1,4-dioxane supports the assumption of an ionic mechanism which is rather the exception in photochemistry The fact that photoexcited acetone fails to sensitize the novel rearrangemant also fits into this picture Certainly, the existing experimental results are not suitable to decide if the rearrangement starts with protonation of the cyano group bearing C-atom of photochemically excited **1** (e.g of **5b**) or with the proposed 1,3-carbalkoxy shift proceeding *via* the dipolar structure **6** (Scheme 2) The preponderance of **2** over **3** in MeOH and of **3** over **2** in t-BuOH (Tab 2) may be due to the sterical arrangement of the methyl groups on C(7a) and C(7b) of **1** which allows protonation with MeOH from above but prevents the bulky t.-BuOH to approach from the same side, consequently producing the inverse configuration C(9)-H_α with **3** (Scheme 1)



Scheme 2

Proposed mechanism for the photochemical 1,3-carbalkoxy shift

EXPERIMENTAL PART

General

All compounds are racemates UV spectra were recorded on an Uvikon 860 from Kontron All NMR spectra were acquired on AM-400 and WH-270 Bruker FT-NMR spectrometers using DMSO-d_6 as solvent Corresponding experimental details and the pulse sequences used as well as further general remarks were described in the preceding paper[5]

Materials

2,2a,3,4,5,7a,7b-Octahydro-2aβ-hydroxy-5,5,7aβ,7bβ-tetramethyl-2-oxoindeno[1,7-bc]furan-6-carbonitrile (**1**) was prepared according to the previously described procedure[5] All solvents used were puriss and obtained from Fluka

Light sources

High-intensity low-pressure Hg-lamp XI-2-70 from ABB (Baden/Switzerland)
Low-pressure Hg-lamp NK 6/20 from Heraeus (Hanau/FRG)
High-pressure Hg-lamp TQ 150 from Heraeus (Hanau/FRG.)

Table 3. Characteristic Data of the Applied Light Sources

Lamp	Electrical power input [w]	Relevant light emission [Einstein h^{-1}]		
		254 nm	302 nm	313 nm
XI-2-70	1500	3 8 x 10^{-1}	6 8 x 10^{-3}	3 5 x 10^{-2}
NK6/20	10	6 9 x 10^{-3}	3 3 x 10^{-5}	2 4 x 10^{-4}
TQ 150	150	1 6 x 10^{-2}	5 0 x 10^{-3}	1 7 x 10^{-2}

Irradiation Experiments

1 Through the photoreactor and an external heat exchanger a solution of **1** (35 g, 0 14 mol) in 5.5 L MeOH was circulated by a pump Using a XI-2-70 lamp its irradiation was performed under N_2 at 20 - 22° C for 1 h Then the volume was reduced at 45° C *in vacuo* to 150 ml, chilled to 0° C and filtered after 2 h. The precipitated **2** was washed with MeOH of 0° C and dried The mother liquor was subjected to repeated medium pressure chromatography on silica gel (pre-packed columns LiChroprep Si 60, 40 - 63 µm from Merck) with dichloromethane/2-propanone mixtures 98:2 and 95 5, respectively The amounts of the isolated compounds are given in Tab.4. Considering the

recovered 1 41 g **1** and the molecular weights of the photoproducts the yields (given in brackets) are expressed in percent of the actually converted 33 59 g **1**.

Table 4 Experiment 1 Amounts (in g) of the Isolated Compounds

1	**2**	**2a**	**2b**	**2c**	**3**	**3a**
1 41	16 95 (50 5%)	4 65 (12 3%)	0 48 (1 3%)	0 50 (1 5%)	1.05 (3.1%)	0 65 (1 7%)

Analytical Data for the Products 2, 2a-c, 3, and 3a

1β,4,4,7aβ-Tetramethyl-3,7-dioxo-1,4,5,6,7,7a-hexahydro-3H-1,3a-ethano-isobenzofuran-9α-carbonitrile (2).

