209. Studies on the Carbon Zip Reaction of 2-Oxocycloalkane-1-carbonitriles

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As a part of continuing interest in the zip reaction, we present the results on a carbon ring-enlargement reaction of activated ketones with a CN group as a charge stabilizer. Two series of (1-cyano-2-oxocycloalkyl)alkanoates were prepared from 8- and 12-membered cyano-ketones **1** and **2**, respectively, namely the propanoates **3** and **4**, the butanoates **6**, **8** and **9** as well as the pentanoates **12** and **15**. While treatment with *t*-BuOK of the former two homologous esters resulted in both ring enlargement and competitive transesterification, the pentanoates **12** and **15** afforded mostly the diastereoisomeric mixtures of bicyclic alcohols **20a–c** and **31a,b**, respectively, which remained intact on further exposure to base. It was shown that – apart from the base used (*t*-BuOK *vs.* $Li(i\text{-}Pr)_2N$ – the distribution of products was greatly influenced by the ring size of substrates. This is further illustrated by treatment of ketones **34** and **35** with *t*-BuOK. While the former rearranged smoothly to diketone **36**, no reaction at all took place with the latter. The behavior of the substrates is discussed in terms of steric and energetic reasons.

In the past, we have published ring-enlargement reactions of cycloalkanones which were substituted in position 2 by an NO_2 group as an electron-attracting residue [1]. For example, methyl 3-oxo-5-(1-nitro-2-oxocyclooctyl)pentanoate was converted on treatment with tetrabutylammoniumfluoride (Bu_4NF) in tetrahydrofurane (THF) to methyl 5-nitro-2,12-dioxocyclododecane-1-carboxylate in 93% yield. Instead of NO_2 other functional groups can be used: In their synthesis of muscone from a 12-membered precursor, *Trost* and *Vincent* [2] have introduced the phenylsulfonyl group; for similar reactions, see [3]. In the following, we report on the employment of the CN group as a charge stabilizer in ring enlargement of cycloalkanones.

1. Ester Derivatives of 2-Oxocyclooctane- (1) and 2-Oxocyclododecane-1-carbonitrile (2). – The 2-oxocyclooctane-1-carbonitrile (**1**) was prepared by reaction of cyclooctanone with $ClSO_2NCO$ and dimethylformamide (DMF) in CH_2Cl_2 [4]. In an analogous manner, cyclododecanone was converted to 2-oxocyclododecane-1-carbonitrile (**2**). Several methods were checked for an introduction of the methyl-propanoate unit into position 1. The best results were observed with methyl acrylate in THF in presence of an aq. solution of *Triton-B* (benzyltrimethylammonium hydroxide). The *Michael* adducts **3** from **1** *(Scheme 1)* and **4** from **2** *(Scheme 2)* were formed in 78 and 82% yield, respectively. Alternatively, compound **4** was synthesized from **2** and methyl acrylate by treatment with

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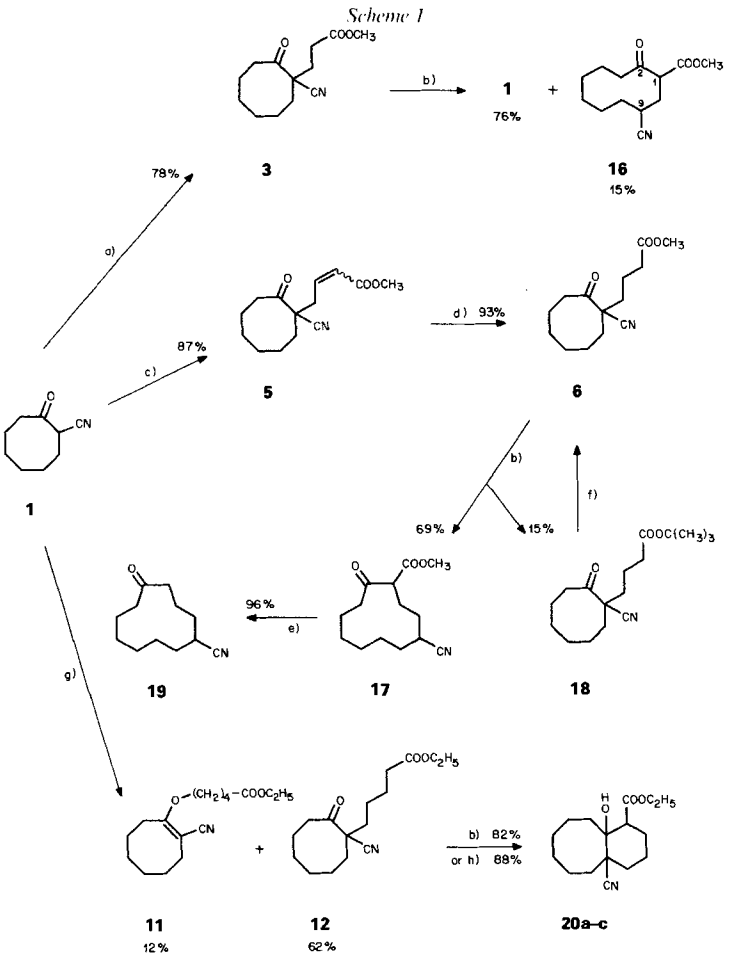
Scheme 1

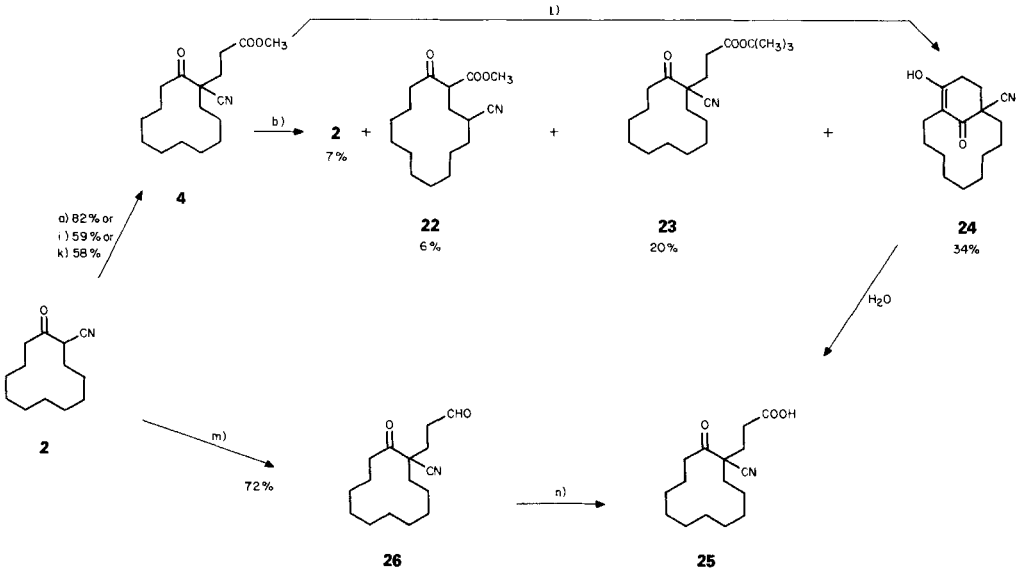


a) CH_2=CHCOOCH$_3$/*Triton-B*/THF. b) *t*-BuOK/THF. c) $BrCH_2CH$=CHCOOCH$_3$/Bu_4NHSO_4/NaOH/CH_2Cl_2/H_2O. d) H_2/Pd/$BaSO_4$/MeOH. e) KOH/MeOH/H_2O. f) MeOH/HCl. g) $BrCH_2(CH_2)_3$COOEt (**13**)/Bu_4NOH/CH_2Cl_2/H_2O. h) Li(i-Pr)$_2$N/THF.