M p 207° C (from MeOH) (Found C,68.79; H,7 26, N,5 35 $C_{15}H_{19}NO_3$ requires C,68 94, H,7 33, N,5 36%). IR ν_{max}/cm^{-1} 2247 (CN), 1776 (5-ring lactone C=O), 1714 (ketone C=O), ^{1}H-NMR δ 1 201 (3H, s, 7aβ-Me), 1 249 (3H, s, 4β-Me), 1.431 (3H, s, 4α-Me), 1 589 (3H, s, 1β-Me), 1 619 (1H, d x d, J ~14, 5.5, 5β-H), 1 904 (1H, d x d, J 14, 4.5, 9α-H), 1.970 (1H, t x d, J ~15, ~5, 5α-H), ~2 035 (1H, d x d, J ~15, ~5, 6β-H), 2 441 (1H, d x d, J 14, 10.7, 8β-H), 2 978 (1H, d x d x d, J 15, 14, ~7, 6α-H), 4 025 (1H, d x d, J 10.5,4 5, 9β-H)

Relevant 1D NOE difference results

Irradiation at		Enhancement (in %)			
7aβ–Me	(1.201 ppm)	9β-H 10,	8β-H 5 4,	6β-H ~3 6,	1β-Me ~1,
4β-Me	(1.249 ppm)	9β-H 11,	6β-H 5 4;	5β-H ~4.5,	4α-Me 1 8
4α-Me	(1 431 ppm)	5α-H 3,	9β-H 1 8	4β-Me 1 8	
1β-Me	(1 589 ppm)	8β-H 8,	7aβ-Me ~1		

^{13}C-NMR: Assignment by DEPT-135, ^{1}H-detected one-bond and multiple-bond ^{1}H,^{13}C-COSY
δ 13.86 (1-Me), 14.71 (7aβ-Me), 22.87 (4β-Me), 24.84 (4α-Me), 23 24 (9-C), 33.26 (4-C), 35 75 (6-C), 36.49 (5-C), 39.41 (8-C), 62.80 (7a-C), 64.20 (3a-C), 88.59 (1-C), 120 54 (CN), 172 48 (3-C), 209.00 (7-C) MS m/z 217 (48), 202 (24), 190 (26), 162 (30), 161 (39), 160 (21), 148 (17), 147 (79), 146 (28), 138 (17), 137 (21), 134 (24), 121 (18), 120 (16), 119 (26), 91 (24), 79 (17), 77 (22), 69 (29), 67 (17), 55 (33), 53 (23), 43 (100), 41 (65), 39 (35), 29 (27). CI (NH_3) 279 [$(M + NH_4)^+$, 100], 262 [$(M + H)^+$, 4] Exact mass calcd. for $C_{15}H_{19}NO_3$ 261 32

X-Ray Crystallographic Structure Determination of **2**

Crystal size 0.35 x 0.35 x 0 4 mm^3. Data were collected on a Nicolet R3m four circle Diffractometer fitted with a graphite monochromator amd the LT1 cooling apparatus. Scan mode omega, scan speed 1 2° min^{-1}, minimum speed Strong reflections were measured up to 15 0°/ min^{-1}, scan width 0.9°. 2Θ range 0 - 50°. Peak-background ratio 5 1 Total reflections observed 1997; rejection criterion $I > 2.5\sigma(I)$ Structure determination and refinement: The structure was determined by direct methods using SHELXTL-86 system[7] Refinement proceeded smoothly to convergence at R = 0.039 with anisotropic refinement of all non-H atoms Weights $w = 1/\sigma^2(F) + 0, 01\, |F|^2$

Crystal data $C_{15}H_{19}NO_3$, M = 261 32, monoclinic, space group $P2_1/c$, a = 6 317(3), b = 12 328(4), c = 16.987(6) Å, β = 97.03(3)°, Z = 4, D = 1 30 g cm^{-3}, μ(Mo-K$_a$) = 0 09 mm^{-1}, F(000) = 560, λ = 0 71069 Å, T = 190 K

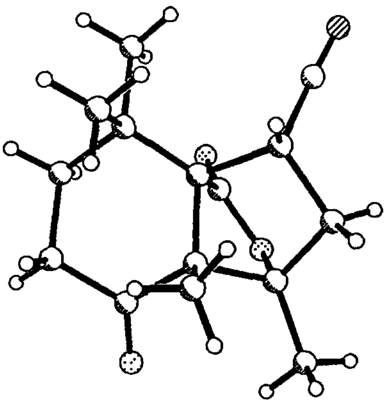


Figure 2 Projection of **2**

4-(5'α-Cyano-1'β,7'β-dimethyl-3'-oxo-2'-oxabicyclo[2.2.1]hept-4'β-yl)-4-methyl-pentanoic acid methyl ester (2a)

Oil (Found C,65.48, H,8 00, N,4 72 $C_{16}H_{23}NO_4$ requires C,65.51, H,7.90, N,4 77%) IR. ν_{max}/cm^{-1} 2240 (CN), 1772 (5-ring lactone C=O), 1736 (ester C=O) ^{1}H-NMR δ 0.938 (3H, d, J 6 9, 7'β-Me), 1 055 and 1 145 (2 x 3H, 2s, 2 x 4-Me), 1 375 (3H, s, 1'β-Me), 1 810 (2H, m, 3-CH$_2$), 1 951 (1H, d x d x q, J 14, 4, ~1, 6'α-H), 2.346 (2H, m, 2-CH$_2$), 2.370 (1H, q x d, J ~7, 1, 7'α-H), 2.463 (1H, d x d, J 14, 11, 6'β-H), 3 590 (3H, s, MeO), 3 962 (1H, d x d, J 10.7, 4, 5'β-H)

Relevant 1D NOE difference results·

Irradiation at		Enhancement (in %)					
7'β-Me	(0 938 ppm)	5'β-H	4 5,	6'β-H	2 8		
		4-Me (1 055 ppm)	2 2,	4-Me (1.145 ppm)	1 9,	1'β-Me	1 1
4-Me	(1 055 ppm)	5'β-H	6 8,	2-CH_2	2 8		
4-Me	(1,145 ppm)	5β-H	5 7,	2-CH_2	~ 3,	3-CH_2	~ 1
		4-Me (1 055 ppm)	0 6				

^{13}C-NMR Assignment by DEPT-135, ^{1}H-detected one-bond and multiple-bond $^{1}H,^{13}C$-COSY δ 10 94 (7'β-Me), 15.24 (1'-Me), 22 31 and 22 63 (2 x 4-Me), 24 69 (5'-C), 28.46 (2-C), 32 51 (3-C), 34 88 (4-C), 39 95 (6'-C), 50 81 (7'-C), 51 41 (MeO), 63.96 (4'-C), 87 86 (1'-C), 121 69 (CN), 173 72 (1-CO), 173.93 (3'-CO) MS m/z 262 (8), 234 (16), 207 (33), 189 (11), 164 (26), 162 (24), 139 (19), 135 (66), 129 (32), 121 (18), 97 (56), 94 (27), 93 (23), 69 (91), 59 (24), 55 (64), 53 (22), 43 (100), 41 (84), 39 (25), 29 (26), CI (NH_3) 311 [(M + NH_4)$^+$, 100], 279 [(M + NH_4) - MeOH, 20] Exact mass calcd for $C_{16}H_{23}NO_4$ 293.36

7-Hydroxy-7-hydroxymethyl-1β,4,4,7aβ-tetramethyl-3-oxo-1,4,5,6,7,7a-hexahydro-3H-1,3a-ethano-isobenzofuran-9α-carbonitrile (2b).

M.p. 119 5° C (from CH_2Cl_2/ethyl acetate) (Found· C,65 31, H,7 85; N,4 73 $C_{16}H_{23}NO_4$ requires C,65 51; H,7 90; N,4.77%) ν_{max}/cm^{-1} 3473 (OH), 2240 (CN), 1758 (5-ring lactone C=O). ^{1}H-NMR. δ 1.012 (3H, s, 7aβ-Me), 1.049 (3H, s, 4β-Me), 1.195 (1H, d x t, J 13 7, 3 5, 5β-H), 1 369 (3H, s, 4α-Me), 1 420 (1H, t x d, J ~13 5, ~2, 6α-H), 1.442 (3H, s, 1β-Me), 1 536 (1H, t x d, J 14, 3 5, 5α-H), 1 798 (1H, d x d, J 13 5, 4, 8α-H), 1 832 (1H, d x t, J 13, 3, 6β-H), 2 386 (1H, d x d, J 13 5, 10 5, 8β-H), 3 400 and 3 477 (1H, d x d, J 11 3, 5 and 1H, d x d, J 11 3, 6, 7-CH_2OH), 3 841 (1H, d x d, 10 5, 4 5, 9β-H), 4 269 (1H, s, 7-HO), 4 809 (1H, d x d, HO-CH_2)