KF/dimethylsulfoxide (DMSO) (59%) or with $(C_4H_9)_3P$/THF (58%)[3]. A second series of alkyl-carboxylate derivatives, namely the butanoates **6** *(Scheme 1)* and **8** *(Scheme 3)*, were prepared from **1** and methyl 4-bromo-2-butenoate *via* **5** by phase-transfer catalysis (tetrabutylammonium hydrogensulfate (Bu_4NHSO_4)/CH_2Cl_2/2N aq. NaOH), followed by catalytic hydrogenation and *via* **7** using the same conditions in 81 and 84% yield, respectively. Analogous to the preparation of **8**, the ethyl ester **9** was synthesized by direct

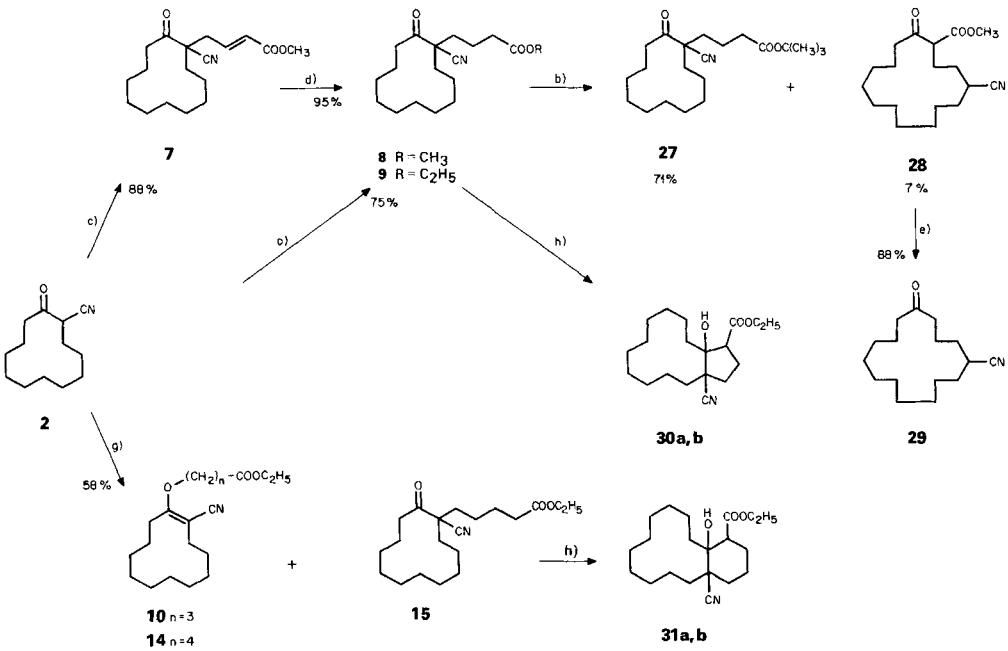
[3]) It should be mentioned that **1** (or **2**) could not be transformed with methyl acrylate to **3** (or **4**) under the following reaction conditions: tetrabutylammonium fluoride (Bu_4NF)/abs. THF at various temperatures; KF/abs. THF with or without [18]crown-6; $(C_6H_5)_3P$ or $(C_6H_5)_2CH_3P$/abs. THF or NaH/abs. DMSO. Furthermore, experiments with methyl 3-bromopropanoate under different conditions turned out to be fruitless.

Scheme 2



a) b) See *Scheme 1.* i) CH_2=CHCOOCH$_3$/KF/DMSO. k) CH_2=CHCOOCH$_3$/(C_4H_9)$_3$P/THF. l) *Triton-B*/THF. m) CH_2=CHCHO/Bu_4NF/THF. n) CrO_3/acetone.

Scheme 3



b)–e) g) h) See *Scheme 1.* o) $BrCH_2(CH_2)_2COOEt/Bu_4NOH/CH_2Cl_2$.

treatment of **2** with ethyl 3-bromobutanoate. Besides the *C*-alkylation product **9** (45%), the corresponding enol ether **10** was also formed *(Scheme 3)*.

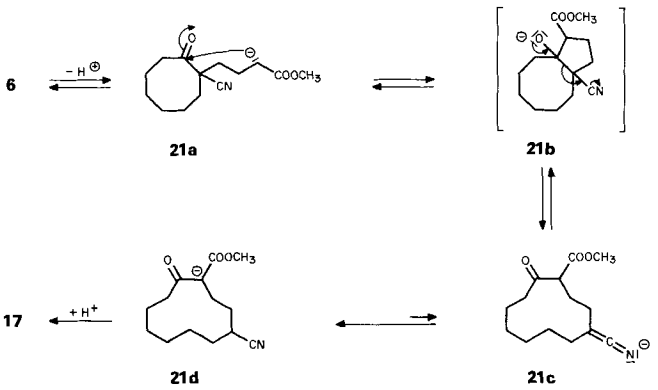
The syntheses of the corresponding ethyl pentanoate derivatives of **1** and **2**, namely **12** *(Scheme 1)* and **15** *(Scheme 3)*, respectively, were achieved with ethyl 5-bromopentanoate (**13**) by phase transfer catalysis, (**12**:**1**/**13**/Bu_4NOH 1:2:2 in CH_2Cl_2/H_2O; **15**:**2**/**13**/Bu_4NHSO_4/NaOH 1:2:1:2 in $CHCl_3/H_2O$ (*cf.* [5]) or **2**/**13**/Bu_4NOH 1:1:2 in CH_2Cl_2/H_2O). Side products in both cases were the *O*-alkylation products **11** and **14**. *Clark* and *Miller* [6] have reported that 1,3-dicarbonyl derivatives were *C*-alkylated preferently when Bu_4NF was used as a catalyst. However, treatment of **1** or **2** with **13** in the presence of Bu_4NF/THF resulted in the formation of a nearly 1:1 mixture of *C*- and *O*-alkylated products in low yield.

2. Rearrangement Experiments. – Treatment of compound **3** with *t*-BuOK in abs. THF at −60° for 20 min gave a mixture of the *retro-Michael* product **1** (76%) and the rearrangement product methyl 9-cyano-2-oxocyclodecanecarboxylate (**16**; 15%; *Scheme 1*). *retro-Michael* products were observed in some cases as the main products of related cyclooctanone derivatives [1] [3] under similar conditions. Under different conditions (*Triton-B* in THF/0° or Bu_4NF/THF/different temperatures), no conversion of **3** to **16** or even to **1** was observed. In the presence of NaOMe/THF at −40→−20° **3** was converted to **1** only, while with NaOMe/MeOH at 20°, no reaction took place. The rearrangement product **16**, compared with its isomeric starting material **3**, shows diagnostic spectroscopic differences for H–C(1) in the ^{1}H-NMR and for C(1) and C(9) (2 *d*) in the ^{13}C-NMR spectrum.

From the base-catalyzed (*t*-BuOK/THF/0°) reaction of the homologous ester **6** resulted the rearrangement product methyl 9-cyano-2-oxocycloundecanecarboxylate (**17**; *Scheme 1*) in an yield of 69%. Besides that, 15% of transesterified compound **18** were isolated. For their characterization, **17** was hydrolyzed and decarboxylated to give **19**, and **18** was converted back to **6** with MeOH/HCl.

The third cyclooctanone derivative **12** afforded, under similar reaction conditions to those discussed above (*t*-BuOK/THF at −50→−10°) or with lithium diisopropylamide [Li(i-Pr)$_2$N]/THF at −78°, a mixture of different diastereoisomers of *Formula* **20** together with 10% of starting material. Depending on the base used, the ratio of the individual

Scheme 4



components **20a–c** was different; until now it was not possible to determine their relative configurations. All attempts to convert **20a–c** to the ring-enlarged product failed, only a few unidentified products being detected.

The mechanism of the ring enlargement is exemplified in *Scheme 4* for the transformation **6**→**17**. Intramolecular attack of the *C*-nucleophile in **21a** gives rise to the bicyclic alkoxide ion **21b** which fragments by cleaving the cross-piece bond to afford the anion **21c**. The latter step is facilitated by the electron-attracting ability of the CN group. The *retro* process **21c**→**21b**, although in principle feasible (see results on similar systems [7]), is suppressed by formation of the species **21d**.

The base-catalyzed treatment of the homologous esters **3**, **6**, and **12** gives only in the first two cases the products of ring enlargement. In addition, the limitation to enlargement in the anion generated from **3** (corresponding to **21b**) is due to the competitive *retro-Michael* reaction (→**1**), a process impossible in the other two cases. From the product analysis it can be inferred that the oxido-substituted bicyclo[6.2.0]decane (from **3**) and bicyclo[6.3.0]undecane (from **6**) are more strained than the oxido-substituted bicyclo[6.4.0]dodecane (from **12**). Therefore, under the assistance of the CN group, the former two react to give the 10- and 11-membered compounds **16** and **17**, respectively. The behavior of corresponding compounds containing a NO_2 instead of a CN group was not investigated until now. Hence, conclusions concerning steric and electronic effects on the course of the reaction cannot be drawn yet.

The base-catalyzed treatment of the cyclododecanone derivatives **4** *(Scheme 2)*, **8**, and **15** *(Scheme 3)* gave similar results to that of **3**, **6**, and **12** *(Scheme 1)*. Compound **4** afforded a mixture which contained, besides starting material (23%), four components (*t*-BuOK/THF): The *retro-Michael* product **2** (7%), the *t*-butyl ester **23** (20%), the expected rearranged 14-membered ring compound **22** (6%), and the bicyclic material **24** (34%; *Scheme 2*). Variation of the reaction conditions brought partly quite different ratios of the components. Increase of the *t*-BuOK concentration or the inverse addition of the reaction components resulted in a higher yield of **23**. At higher temperature ($> -20°$), only small quantities of **23** were formed; instead, **24** was the main product and **22** was missing completely.

In the presence of 2.5 equiv. of $Li(i\text{-}Pr)_2N$ in THF, **4** was transformed to **2** only, not even a trace of **24** was detectable in the reaction mixture. On the other side, **24** was formed from **4** with all other bases so far investigated (*t*-BuOK/THF/reflux; KF/DMSO/$> 130°$; *Triton-B*/THF/0°). This result underlines the high selectivity of $Li(i\text{-}Pr)_2N$ to **4**. The enolic structure **24** was determined by comparison of similar compounds of known structure [8]. Compound **24** is crystalline, and in this form it is stable. By chromatography (silica gel, benzene/MeOH) or by reaction with H_2O, **24** was partly converted to the carboxylic acid **25**. Therefore, **24** and **25** can not be separated by chromatographic systems containing traces of H_2O. The structure of **25** was proven by direct comparison with a material synthesized from **2** *via* **26** according to *Scheme 2*.

Treatment of the butanoate **8** with *t*-BuOK afforded the ring enlarged **28** (7%) and the *t*-butyl ester **27** (71%; *Scheme 3*). This result is comparable with that of the 8-membered ring compound **6**, but there the yield of the ring-enlarged **17** was much higher than that of the *t*-butyl ester **18** *(Scheme 1)*. Transesterification of **27** with MeOH/HCl gave **8**. The structure assignment of **28** was supported by spectral data as well as by its conversion to the hydrolysis and decarboxylation product **29**. Under different reaction conditions

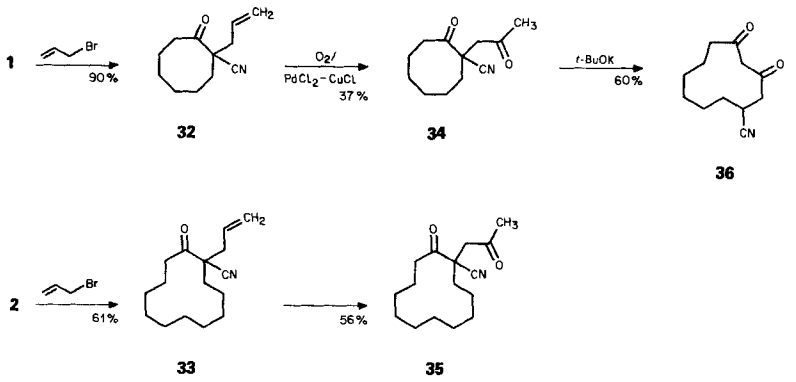
(Li(i-Pr)$_2$N/THF), the ethyl ester **9** was transformed to a mixture of diastereoisomeric products **30a** and **30b** (ratio *ca.* 1:10; *Scheme 3*). Under these conditions, no rearrangement product was observed.

In contrast to the pentanoate **12**, the pentanoate **15** resisted to treatment with *t*-BuOK or Bu_4NF in THF. However, with Li(i-Pr)$_2$N/THF, **15** was partly (20% recovered **15**) transformed into a *ca.* 1:11 mixture of the diastereoisomeres **31a** and **31b** *(Scheme 3)*.

Besides the formation of **24** from **4** the results of both reaction series (starting from **1** and **2**, respectively) are similar. It is obvious that the 8-membered-ring esters show higher tendency to rearrange than the 12-membered analogue. But this result can not be generalized because with other systems different observations were made [1] [7] [9].

It should be mentioned that in no case, a rearrangement product was observed containing a *t*-Bu instead of a Me or Et ester group.

Scheme 5



The reaction properties of the cyano-oxo-ketones are in good agreement with those of cyano-oxo-esters of comparable structures as shown in *Scheme 5*. Under phase-transfer conditions, **1** and **2** reacted with allyl bromide to form **32** and **33**, respectively. The allyl groups were oxidized with $O_2/PdCl_2$-CuCl [10] to form the ketones **34** and **35**, respectively. While under base catalysis (*t*-BuOK/THF) the ketone **34** was transformed to the ring-enlarged product **36** in a yield of 60% (*cf.* **6**→**17**, *Scheme 1*), with the 12-membered analogue **35**, no reaction took place at all. The success of the ring enlargement in the former case relies upon the release of energy as already discussed [1].

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Experimental Part

General. If not otherwise mentioned, the following conditions were used: Before evaporation, org. solns. were dried over Na_2SO_4 or $MgSO_4$. Bu_4NF was dried at 60°/10^{-5} Torr according to [11]. Column chromatography: silica gel *60* (0.063–0.200 mm, *Merck*). M.p.: *Mettler-FP-52* apparatus; IR (cm^{-1}): in $CHCl_3$ on *Perkin-Elmer 297*. ^{1}H-NMR: *Varian XL-200* at 200 MHz (90 MHz on *Varian EM-390*) in $CDCl_3$; δ in ppm, J in Hz. Tetramethylsilan as internal standard (= 0 ppm). ^{13}C-NMR: *Varian XL-100-12* at 25.2 MHz. EI-MS: *Varian MAT 112 S; m/z* (rel. intensity > 5%). CI-MS: *Varian MAT 112* (2-methylpropane).

1. *Derivatives of 2-Oxocyclooctanenitrile* (**1**). 1.1. *Methyl 3-(1-Cyano-2-oxocyclooctyl)propanoate* (**3**). Compound **3** was prepared using *Method A* of *2.1* from **1** (604 mg, 4 mmol)[4]) and methyl acrylate (439 mg, 5.1 mmol) in THF (35 ml): 735 mg (78%). M.p. 44.5–45.2° (Et_2O/hexane 3:1). IR (KBr): 2950 (br.), 2875, 2255, 1740 (sh), 1730, 1710 (sh), 1705. IR (film): 2940, 2865, 2250, 1740 (br.), 1710. ^{1}H-NMR: 3.68 (*s*, CH_3O); 2.72–1.21 (*m*, 16 H). CI-MS: 238 ([M + 1]$^+$), 206. EI-MS: 237 (2, M^+), 206 (11), 164 (10), 151 (10), 150 (6), 136 (22), 133 (13), 123 (14), 121 (10), 109 (12), 108 (40), 98 (48), 95 (18), 94 (17), 81 (17), 80 (22), 79 (10), 74 (28), 70 (13), 69 (17), 67 (22), 56 (14), 55 (100), 53 (32), 43 (36), 42 (39), 41 (81).

1.2. *Methyl 9-Cyano-2-oxocyclodecane-1-carboxylate* (**16**). *Method A.* To a stirred soln. of **3** (1.0 g, 4.2 mmol) in abs. THF (20 ml), a soln. of freshly sublimed *t*-BuOK (504 mg, 4.5 mmol) in abs. THF (20 ml) was added at −65° within 5–7 min under Ar. After 20 min, AcOH (0.5 ml) was added and evaporated (20°), the residue dissolved in CH_2Cl_2 (50 ml), and the org. layer washed with H_2O, sat. NaCl soln., and dried. After evaporation, the residue was chromatographed (80 g of silica gel, Et_2O/hexane 1:2): **1** (370 mg, 58.3%; fast running), **16** (160 mg, 16%)[5]).

Method B. After adding a soln. of **3** (1.0 g) in abs. THF to a soln. of *t*-BuOK (504 mg) in abs. THF (20 ml) under Ar within 5 min and working up after 30 min with AcOH (0.5 ml) following *Method A*, **1** (480 mg, 75.7%) and **16** (150 mg, 15.1%) resulted. **16**: Oil. IR (film): 2940 (br.), 2870, 2260, 1740 (br.), 1720 (sh). ^{1}H-NMR: 3.78–3.71 (*m*, CHCOO); 3.69 (*s*, CH_3O); 2.53–2.31 (*m*, CHCN); 2.21–1.28 (*m*, 14 H). ^{13}C-NMR: 208.6 (C(2)); 173.5 (*C*OOCH$_3$); 116.5 (CN); 51.7 (CH_3O); 47.3 (C(1)); 45.7 (C(9)); 35.8; 31.5; 28.1; 26.2; 24.8; 24.3; 23.6. Ester **16** is a mixture of diastereoisomers and/or conformers: the intensities of the NMR signals of the second component is less than 10% compared with the main signal. EI-MS: 237 (3, M^+), 206 (6), 178 (8), 177 (7), 156 (6), 150 (11), 149 (16), 148 (12), 136 (19), 134 (13), 128 (13), 123 (15), 122 (15), 121 (11), 120 (14), 109 (13), 106 (15), 100 (13), 96 (23), 94 (23), 84 (35), 83 (26), 82 (21), 81 (23), 74 (61), 68 (28), 67 (32), 59 (25), 55 (82), 41 (100).