Relevant 1D NOE difference results

Irradiation at		Enhancement (in %)							
7aβ-Me	(1 012 ppm)	9β-H	13 5,	8β-H	7 1,	7-OH	5 8;	1β-Me	1 7
4β-Me	(1.049 ppm)	9β-H	10	5β-H	3 2,	4α-Me	2.6		
4α-Me	(1 369 ppm)	4β-Me	1 9						
1β-Me	(1 442 ppm)	CH_2 (3.400 ppm)	4 7,	7-OH	2 6;	7aβ-Me	1 6		

^{13}C-NMR Assignments by DEPT-135, ^{1}H-detected one-bond and multiple-bond $^{1}H,^{13}C$-COSY δ 13 76 (1-Me), 15 84 (7aβ-Me), 23 84 (4β-Me), 24 72 (9-C), 25 45 (4α-Me), 27 17(6-C), 32 91 (4-C), 35 37 (5-C), 40 66 (8-C), 59 58 (7a-C), 61 41 (3a-C), 62.32 (CH_2OH), 75 55 (7-C), 89.27 (1-C), 121 15 (**CN**), 174 45 (3-**CO**) MS m/z 262 (49), 234 (13), 218 (52), 216 (60), 152 (17), 138 (25), 129 (27), 93 (19), 91 (18), 69 (36), 55 (41), 43 (100), 41 (53), 31 (20) CI (NH_3) 311 [$(M + NH_4)^+$, 100],, 299 [$(M + NH_4) - H_2O$, 19], 279 (20), 277 (20) Exact mass calcd for $C_{16}H_{23}NO_4$: 293 36

7β-Hydroxy-1β,4,4,7aβ-tetramethyl-3-oxo-1,4,5,6,7,7a-hexahydro-3H-1,3a-ethano-isobenzofuran-9α-carbonitrile (2c).

M.p 204° C (from acetone/hexane) (Found C,68 12, H,8 00, N,5.22 $C_{15}H_{21}NO_3$ requires C,68 42, H,8 04, N,5 32%) IR ν_{max}/cm^{-1} 3478 (OH), 2240 (CN), 1757 (5-ring lactone C=O), 1046 ^1H-NMR δ 0 901 (3H, s, 7aβ-Me), 0 986 (3H, s, 4β-Me), 1 231 (1H, ~d x t, J 13, ~2, 5β-H), 1 326 (3H, s, 4α-Me), 1 387 (3H, s, 1β-Me), ~1 52 (2H, m, 6-CH_2), ~1.622 (1H, m, 5α-H), 1 845 (1H, d x d, J 14, 4 4, 8α-H), 2 421 (1H, d x d, J 13 7, 10 5, 8β-H), 3 565 (1H, d x d x d, J 9, 6 5, 5.5, 7α-H), 3 840 (1H, d x d, J 10 5, 4 2, 9β-H), 4 908 (1H, d, J 5.4, 7β-OH)

Relevant 1D NOE difference results

Irradiation at		Enhancement (in %)
7aβ-Me	(0 901 ppm)	9β-H 11 6, 8β-H 5 4, 7β-OH 3 6, 1β-Me 1 5, 4β-Me 1 5
4β-Me	(0 986 ppm)	9β-H 11, 4α-Me ~2, 7aβ-Me ~1
4α-Me	(1 326 ppm)	9β-H ~2, 4β-Me ~3
1β-Me	(1 387ppm)	7β-OH 3, 7β-H ~3, 8β-H ~3, 7α-H ~3
9β-H	(3 840 ppm)	8β-H 4 5, 7aβ-Me 2 1; 4β-Me 1 8

^{13}C-NMR Assignment by DEPT-135, ^1H-detected one-bond and multiple-bond $^1H,^{13}C$-COSY δ 11 11 (7aβ-Me), 13 97 (1-Me), 23 28 (4β-Me), 24 40 (9-C), 25 26 (4α-Me), 28.03 (6-C), 33 08 (4-C), 35 64 (5-C), 39 47 (8-C), 56 98 (7a-C), 62 28 (3a-C), 67 41 (7-C), 88 90 (1-C), 121 17 (**CN**), 174 19 (3-C). MS m/z 204 (45), 163 (33), 148 (18), 139 (59), 136 (23), 121 (17), 120 (20), 81 (19), 69 (21), 57 (16), 55 (28), 53 (16), 43 (100), 41 (46), 39 (19), 29 (24) CI (NH_3) 281 [$(M + NH_4)^+$, 100] Exact mass calcd for $C_{15}H_{21}NO_3$ 263 34

1β,4,4,7aβ-Tetramethyl-3,7-dioxo-1,4,5,6,7,7a-hexahydro-3H-1,3a-ethano-isobenzofuran-9β-carbonitrile (3).