1.3. *Methyl 4-(1-Cyano-2-oxocyclooctyl)-2-butenoate* (**5**). To a soln. of **1** (3.78 g, 25 mmol) and methyl 4-bromo-2-butenoate (*Fluka;* mainly (*E*)-isomer; 6.27 g, 35 mmol) in CH_2Cl_2 (20 ml) was added a soln. of Bu_4NHSO_4 (*Fluka;* 8.49 g, 25 mmol) in 2N aq. NaOH (26 ml) within 3 min under stirring. After 1 h stirring at 20°, the org. layer was separated, dried, evaporated *in vacuo*, and chromatographed (252 g of silica gel, hexane/Et_2O) to give **5** (5.42 g, 87%) as an oil. IR: 2238, 1718, 1660, 1280, 980. ^{1}H-NMR (90 MHz): 6.97, 6.78 (*ABX*, J = 16, 7.5, 1 H); 5.95 (*d*, J = 16, 1 H); 3.77 (*s*, CH_3O); 2.97–2.33 (*m*, 4 H); 2.31–1.13 (*m*, 10 H). EI-MS: 249 (4, M^+), 221 (5), 218 (22), 217 (32), 178 (13), 162 (20), 152 (27), 120 (100), 98 (31), 55 (81).

1.4. *Methyl 4-(1-Cyano-2-oxocyclooctyl)butanoate* (**6**). A mixture of **5** (4.99 g, 20 mmol) and 5% $Pd/BaSO_4$ (*Fluka;* 0.2 g) in MeOH (35 ml) was stirred under H_2 for 3 h. The soln. was diluted with CH_2Cl_2, filtered through *Celite*, washed, dried, and evaporated *in vacuo*. Crystallization from MeOH gave **6** (4.69 g, 93.3%), m.p. 60.9–62.8°. IR: 2240, 1720 (br.), 1162. ^{1}H-NMR (90 MHz): 3.70 (*s*, CH_3O); 2.83–1.05 (*m*, 18 H). EI-MS: 251 (14, M^+), 220 (15), 219 (14), 193 (8), 174 (17), 151 (15), 150 (15), 136 (32), 122 (77), 111 (42), 98 (100), 94 (48), 55 (98).

1.5. *Treatment of* **6** *with* t-*BuOK.* A soln. of **6** (1.508 g, 6.0 mmol) in THF (25 ml) was added dropwise within 30 min under stirring to an ice-cold soln. of *t*-BuOK (2.35 g, 21.0 mmol) under N_2. After addition of 1N KH_2PO_4/H_2O (35 ml), benzene (50 ml), and Et_2O (10 ml), the org. layer was separated, washed with H_2O (2 × 20 ml) and brine (30 ml), and dried. After evaporation, the residue was chromatographed (46 g of silica gel, hexane/Et_2O) to yield the oily *methyl 9-cyano-2-oxocycloundecanecarboxylate* (**17**; 1.037 g, 68.8%) and tert-*butyl 4-(1-cyano-2-oxocyclooctyl)butanoate* (**18**; 0.266 g, 15.1%)[6]). Data of **17**: IR: 2238, 1741, 1708, 1640, 1600. ^{1}H-NMR (keto/enol tau-

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[4]) Synthesis of **1** and **2** according to [4] (we could not repeat the published yields). Purification of **2** by destillation (b.p. 140–145°/3 × 10^{-5} Torr). The colorless compounds **1** and **2** are decomposed in soln. after 2–3 days; **1** in crystalline state, after *ca.* 3 weeks, turned yellowish (TLC and m.p.). Note that **1** and **2** should be prepared and handled in the hood (avoid skin contact).

[5]) The same yield of **1** was observed at higher temp. (*e.g.* −50 or −40°) following *Method A*, but the yield of **16** decreased.

[6]) A sample of **18** was added to abs. MeOH/HCl. After dissolution (*ca.* 10 min), the mixture was evaporated and the residue was found to be identical with **6**.

tomers): 13.07 (*s*, 0.35 H); 3.80 (*s*, 1.4 H); 3.72 (*s*, 1.1 H); 3.71 (*s*, 0.5 H); 3.70–3.55 (*m*, 0.65 H); 2.72–1.04 (*m*, 17 H). EI-MS: 251 (13, M^+), 220 (14), 208 (12), 180 (6), 176 (7), 164 (24), 154 (12), 141 (51), 116 (22), 109 (42), 98 (26), 87 (16), 81 (25), 55 (100).

1.6. *5-Oxocycloundecane-1-carbonitrile* (**19**). The mixture of **17** (0.799 g, 3.18 mmol) and KOH (0.28 g, 5.0 mmol) in MeOH (30 ml) and H_2O (7 ml) was heated at 80° for 1.5 h, cooled, and diluted with H_2O (40 ml). After concentration to 2/3 of the original volume, the soln. was extracted with Et_2O (2 × 10 ml) and the combined extracts were washed with H_2O and brine and dried. Evaporation gave the oily **19** (0.587 g, 95.5%). IR: 2240, 1702. ^{1}H-NMR (90 MHz): 2.68–2.37 (*m*, 4 H); 2.30–0.95 (*m*, 15 H). EI-MS: 193 (5, M^+), 164 (20), 150 (16), 136 (16), 123 (14), 122 (14), 109 (21), 98 (25), 96 (24), 83 (100), 55 (34).

1.7. *Ethyl 5-(2-Cyano-1-cycloocten-1-yloxy)pentanoate* (**11**) *and Ethyl 5-(1-Cyano-2-oxocyclooctyl)pentanoate* (**12**). A mixture of **1** (4.53 g, 30 mmol), ethyl 5-bromopentanoate (**13**; 12.54 g, 60 mmol), Bu_4NOH (15.5 g, 60 mmol, 40% aq. soln.) and CH_2Cl_2 (20 ml) was stirred for 50 h. The org. layer was washed 2× with H_2O and brine and filtered (20 g of silica gel). After evaporation, the residue was chromatographed (180 g of silica gel, hexane/Et_2O 3:1) to give **11** (fast running; 1.0 g, 11.9%) and **12** (5.21 g, 62.2%). Data of **11**: Oil. IR (film): 2960 (sh), 2935, 2860, 2220, 1740, 1635. ^{1}H-NMR: 4.18–4.04 (*m*, 2 CH_2O); 2.42–2.24 (*m*, 6 H); 1.82–1.51 (*m*, 12 H); 1.26 (*t*, CH_3). CI-MS: 280 ($[M + 1]^+$), 234. EI-MS: 234 (9), 152 (6), 130 (7), 129 (100), 101 (52), 83 (22), 55 (28), 41 (14).

Data of **12**: M.p. 38.2–39.1° (pentane/Et_2O). IR: 2940, 2870, 2250, 1735–1715. IR (film): 1740 (sh), 1735, 1715. IR (KBr): 1740–1730, 1710. ^{1}H-NMR: 4.12 (*q*, J = 7, CH_2O); 2.65–1.31 (*m*, 20 H); 1.26 (*t*, J = 7, CH_3). CI-MS: 280 ($[M + 1]^+$), 234. EI-MS: 279 (1, M^+), 251 (4), 234 (18), 205 (5), 178 (10), 164 (15), 162 (6), 161 (6), 152 (10), 151 (14), 136 (32), 129 (20), 124 (12), 123 (22), 122 (13), 111 (42), 109 (13), 108 (19), 101 (26), 98 (81), 94 (18), 83 (30), 81 (28), 80 (22), 67 (38), 55 (100), 53 (25), 42 (46), 41 (94).

1.8. *Ethyl 1-Cyano-8-hydroxybicyclo[6.4.0]dodecane-9-carboxylates* (**20a–c**). *Method A.* To a stirred soln. of **12** (830 mg, 2.97 mmol) in abs. THF (20 ml) was added a soln. of freshly sublimed *t*-BuOK (348 mg, 3.1 mmol) in abs. THF (10 ml) within 10 min at −50° under Ar. The mixture was warmed up within 2 h to −10° and worked up with AcOH (1 ml). After evaporation of THF, the residue was dissolved in CH_2Cl_2 (50 ml), washed with H_2O and brine, and dried. After evaporation, 3 products were isolated by column chromatography (90 g of silica gel, hexane/Et_2O 3:1): **20a** (fast running; 370 mg, 44.6%), **20b** (310 mg, 37.4%), **12** (90 mg, 10.9%).