M p 188° C (from CH_2Cl_2/acetone) (Found C,68.74, H,7.49, N,5 39 $C_{15}H_{19}NO_3$ requires C,68 94, H,7 33, N,5 36%) IR ν_{max} 2238 (CN), 1765 (5-ring lactone C=O), 1720 (ketone C=O) ^1H-NMR δ 1 406 (3H, s, 4α-Me), 1 451 (3H, s, 7aβ-Me), 1 549 (3H, s, 4β-Me), ~1 562 (1H, m, 5β-H), 1 630 (3H, s, 1β-Me), 2 010 (1H, d x d x d, J ~14 3, 14, 5, 5α-H), ~2 080 (1H, d x m, 6β-H), ~2.087 (1H, d x d, J 14, 9, 8α-H), ~2 350 (1H, d x d, J ~14, 5 5, 8β-H), 3.010 (1H, d x d x d, J 16, 14, 7 9, 6α-H), 3.581 (1H, d x d, J 9, 5.5, 9α-H)

Relevant 1D NOE difference results

Irradiation at		Enhancement (in%)							
4α-Me	(1 406 ppm)	9α-H	8 1,	5α-H	3,	4β-Me	3		
7aβ-Me	(1 451 ppm)	8β-H	5.1,	6β-H	3.7,	4β-Me	2.2,	1β-Me	1 5
4β-Me	(1 549 ppm)	6α-H	9,	6β-H	6,	4α-Me	~3,	7aβ-Me	~3
1β-Me	(1.630 ppm)	8α,β-H	~2,	7aβ-Me	1.5				

^{13}C-NMR. Assignment by DEPT 135, ^{1}H-detected one-bond and multiple-bond ^{1}H,^{13}C-COSY δ 13.99 (1-Me), 15.23 (7aβ-Me), 22 82 and 24 38 (2 x 4-Me), 23.52 (9-C), 33 39 (4-C), 36.01 (6-C), 36.98 (5-C), 39.30 (8-C), 62.80 (7a-C), 63 16 (3a-C), 89.33 (1-C), 121.13 (**CN**), 173 35 (3-C), 209.22 (7-C) m/z 217 (77), 202 (21), 162 (34), 161 (34), 148 (17), 147 (90), 146 (27), 139 (16), 138 (20), 137 (19), 134 (23), 121 (21), 120 (18), 119 (27), 91 (26), 81 (16), 79 (19), 77 (24), 69 (32), 67 (17), 65 (17), 55 (36), 53 (27), 43 (100), 41 (68), 39 (37), 29 (24) CI (NH_3) 279 [(M + NH_4)$^+$, 100] Exact mass calcd. for $C_{15}H_{19}NO_3$ 261.32

4-(5'β-Cyano-1'β,7'β-dimethyl-3'-oxo-2'-oxabicyclo[2.2.1]hept-4'β-yl)-4-methylpentanoic acid methyl ester (3a).

M.p.121° C (from CH_2Cl_2/acetone) (Found· C,65.51, H,8.03, N,4.79. $C_{16}H_{23}NO_4$ requires C,65.51; H,7.90; N,4.77%). IR: ν_{max} 2238 (CN), 1776 (5-ring lactone C=O), 1731 (ester C=O) ^{1}H-NMR. δ 1 157 and 1.206 (2 x 3H, 2s, 2 x 4-Me), 1 198 (3H, d, J 7, 7'β-Me), 1 425 (3H, s, 1'β-Me), ~1.81 and ~2 10 (both signals broadened due to hindered rotation, 2 x 1H, 4-CH_2), ~2.272 (1H, d x d, J ~13.6, 5 8, 6'β-H), ~2.330 (1H, m, 6'α-H, overlapped with m, 2-CH_2), 2.430 (1H, ~q , J 6 8, 7'α-H), 3.465 (1H, d x d, J 9, 5.7, 5'α-H), 3.595 (3H, s, MeO) ^{13}C-NMR: Assignment by ^{1}H-detected one-bond and multiple-bond ^{1}H,^{13}C-COSY δ 11.57 (7'β-Me), 15.19 (1'-Me), 22 12 and 22 84 (broad, 2 x 4-Me), 25.76 (5'-C), 28.34 (2-C), 32.13 (very broad, 3-C), 34.83 (4-C), 38 52 (6'-C), 49.82 (7'-C), 51.36 (MeO), 63.39 (4'-C), 88.42 (1'-C), 121.86 (**CN**), 173.65 (1-**CO**), 174 50 (3'-**CO**) MS: m/z 234 (16), 217 (18), 208 (16), 202 (20), 164 (22), 162 (30), 161 (21), 139 (26), 136 (16), 135 (77), 129 (31), 121 (21), 120 (21), 107 (21), 97 (38), 94 (24), 93 (25), 91 (21), 79 (20), 77 (20), 69 (87), 67 (21), 59 (22), 55 (65), 53 (21), 43 (100), 41 (82), 39 (24), 29 (26). CI (NH_3) 311 [(M + NH_4)$^+$, 100], 294 [(M + H)$^+$, 73], 279 [(M + NH_4) - MeOH, 31]. Exact mass calcd. for $C_{16}H_{23}NO_4$· 293 36.

X-Ray Crystallographic Structure Determination of **3a**.

Crystal size 0.28 x 0.38 x 0.38 mm^3 Data were collected on the above described apparatus. Scan mode omega; scan speed 3.26° min^{-1}, minimum speed. Strong reflections were measured up to 15° min^{-1}, scan width 1.2° 2Θ range 0 - 56° Peak-background ratio 5 1 Total data measured· 2086 excluding standards Total reflections observed 1788, rejection criterion $I > 2.5\sigma(I)$. Structure determination and refinement: The structure was determined by direct methods using SHELXTL-86 system[7] Refinement proceeded smoothly to convergence at R = 0 05 with anisotropic refinement of all non-H atoms. Number of parameters: 190; weights $w = 1/\sigma^2(F) + 0\ 002\ |F|^2$.

Crystal data. $C_{16}H_{23}NO_4$, M = 293 36, monoclinic, space group $P2_1$, a = 9 622(2), b = 6 593(1), c = 11 993(2) Å, β = 90 49°, Z = 2, D = 1 211 g cm^{-3}, $\mu(Mo\text{-}K_\alpha)$ = 0 086 mm^{-1}, F(000) = 316, λ = 0 71069 Å, T = 190 K.

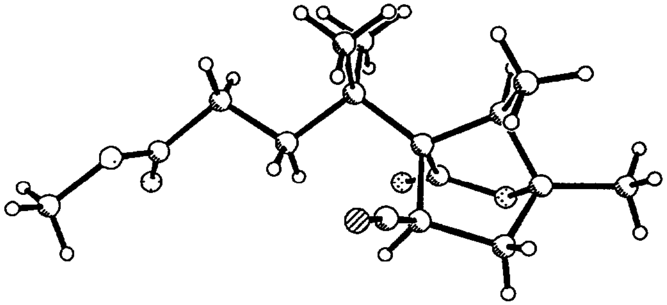


Figure 3 Projection of **3a**.

2 A solution of **1** (2 g, 7.65 mmol) in 250 ml t.-butanol was irradiated under N_2 with the lamp NK 6/20 at 40° C for 9 h. The irradiation solutions of 12 identical experiments were combined and the solvent was evaporated *in vacuo*. Then the residue was dissolved in boiling MeOH, chilled to 0° C, and filtered after 2 h The precipitate was washed with MeOH of 0° C and dried to give 13 46 g **3** To the reduced mother liquor (150 ml) 25 ml dichloromethane were added From this mixture crystallized after chilling 1 18 g **1** The second mother liquor was also evaporated to dryness. The residue was dissolved in dichloromethane and subjected to medium pressure chromatography on silica gel (see above) with dichloromethane as eluent The amounts of the compounds isolated by crystallization and by chromatography are given in Tab 4 Considering the recovered 1.18 g **1** and the fact that the molecular weight remains constant the yields of **2** and **3** (given in brackets) are expressed in percent of the actually converted 22 82 g **1**