Method B. A soln. of Li(i-Pr)$_2$N (12.5 mmol) in abs. THF (20 ml) was added within 10 min to **12** (1 g, 3.58 mmol) in abs. THF (30 ml) at −78° with stirring unter Ar. After 1.5 h, the reaction was quenched with AcOH (2 ml), worked up as described for *Method A*, and chromatographed (100 g of silica gel, hexane/Et_2O 4:1): **20a** (fast running; 100 mg, 10%), **20c** (550 mg, 55%), **20b** (230 mg, 23%), **12** (30 mg, 3%). Data of **20a**: M.p. 56.3–57.1° (pentane/Et_2O). IR: 3500 (br.), 2940, 2880, 2860, 2240, 1740 (sh), 1715–1705. IR (KBr): 3500, 3000, 2950, 2870–2860, 2220, 1725 (sh), 1715. ^{1}H-NMR: 4.16 (2*q*, shifted by 0.6 Hz, each J = 7, CH_2O); 3.98 (br. *s*, OH, exchangeable with D_2O); 2.81–2.73 (*m*, H–C(9)); 2.33–1.35 (*m*, 18 H); 1.28 (*t*, J = 7, CH_3). ^{13}C-NMR: 176.8 (COO); 122.2 (CN); 71.9 (C(8)); 60.8 (CH_2O); 50.4 (C(9)); 47.5 (C(1)); 34.9; 34.7; 31.3; 25.9; 25.5; 25.3; 24.7; 21.8; 21.4; 14.0 (CH_3). CI-MS: 280 ($[M + 1]^+$), 262. EI-MS: 279 (5, M^+), 261 (3), 251 (3), 234 (6), 233 (10), 222 (5), 211 (15), 196 (10), 195 (50), 188 (14), 170 (14), 169 (9), 150 (11), 149 (20), 141 (11), 137 (13), 136 (16), 130 (17), 123 (38), 111 (16), 109 (15), 101 (29), 98 (28), 97 (22), 96 (21), 95 (25), 94 (18), 93 (25), 91 (12), 83 (28), 81 (38), 79 (24), 73 (29), 69 (23), 68 (20), 67 (36), 55 (100), 41 (100). Anal. calc. for $C_{16}H_{25}NO_3$ (279.38): C 68.78, H 9.01, N 5.01; found: C 68.82, H 8.75, N 4.82.

Data of **20b**: M.p. 68.2–68.8° (pentane/Et_2O). IR (KBr): 3515, 2950, 2880, 2245, 1708 (br.). IR (film): 3500 (br.), 2940, 2880, 2240, 1735 (sh), 1710. ^{1}H-NMR: 4.25–4.10 (*m*, CH_2O); 3.84 (br. *s*, OH, exchangeable with D_2O); 2.84 (*dd*, J = 4, 12, H–C(9)); 2.61–1.33 (*m*, 18 H); 1.28 (*t*, CH_3). ^{13}C-NMR: 175.3 (COO); 122.5 (CN); 73.0 (C(8)); 61.0 (CH_2O); 46.5 (C(1)); 44.4 (C(9)); 37.2; 36.9; 31.1; 27.2; 25.6; 25.5; 25.1; 21.4; 19.3; 14.1 (CH_3). CI-MS: 280 ($[M + 1]^+$), 262. EI-MS: 279 (3, M^+), 261 (< 1), 251 (2), 234 (7), 233 (11), 206 (6), 205 (8), 195 (66), 188 (21), 178 (9), 177 (7), 162 (10), 161 (11), 150 (12), 149 (36), 136 (17), 130 (31), 123 (26), 122 (17), 121 (11), 111 (16), 109 (17), 108 (14), 101 (28), 98 (32), 97 (23), 83 (31), 81 (34), 73 (19), 67 (37), 55 (100), 41 (87). Anal. calc. for $C_{16}H_{25}NO_3$ (279.38): C 68.78, H 9.01, N 5.01; found: C 67.18, H 8.16, N 5.03.

Data of **20c**: M.p. 50.6–51.3° (pentane/Et_2O). IR (KBr): 3450, 3020, 2970, 2940, 2880, 2240, 1705 (sh), 1690. ^{1}H-NMR: 4.56 (*s*, OH, exchangeable with D_2O); 4.32–4.14 (*m*, CH_2O); 2.86 (*dd*, J = 3.4, 13, H–C(9)); 2.24–2.00 (*m*, 2 H); 1.98–1.35 (*m*, 22 H); 1.35 (*t*, CH_3). ^{13}C-NMR: 174.1 (COO); 123.5 (CN); 74.0 (C(8)); 61.2 (CH_2O); 53.9 (C(9)); 48.7 (C(1)); 33.2; 32.7; 29.2; 26.0; 24.9; 24.5; 24.0; 21.9; 20.9; 14.1 (CH_3). CI-MS: 280 ($[M + 1]^+$), 262, 234. EI-MS: 279 (2, M^+), 251 (2), 234 (8), 233 (6), 215 (5), 211 (18), 206 (8), 205 (7), 196 (6), 195 (9), 188 (12), 178 (8), 177 (7), 169 (7), 165 (5), 164 (5), 150 (9), 149 (10), 148 (8), 136 (12), 134 (11), 130 (10), 123 (18), 111 (11), 109 (11), 108 (12), 101 (19), 98 (26), 97 (17), 96 (10), 95 (16), 94 (17), 93 (15), 91 (16), 83 (18), 81 (29), 73 (28), 69 (17), 68 (14),

67 (30), 55 (100), 41 (73). Anal. calc. for $C_{16}H_{25}NO_3$ (279.38): C 68.78, H 9.01, N 5.01; found: C 68.58, H 9.21, N 4.93.

2. *Derivatives of 2-Oxocyclododecane-1-carbonitrile* (**2**). 2.1. *Methyl 3-(1-Cyano-2-oxocyclododecyl)propanoate* (**4**). *Method A.* A 40% aq. soln. of *Triton-B* (0.1 ml) was added at 20° under Ar to a mixture of **2**[4]) (0.828 g, 4 mmol) and methyl acrylate (0.439 g, 5.1 mmol) in THF (35 ml). After 10 h stirring, the same amount of *Triton-B* was added. After additional 10 h, the mixture was treated with AcOH (0.5 ml) at 0°, evaporated at 20°, and the residue dissolved in CH_2Cl_2 (50 ml). Further workup as in *1.8* and chromatography (65 g of silica gel, hexane/Et_2O 2:1) yielded **4** (960 mg, 81.9%).

Method B. A soln. of **2** (1.03 g, 5 mmol), methyl acrylate (473 mg, 5.5 mmol), and dried [11] KF in abs. DMSO (20 ml) was stirred 10 h at 60° under N_2. The mixture was poured into 1N aq. HCl (110 ml) and extracted with AcOEt and the org. layer washed with H_2O until neutral and dried. Workup and chromatography as described in *Method A* gave **4** (870 mg, 59.4%), *cf.* [12].

Method C. To a soln. of **2** (1.03 g, 5 mmol) and methyl acrylate (473 mg, 5.5 mmol) in abs. THF (30 ml), $(C_4H_9)_3P$ (202 mg, 1 mmol) was added dropwise under Ar. After 20 h stirring at 45–50°, CH_3I (0.2 ml) was added. Workup as described under *Method A* yielded **4** (850 mg, 58%). M.p. 82.5–83.7° (hexane/Et_2O). IR: 2920, 2860, 2240, 1720–1710. IR (KBr): 2925, 2860, 2240, 1735, 1705. ^{1}H-NMR: 3.69 (*s*, CH_3O); 2.87–1.20 (*m*, 24 H). CI-MS: 294 ($[M + 1]^+$), 263. EI-MS: 293 (2, M^+), 262 (5), 220 (9), 192 (16), 182 (7), 164 (8), 150 (9), 136 (12), 126 (18), 123 (13), 112 (20), 111 (11), 108 (33), 98 (81), 97 (15), 95 (17), 84 (20), 80 (21), 79 (11), 74 (25), 69 (18), 67 (22), 56 (19), 55 (78), 43 (39), 41 (100).