Table 5 Experiment 2. Amounts (in g) of the Isolated Compounds

1	**2**	**3**
1 18	1 30 (5 70%)	14 79 (64 81%)

3 A solution of **3** (2 g, 7 65 mmol) in 250 ml MeOH was irradiated under N_2 with the lamp TQ 150 through 1 5 mm pyrex glass at 20° C for 24 h Then the solvent was evaporated to dryness and the in dichloromethane dissolved residue was subjected to medium pressure chromatography on silica gel (see above) using dichloromethane with 0 to 4% 2-propanone as eluent The amounts of the isolated compounds are given in Tab 5 The yields of **3a-c** (given in brackets) are expressed in percent of the actually converted 1 55 g **3** considering the recovered 0 45 g **3** and the respective molecular weights of the products

Table 6 Experiment 3 Amounts (in g) of the Isolated Compounds

3	**3 a**	**3 b**	**3 c**
0 45	1.30 (74 7%)	0 14 (8 1%)	0 11 (7 0%)

Analytical Data for the Products 3b and 3c.

7-Hydroxy-7-hydroxymethyl-1β,4,4,7aβ-tetramethyl-3-oxo-1,4,5,6,7,7a-hexahydro-3H-1,3a-ethano-isobenzofuran-9β-carbonitrile (3b)

M p 190° C (from CH_2Cl_2). (Found C,65 40, H,7.86, N,4 74 $C_{16}H_{23}NO_4$ requires C,65 51, H,7 90, N,4 77%) IR ν_{max}/cm^{-1} 3494 (OH), 2236 (CN), 1760 (5-ring lactone C=O) ^{1}H-NMR δ 1 150 (1H, m,5β-H), 1 301 (3H, s, 7aβ-Me), 1 323 (s, 4α-Me), 1 365 (3H, s, 4β-Me), ~1 480 (1H, m, 6α-H), 1 485 (3H, s, 1β-Me), 1 545 (1H, t x d, J ~13, ~1 5, 5α-H), 1 863 (1H, m, 6β-H), 2 217 (1H, d x d, J 13, 6, 8β-H), 2.260 (1H, d x d, J 13, 8 7, 8α-H), 3 367 (2H, m, **H_2C-OH**) overlapped with ~3.392 (1H, d x d, J 8 5, 6 2, 9α-H), 4 306 (1H, s, 7-**OH**), 4 811 (1H, d, J 5 5, CH_2-**OH**)

Relevant 1D NOE difference results

Irradiation at		Enhancement (in %)		
4α-Me	(1 323 ppm)	9α-H 7 5,	4β-Me ~3	
4β-Me	(1 365 ppm)	9α-H ~3,	4α-Me >0,	7aβ-Me >0
1β-Me	(1 485 ppm)	**CH_2**-OH ~2 5,	7-**OH** ~2 5,	8α,β-H >0

^{13}C-NMR Assignments by ^{1}H-detected one-bond and multiple-bond ^{1}H,^{13}C-COSY δ 13 69 (1-Me), 16 43 (7aβ-Me), 24 09 (4β-Me), 24 63 (9-C), 25 23 (4α-Me), 27 30 (6-C), 33 43 (4-C), 36 34 (5-C), 40 57 (8-C), 59 62 (7a-C), 61 28 (3a-C), 62 52 (**CH_2OH**), 75 41 (7-C), 89 72 (1-C), 121 77 (**CN**), 175 27 (3-**CO**) MS m/z 262 (43), 234 (16), 218 (47), 217 (18), 216 (84), 153 (20), 152 (19), 138 (26), 135 (18), 129 (30), 93 (20), 91 (119), 77 (17), 69 (35), 67 (15), 55 (40), 53 (16), 43 (100), 41

(51), 39 (19), 31 (23), 29 (23) CI (NH_3) 311 [$(M + NH_4)^+$, 100], 299 [$(M + NH_4) - H_2O$, 18], 279 (25) Exact mass calcd for $C_{16}H_{23}NO_4$ 293 36

7β-Hydroxy-1β,4,4,7aβ-tetramethyl-3-oxo-1,4,5,6,7,7a-hexahydro-3H-1,3a-ethano-isobenzofuran-9β-carbonitrile (3c)

M.p 168° C (from CH_2Cl_2) (Found C,68 23, H,8.02, N,5 24 $C_{15}H_{21}NO_3$ requires C,68 42, H,8.04, N,5 32%) IR: ν_{max}/cm^{-1} 3499 (OH), 2240 (CN), 1758 (5-ring lactone C=O) ^{1}H-NMR δ 1 180 (3H, s, 7aβ-Me), ~1 194 (1H, m, 5β-H), 1 293 (6H, s, 2 x 4-Me), 1 419 (3H, s, 1β-Me), ~1 55 (2H, m, 6-H_2C), 1 633 (1H, m, 5α-H), ~2 243 (1H, d x d, J 13 7, 6, 8β-H), ~2 285 (1H, d x d, J 13 8, 8 7, 8α-H), 3 404 (1H, d x d, J 8 7, 6, 9α-H), 3 530 (1H, m, 7α-H), 4 937 (1H, d, J 5 5, 7β-OH)

Relevant 1D NOE difference results

Irradiation at		Enhancement (in %)			
7aβ-Me + 5β-H	(1 180 ppm)	4-Me ~5,	7β-OH 3 5,	7aβ-Me 1 5,	(5α-H ~15)
4α-Me + 4β-Me	(1 293 ppm)	9α-H 13,	5α-H 8,	7aβ-Me 2	
1β-Me	(1 419 ppm)	7α-H 5,	7β-OH 3,	4-Me ~4,	7aβ-Me ~4
9α-H	(3 404 ppm)	8α,β-H ~3,	4-Me ~4 5		

^{13}C-NMR Assignment by ^{1}H-detected one-bond and multiple-bond ^{1}H,^{13}C-COSY δ 11 66 (7aβ-Me), 13 89 (1β-Me), 23 47 (4-Me), 24 67 (9-C), 24 89 (4-Me), 28 07 (6-C), 33 29 (4-C), 36 63 (5-C), 39 40 (8-C), 56 78 (7a-C), 61 55 (3a-C), 67 27 (7-C), 89 33 (1-C), 121 67 (**CN**), 175 00 (3-**CO**) MS m/z 204 (34), 186 (18), 177 (20),163 (30), 148 (10), 139 (82), 136 (23), 121 (17), 120 (22), 91 (16), 81 (17), 77 (15), 55 (27), 53 (17), 43 (100), 41 (46), 39 (21), 29 (24) CI (NH_3) 281 [$(M + NH_4)^+$, 100], 264 [$(M + H)^+$, 9] Exact mass calcd for $C_{15}H_{21}NO_3$ 263 34

4 A solution of **1** (1 0 g, 3 8 mmol) in 250 ml 1,4-dioxane was irradiated under N_2 with the lamp NK 6/20 through quartz glass at 35 - 40° C for 8 h With TLC (CH_2Cl_2-MeOH 9 1) only starting material **1** could be detected and was then completely recovered.

5 A solution of **1** (1 0 g, 3 8 mmol) in 250 ml 2-propanone was irradiated under N_2 with the lamp TQ 150 through 1 5 mm pyrex glass at 35 - 40° C for 8 h With a path length of 0 5 cm only the Hg-line 313 nm was absorbed (absorption A = 4 000), whereas **1** was protected by the pyrex cut-off filter The result was the same as in exp 4

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REFERENCES AND NOTES

1. McCullough, J.J.; Manning, C. J. Org. Chem. 1978, 43, 2839.
2. Akhtar, I.A.; McCullough, J.J.; Vaitekunas, S.; Faggiani, R.; Lock, C.J.L. Can. J. Chem. 1982, 60, 1657.
3. Hixson, S.S.; Day, R.O.; Franke, L.A.; Rao, R.V. J. Am. Chem. Soc. 1980, 102, 412
4. Morrison, H.; Miller, A. J. Am. Chem. Soc. 1980, 102, 372.
5. Pfoertner, K.H.; Englert, G.; Schoenholzer, P. Tetrahedron, preceding publication.
6. These yields were calculated considering also the amounts and molecular weights of the products derived from secondary reactions, i.e. **2a-c** and **3a**, respectively.
7. Sheldrick, G.M.; University of Goettingen, FRG. Coordinates and thermal parameters have been deposited at the Crystallographic Data Centre, Cambridge, University Chemical Lab., Cambridge CB2 1EW, UK.