2.2. *Treatment of* **4** *with* t-*BuOK.* A soln. of freshly sublimed *t*-BuOK (896 mg, 8 mmol) in abs. THF (25 ml) was added dropwise within 10 min to a stirred soln. of **4** (1.0 g, 3.41 mmol) in abs. THF (50 ml) at –40° under Ar. Workup after 25 min and chromatography (100 g of silica gel, hexane/Et_2O 5:1→hexane/Et_2O/MeOH 10:10:1) as described under *1.2 (Method A)* gave tert-*butyl 3-(1-cyano-2-oxocyclododecyl)propanoate* (fast running; **23**; 230 mg, 20.1%), **4** (230 mg, 23%), **2** (50 mg, 7.1%), *methyl 13-cyano-2-oxocyclotetradecanecarboxylate* (**22**; 60 mg, 6%), and *12-hydroxy-15-oxobicyclo[9.3.1]pentadec-11-ene-1-carbonitrile* (**24**; 300 mg, 34%; see *2.3*)[7]).

Data of **22**: M.p. 80–83° (pentane/Et_2O). IR (KBr): 2930, 2900, 2870, 2250, 1745, 1735 (sh), 1718. ^{1}H-NMR: 4.11–4.06 (*m*, H–C(1)); 3.69 (*s*, CH_3); 3.08–2.92 (*m*, H–C(13)); 2.35 (*t*, 2 H–C(3)); 2.15–1.16 (*m*, 20 H). CI-MS: 294 ($[M + 1]^+$), 262. EI-MS: 293 (< 1, M^+), 262 (5), 234 (2), 220 (7), 192 (7), 166 (6), 164 (6), 162 (6), 152 (10), 151 (6), 150 (9), 137 (12), 136 (11), 128 (12), 123 (13), 110 (18), 98 (38), 97 (55), 96 (31), 84 (22), 83 (38), 81 (24), 74 (27), 69 (24), 67 (35), 55 (100), 41 (86).

Data of **23**: M.p. 85.8–86.4° (pentane/Et_2O): IR (KBr): 3000, 2970, 2960, 2940, 2910, 2880, 2870, 2855, 2250, 1725, 1705. ^{1}H-NMR: 2.85–1.26 (*m*, 24 H); 1.44 (*s*, 3 CH_3). CI-MS: 336 ($[M + 1]^+$), 280, 262. EI-MS: 279 (7), 262 (8), 164 (6), 136 (6), 126 (22), 112 (12), 98 (42), 84 (12), 81 (11), 80 (12), 57 (100), 56 (11), 55 (56), 53 (11), 41 (67).

2.3. *12-Hydroxy-15-oxobicyclo[9.3.1]pentadec-11-ene-1-carbonitrile* (**24**). To a soln. of **4** (1.0 g, 3.41 mmol) in THF (50 ml), a 40% aq. soln. of *Triton-B* (1.34 g, 8 mmol) was added dropwise within 5 min at 0° under N_2. After 30 min, the mixture was warmed up to 20° and worked up 20 min later as described in *1.8*. The final residue was crystallized from Et_2O (10 ml) to give **24** (230 mg, m.p. 184–187°). The mother liquor contained **24** and a small amount of **25**, see *2.5*. IR (KBr): 3370 (br.), 2940, 2870, 2850, 2260, 1655, 1618. ^{1}H-NMR: 6.40 (br. *s*, OH, exchangeable with D_2O); 2.85–0.99 (*m*, 22 H). ^{13}C-NMR: 192.6 (C(15)); 166.7 (C(12)); 120.0 (CN); 112.6 (C(11)); 48.6 (C(1)); 32.0; 30.0; 26.2; 25.5; 24.6; 23.6; 23.0; 22.0; 21.8; 21.7; 20.3. CI-MS: 262 ($[M + 1]^+$). EI-MS: 261 (17, M^+), 164 (5), 154 (8), 151 (11), 150 (12), 140 (34), 139 (19), 126 (58), 125 (14), 122 (12), 112 (11), 111 (19), 109 (12), 108 (14), 98 (31), 97 (21), 95 (19), 94 (10), 93 (10), 84 (29), 83 (18), 80 (14), 79 (19), 70 (33), 67 (23), 55 (81), 43 (68), 42 (49), 41 (100), 39 (41).

2.4. *1-(2-Formylethyl)-2-oxocyclododecane-1-carbonitrile* (**26**). To a stirred soln. of **2** (4.9 g, 23.7 mmol), acrylaldehyde (1.33 g, 27 mmol), and abs. THF (120 ml), Bu_4NF (104 mg, 0.4 mmol) in THF (10 ml) was added within 10 min under Ar. After 2 h, it was worked up with AcOH (1 ml) according to *1.8*. The residue was crystallized from hexane/Et_2O to afford **26** (4.5 g, 72.2%). M.p. 85.2–86.3°. IR: 2950, 2880, 2870, 2740, 2250, 1730 (br.). IR (KBr): 3430, 2940, 2920, 2880, 2860, 2750, 2250, 1730, 1720. ^{1}H-NMR: 9.80 (*s*, CHO); 2.97–1.15 (*m*, 24 H). ^{13}C-NMR: 203.0 (C(2)); 199.1 (CHO); 119.5 (CN); 54.2 (C(1)); 39.7; 35.0; 34.9; 26.1 (2 C); 25.8; 23.4; 22.6; 22.3; 22.2; 21.3; 20.6. CI-MS: 264 ($[M + 1]^+$). EI-MS: 263 (2, M^+), 220 (19), 192 (17), 150 (9), 136 (11), 126 (10), 122 (9), 112 (11), 110 (9), 108 (8), 98 (27), 83 (8), 69 (9), 56 (37), 55 (100), 41 (34).

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[7]) Partly hydrolyzed to 3-(1-cyano-2-oxocyclododecyl)propionic acid (**25**) during chromatographic purification; see *2.5*.

2.5. *3-(1-Cyano-2-oxocyclododecyl)propanoic Acid* (**25**). A sample of **26** in acetone was oxidized at 0° with an excess of *Jones* reagent. i-PrOH was added, the mixture was evaporated, and the residue extracted with Et_2O. After evaporation, the residue was crystallized from Et_2O. M.p. 143.8–145.1°. IR (KBr): 3440 (br.), 2940, 2870, 2250, 1710. ^{1}H-NMR: 2.91–1.12 (*m*). CI-MS: 280 ([*M* + 1]$^+$), 262, 246. EI-MS: 279 (2, *M*$^+$), 220 (12), 208 (5), 192 (20), 150 (11), 136 (15), 126 (13), 123 (13), 122 (12), 112 (15), 108 (38), 98 (57), 95 (18), 94 (14), 84 (19), 80 (22), 69 (21), 67 (20), 57 (13), 56 (23), 55 (58), 53 (25), 43 (33), 41 (100).

2.6. *Methyl 4-(1-Cyano-2-oxocyclododecyl)-2-butenoate* (**7**). Following *1.3*, **2** [4] (5.18 g, 25 mmol) was alkylated to yield **7** (6.74 g, 88.3%), m.p. 122.5–122.6° (MeOH). IR: 2235, 1722, 1660, 1282. ^{1}H-NMR (90 MHz): 6.97, 6.78 (*A* of ABX_2, *J* = 16, 7, 1 H); 5.98 (*B* of ABX_2, *J* = 16, 1.5, 1 H); 3.74 (*s*, 3 H); 3.23–2.40 (*m*, 4 H); 2.26–0.95 (*m*, 18 H). EI-MS: 305 (7, *M*$^+$), 274 (15), 273 (33), 152 (15), 120 (48), 98 (63), 55 (73), 41 (100).

2.7. *Methyl 4-(1-Cyano-2-oxocyclododecyl)butanoate* (**8**). The hydrogenation of **7** (4.77 g, 15.6 mmol) in the presence of 5% Pd/$BaSO_4$ was run according to *1.4*, to give **8** (4.53 g, 94.6%), m.p. 75.0–75.6° (MeOH). IR: 2233, 1735 (sh), 1725, 1717 (sh). ^{1}H-NMR (90 MHz): 3.69 (*s*, 3 H); 2.91–2.68 (*m*, 2 H); 2.53–2.27 (*m*, 2 H); 2.17–0.80 (*m*, 22 H). EI-MS: 307 (11, *M*$^+$), 276 (15), 275 (18), 220 (13), 192 (15), 164 (12), 150 (12), 126 (14), 122 (37), 98 (99), 55 (79), 41 (100).

2.8. *Treatment of* **8** *with* t-*BuOK*. Reaction of **8** (1.845 g, 6.0 mmol) with *t*-BuOK described in *1.5* yielded, after column chromatography, **8** (86 mg, 4.7%), *methyl 13-cyano-2-oxocyclopentadecanecarboxylate* (**28**; 120 mg, 6.5%), and tert-*butyl 4-(1-cyano-2-oxocyclododecyl)butanoate* (**27**; 1.48 g, 70%; m.p. 74.6–75.4° (MeOH)[8]). Data of **28**: IR: 2239, 1741, 1710, 1642, 1610. ^{1}H-NMR (90 MHz): 12.77 (*s*, 0.2 H); 3.79 (*s*, 0.6 H); 3.74 (*s*, 1.75 H); 3.72 (*s*, 1.15 H); 3.60–3.40 (*m*, 0.8 H); 2.65–1.0 (*m*, 25 H). EI-MS: 307 (5, *M*$^+$), 276 (10), 275 (16), 154 (19), 141 (100), 109 (24), 55 (53), 41 (51).

2.9. *5-Oxopentadecanenitrile* (**29**). Ketoester **28** (85 mg, 0.28 mmol) yielded, by hydrolysis and decarboxylation according to *1.6*, the oily **29** (61 mg, 87.5%). IR: 2240, 1709. ^{1}H-NMR (90 MHz): 2.70–2.38 (*m*, 5 H); 2.15–1.15 (*m*, 22 H). EI-MS: 249 (12, *M*$^+$), 220 (6), 206 (8), 178 (8), 125 (14), 96 (38), 83 (100), 55 (52), 41 (61).

2.10. *Ethyl 4-(1'-Cyano-2'-oxocyclododecyl)butanoate* (**9**). Analogous to *1.7*, **2** (4.14 g, 20 mmol), 40% aq. soln. of Bu_4NOH (26.7 ml), ethyl 4-bromobutanoate (7.8 g, 40 mmol), and CH_2Cl_2 (20 ml) yielded a mixture which was filtered through a column of silica gel (100 g, hexane/Et_2O 4:1) to give a fraction (4.82 g, 15.02 mmol) of the *C*- and *O*-alkylated products. On treatment with pentane/Et_2O 3:2, **9** (2.9 g, 45.2%) crystallized out. M.p. 55.0–57.6°. IR (KBr): 2980, 2940, 2870 (br.), 2250, 1730, 1710. ^{1}H-NMR: 4.15 (*q*, CH_2O), 2.83–2.74 (*m*, 2 H–C(3')); 2.38 (*t*, 2 H–C(2)); 2.06–1.23 (*m*, 25 H). CI-MS: 322 ([*M* + 1]$^+$). EI-MS: 321 (2, *M*$^+$), 276 (8), 275 (10), 220 (9), 204 (5), 192 (8), 164 (7), 151 (7), 150 (9), 149 (6), 136 (12), 133 (10), 126 (19), 122 (26), 112 (14), 111 (13), 110 (14), 109 (17), 102 (12), 98 (78), 97 (26), 96 (21), 95 (20), 94 (23), 91 (34), 41 (100).

2.11. *Ethyl 1-Cyano-12-hydroxybicyclo[10.3.0]pentadecane-13-carboxylates* (**30a, b**). To a stirred soln. of **9** (1.0 g, 3.12 mmol) in abs. THF (50 ml) was added within 10 min a soln. of Li(i-Pr)$_2$N (10 mmol) in abs. THF (10 ml) at −70° under Ar. After 45 min, it was quenched with AcOH (1.5 ml) and worked up as in *1.8*. The following products were isolated by column chromatography (140 g of silica gel, hexane/Et_2O 4:1): **30a** (fast running; 50 mg, 5%), **9** (190 mg, 19%), and **30b** (490 mg, 49%).

Data of **30a**: Oil. IR (film): 3480–3460, 2940 (br.), 2880, 2240, 1740 (sh), 1710. ^{1}H-NMR: 4.21 (2*q*, shifted by 0.6 Hz, CH_2O); 4.18 (*s*, OH, exchangeable with D_2O); 3.14–3.03 (*m*, H–C(13)); 2.23–1.26 (*m*, 27 H), therein at 1.29 (*t*, CH_3). CI-MS: 322 ([*M* + 1]$^+$), 304. EI-MS: 321 (9, *M*$^+$), 293 (7), 276 (27), 275 (31), 248 (9), 247 (18), 233 (7), 230 (11), 220 (9), 205 (7), 197 (28), 192 (11), 182 (6), 181 (10), 176 (8), 168 (19), 164 (9), 163 (8), 162 (9), 155 (33), 151 (11), 150 (13), 149 (12), 148 (11), 137 (12), 136 (32), 135 (17), 130 (11), 123 (22), 122 (42), 111 (14), 110 (38), 108 (23), 105 (11), 101 (12), 98 (35), 97 (37), 96 (46), 95 (51), 94 (32), 83 (27), 81 (21), 73 (17), 69 (25), 67 (28), 55 (100), 41 (88).

Data of **30b**: IR (KBr): 3470, 3000, 2980, 2920, 2870, 2850, 2240, 1705 (sh), 1700. ^{1}H-NMR: 4.20 (*q*, *J* = 7, CH_2O); 3.87 (*s*, OH, exchangeable with D_2O); 2.79–2.71 (*m*, H–C(13)); 2.60–2.46 (*m*, 1 H); 2.22–1.25 (*m*, 26 H), therein at 1.29 (*t*, *J* = 7, CH_3). ^{13}C-NMR: 172.5 (COO); 123.1 (CN); 83.4 (C(12)); 60.1 (CH_2O); 55.1 (C(13)); 52.8 (C(1)); 33.7; 31.2; 27.6; 26.4; 26.2; 25.4; 25.0; 22.9; 22.5; 22.4; 21.7; 20.5; 14.2 (CH_3). CI-MS: 322 ([*M* + 1]$^+$), 304. EI-MS: 321 (6, *M*$^+$), 275 (23), 247 (15), 230 (14), 220 (8), 204 (8), 203 (9), 197 (22), 192 (12), 176 (11), 168 (24), 164 (13), 162 (11), 155 (47), 154 (13), 151 (12), 150 (12), 149 (13), 148 (14), 137 (12), 136 (34), 135 (20), 134 (15), 133 (10), 130 (15), 123 (22), 122 (48), 121 (21), 120 (16), 119 (12), 110 (22), 109 (42), 108 (21), 107 (14), 101 (15), 98 (41), 97 (42), 96 (50), 95 (60), 94 (34), 93 (23), 91 (18), 84 (23), 83 (47), 82 (23), 81 (42), 67 (35), 55 (100), 43 (39), 41 (42).

2.12. *Ethyl 5-(1'-Cyano-2'-oxocyclododecyl)pentanoate* (**15**). *Method A, cf.* [5]. Compound **2** (4.14 g, 20 mmol), in $CHCl_3$ (20 ml) was added to a Bu_4NOH soln., prepared from Bu_4NHSO_4 (7.5 g, 22 mmol), NaOH

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[8]) By treatment of **27** with HCl/MeOH, ester **8** was formed (TLC evidence).

(1.68 g, 42 mmol), and H_2O (20 ml) at 0°. After 1 h stirring, the $CHCl_3$ layer was separated and treated with ethyl 5-bromopentanoate (**13**; 8.36 g, 40 mmol). After 3 h, the mixture was washed with H_2O, the org. layer dried, evaporated, and the residue purified by chromatography (150 g of silica gel, hexane/Et_2O 5:1). The evaporated eluate (**15**/**14**) was crystallized from Et_2O/pentane to give **15** (2.48 g, 37%).

Method B. A soln. of **2** (2.07 g, 10 mmol) and **13** (2.3 g, 11 mmol) in CH_2Cl_2 (20 ml) was stirred together with a 40% aq. soln. of Bu_4NOH (5.18 g, 20 mmol) for 30 h and worked up as described in *1.7*. Chromatography (120 g of silica gel, hexane/Et_2O 4:1) afforded 1.17 g of a mixed fraction from which **15** (735 mg, 21.9%), and afterwards **2** (560 mg, 27%) were isolated. Data of **15**: M.p. 55.6–56.3°. IR (KBr): 2940, 2870, 2250, 1735, 1710. ^{1}H-NMR: 4.12 (*q*, *J* = 7, CH_3CH_2O); 2.77–2.70 (*m*, 2 H–C(3′)); 2.32 (*t*, *J* = 3, 2 H–C(2)); 1.99–1.19 (*m*, 27 H). ^{13}C-NMR: 203.9 (C(2′)); 173.1 (COO); 120.2 (CN); 60.3 (CH_3CH_2O); 55.4 (C(1′)); 35.2; 35.1; 33.9; 33.8; 26.4; 26.2; 24.9; 24.7; 23.6; 22.8; 22.7; 22.4; 21.4; 21.0; 14.2 (CH_3). CI-MS: 336 ([*M* + 1]$^+$), 290. EI-MS: 307 (1), 290 (5), 262 (10), 261 (16), 234 (9), 192 (9), 179 (6), 164 (10), 151 (12), 150 (9), 148 (6), 137 (19), 136 (16), 126 (12), 123 (16), 122 (13), 112 (13), 111 (12), 110 (13), 109 (12), 108 (12), 98 (84), 97 (23), 95 (20), 94 (18), 84 (16), 83 (24), 81 (30), 80 (22), 69 (19), 67 (31), 55 (72), 43 (48), 41 (100). Anal. calc. for $C_{20}H_{33}NO_3$ (335.49): C 71.60, H 9.91, N 4.17; found: C 70.54, H 9.99, N 4.21.

2.13. *Ethyl 1-Cyano-12-hydroxybicyclo[10.4.0]hexadecane-13-carboxylates* (**31a, b**). To a stirred soln. of **15** (1.0 g, 2.99 mmol) in abs. THF (20 ml) was added dropwise (10 min) Li(i-Pr)$_2$N (10 mmol) in abs. THF (20 ml) at −60° under Ar. The mixture was allowed to warm to −45° within 75 min, and after addition of AcOH (1.5 ml), it was worked up as described in *1.8*. Chromatography (100 g of silica gel, hexane/Et_2O 4:1) afforded **31a** (40 mg, 4%; fast running), **31b** (450 mg, 45%), and **15** (200 mg, 20%). Data of **31a**: Oil. IR (film): 3490, 2990, 2940, 2870, 2240, 1710 (br.). CI-MS: 336 ([*M* + 1]$^+$), 318. EI-MS: 335 (6, *M*$^+$), 307 (3), 290 (12), 289 (13), 261 (13), 244 (7), 234 (7), 211 (9), 208 (8), 196 (7), 195 (30), 192 (5), 178 (6), 176 (7), 169 (6), 150 (11), 149 (12), 137 (14), 136 (13), 135 (9), 123 (17), 122 (14), 121 (16), 111 (12), 110 (10), 109 (16), 108 (12), 107 (15), 98 (24), 97 (23), 96 (15), 95 (20), 94 (18), 93 (18), 91 (17), 83 (20), 82 (14), 81 (34), 80 (35), 79 (26), 73 (15), 69 (22), 68 (13), 67 (41), 57 (14), 56 (13), 55 (100), 41 (91).

Data of **31b**: M.p. 103.5–105.5° (Et_2O/pentane 1:1). IR (KBr): 3450, 3010, 2980, 2940 (br.), 2900, 2890, 2870, 2850, 2240, 1695 (br.). ^{1}H-NMR: 4.33 (*s*, OH, exchangeable with D_2O); 4.22 (*q*, *J* = 7, CH_2O); 2.87 (*dd*, *J* = 3.5, 9, H–C(13)); 2.07–1.18 (*m*, 29 H), therein at 1.31 (*t*, *J* = 7, CH_3). ^{13}C-NMR: 173.8 (COO); 122.5 (CN); 74.9 (C(12)); 61.3 (CH_2O); 52.1 (C(13)); 49.7 (C(1)); 34.1; 32.3; 27.5; 26.4; 26.3; 25.9; 24.3; 24.2; 23.4; 22.9; 22.7; 21.6; 21.0; 14.1 (CH_3). CI-MS: 336 ([*M* + 1]$^+$), 318. EI-MS: 335 (4, *M*$^+$), 290 (7), 289 (13), 262 (6), 261 (11), 244 (6), 234 (5), 211 (14), 195 (10), 178 (6), 169 (9), 168 (6), 149 (9), 148 (6), 137 (9), 136 (13), 135 (11), 134 (9), 130 (8), 123 (11), 122 (10), 121 (11), 111 (11), 110 (11), 109 (14), 108 (13), 101 (14), 98 (30), 97 (25), 95 (19), 94 (17), 93 (14), 91 (10), 84 (39), 83 (19), 82 (13), 81 (32), 80 (38), 79 (20), 72 (21), 68 (28), 66 (33), 55 (92), 43 (42), 41 (100). Anal. calc. for $C_{20}H_{33}NO_3$ (335.49): C 71.60, H 9.91, N 4.17; found: C 70.40, H 9.56, N 3.62.

3. *Acetonyl Derivatives.* 3.1. *1-Allyl-2-oxocyclooctane-1-carbonitrile* (**32**) *and 1-Allyl-2-oxocyclododecane-1-carbonitrile* (**33**). Treatment of **1** (4.53 g, 30 mmol) or **2** (6.21 g, 30 mmol) with allyl bromide (5.44 g, 45 mmol) in the presence of Bu_4NHSO_4 (10.19 g, 30 mmol) and 2N NaOH (31 ml) in analogy to *1.3* afforded **32** (5.17 g, 90.2%) and **33** (4.54 g, 61.3%), resp. Data of **32**: Oil. IR: 2950, 2880, 2240, 1712 (br.), 1645. ^{1}H-NMR (90 MHz): 6.03–5.61 (*m*, 1H); 5.33–5.12 (*m*, 2 H); 2.81–1.28 (*m*, 14 H). EI-MS: 191 (79, *M*$^+$), 162 (21), 149 (19), 133 (20), 98 (61), 94 (100).

Data of **33**: M.p. 75.4–76.2° (MeOH). IR: 2930 (br.), 2855, 2240, 1725 (br.), 1655. ^{1}H-NMR (90 MHz): 6.05–5.55 (*m*, 1H); 5.40–5.12 (*m*, 2 H); 2.85–1.19 (*m*, 22 H). EI-MS: 247 (15, *M*$^+$), 204 (7), 190 (8), 178 (6), 176 (10), 164 (6), 162 (7), 150 (10), 148 (8), 137 (10), 136 (13), 126 (31), 123 (11), 122 (12), 120 (9), 112 (21), 109 (14), 98 (100), 94 (30), 84 (24), 81 (20), 69 (22), 67 (41), 55 (54), 43 (27), 41 (84).

3.3. *1-Acetonyl-2-oxocyclooctane-1-carbonitrile* (**34**) *and 1-Acetonyl-2-oxocyclododecane-1-carbonitrile* (**35**). According to [10], **32** (4.97 g, 26 mmol) or **33** (6.4 g, 26 mmol) was converted with CuCl (5.14 g, 52 mmol) and $PdCl_2$ (1.78 g, 10 mmol) in DMF under O_2 to **34** (1.99 g, 37%) and **35** (3.8 g, 55.6%), resp. Data of **34**: IR: 3550, 3420, 3030 (br.), 2980, 2940 (br.), 2890, 2870, 2250, 1725 (sh), 1715. IR (KBr): 3410, 2990, 2970, 2950, 2920, 2890, 2870, 2245, 1712 (br.). ^{1}H-NMR (90 MHz): 3.58–3.18 (*m*, 2 H); 3.04–0.90 (*m*, 12 H), therein at 2.17 (*s*, 3 H). EI-MS: 207 (1, *M*$^+$), 164 (17), 136 (19), 119 (7), 109 (9), 98 (5), 95 (8), 94 (12), 91 (6), 80 (8), 69 (6), 67 (17), 55 (20), 53 (13), 43 (100), 41 (34).

Data of **35**: IR: 2940, 2860, 2240, 1725 (br.). EI-MS: 263 (9, *M*$^+$), 221 (10), 220 (59), 193 (6), 192 (41), 164 (7), 150 (14), 136 (19), 126 (17), 122 (16), 112 (17), 110 (10), 108 (14), 98 (62), 95 (19), 84 (15), 83 (16), 82 (14), 81 (26), 80 (15), 69 (22), 67 (24), 57 (22), 56 (21), 55 (70), 54 (13), 53 (18), 43 (81), 42 (26), 41 (100).

3.3. *3,5-Dioxocycloundecane-1-carbonitrile* (**36**). Compound **34** (829 mg, 4 mmol) was treated with *t*-BuOK (1.12 g, 10 mmol) according to *1.5* to give **34** (149 mg, 18%) and **36** (499 mg, 60.2%; amorphous). IR: 3540 (br.), 3400, 2930, 2860, 2240, 1730, 1695 (br.), 1585 (br.). ^{1}H-NMR (90 MHz): 3.87–3.51 (*m*, 2 H); 3.38–0.94 (*m*, 15 H).

EI-MS: 207 (2, M^+), 189 (6), 164 (21), 151 (8), 150 (41), 149 (17), 137 (15), 136 (21), 123 (16), 122 (33), 121 (10), 111 (20), 110 (25), 109 (18), 108 (15), 98 (39), 97 (66), 96 (26), 95 (25), 94 (22), 84 (38), 83 (20), 81 (31), 80 (20), 69 (44), 68 (33), 58 (44), 55 (77), 54 (40), 53 (32), 43 (57), 42 (43), 41 (100).

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