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FUNCTIONALIZED CHLOROENAMINES IN AMINOCYCLOPROPANE SYNTHESIS - V.[1] SYNTHESIS AND REACTIONS OF AMINOCYCLOPROPYLKETONES

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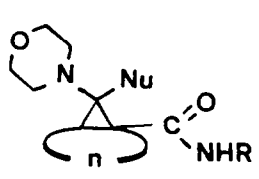
Abstract: Conjugated acylated chloroenamines **5A,C** were available by chlorination of mixtures of acylated enamines **8A,C/9A,C** by NCS at 0°C. Nonconjugated chloroenamines **10Aa** and **10Ba** could be obtained by NCS-chlorination of the conjugated acylenamines **9A,B** at low temperature. Reaction of **5Aa-5Ac,5Ae, 5Af** with cyanide produced morpholinocyclopropylketones **11A**. In two cases aminofurans **12Ad** and **12Ca** resulted as products of this reaction. More generally amino-aryl-furans **12** were formed by thermolysis of the aryl-cyclopropylketones **11**. Amino-alkyl-furans as **12Ae** and **12Af** only could be trapped by a Diels-Alder reaction leading to **16Ae** and **16Af**. Epoxyenamines **29A,B** unexpectedly were produced from the interaction of cyanide with the chloroenamines **10Aa** and **10Ba**.

The reaction of carbamoylated chloroenamines **4**[1-4] with nucleophiles proved to be a useful basis for the synthesis of bicyclic lactams **2**[2] or **3**[1]. The formation of **2** or **3** from **4** consists of a formal combination of a ring contraction and an aza-annulation reaction. This can be effected either by a direct tandem type process[1] or by a cyclization - ring opening - aza-annulation sequence[2] including an aminocyclopropane derivative **1** as isolable intermediate product.



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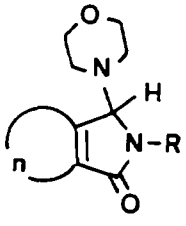

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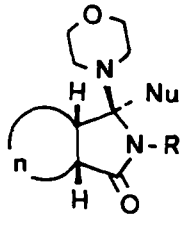
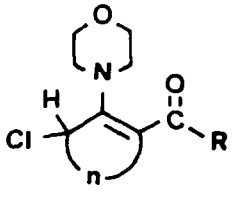
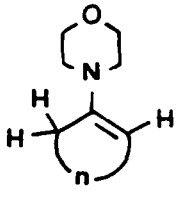


3

Nu: H, CN



4: R = NHR
5: R = Aryl, Alkyl



6

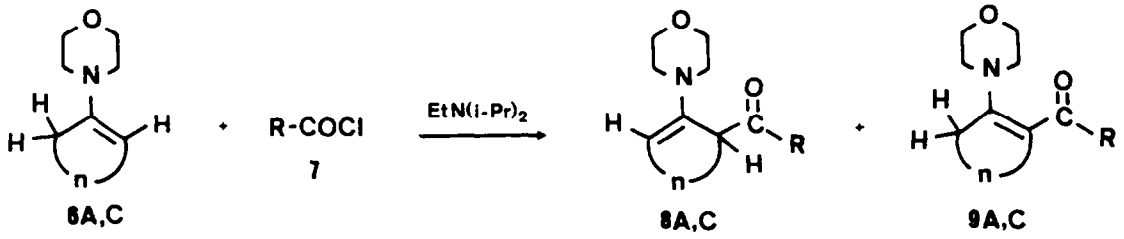
The simple accessibility of acylated chloroenamines of type **4** from enamines **6** prompted us to look for further systems leading to the overall result of a ring contraction - hetero-annulation reaction. We synthesized, therefore, acylated chloroenamines **5** and investigated their reaction with cyanide as a typical nucleophile.

ACYLATED CHLOROENAMINES 5 AND 10

An acylation - chlorination sequence was used as access to the acylated chloroenamines **5** in analogy to the synthesis of carbamoylated chloroenamines **4**[2].

Acylation of enamines **6** by acid chlorides is a well known process[5] leading to a mixture of isomeric acylation products **8/9** (e. g. acylation of **6A** with **7a**[6,7], **7e**[6,8,9] or **7f**[10], **6C** with **7a**[11]). In the case of the benzoylated derivative the conjugated isomer **9Aa** is reported to predominate strongly over the nonconjugated species **8Aa** in the acylation mixture[6,7]; an opposite result is described for the acetylated compound **9Ae**[6,8,9] (see also ref. [12]). Cycloheptenyl morpholine **6B** was benzoylated according to a general procedure for the acylation of enamines[8]. The product obtained in 61% yield almost exclusively consists of **9Ba** (> 90%) as detected by ^{1}H- and ^{13}C NMR spectroscopy.

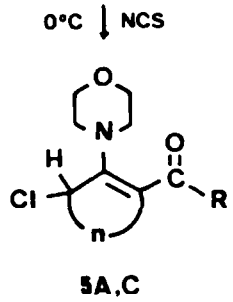
Treating the crude acylation mixtures **8A,C/9A,C** with N-chlorosuccinimide at 0°C gave the desired acylated chloroenamines **5A,C** in 37-62% yield (calculated for **6** as starting material). The CHCl-unit in **5** unequivocally can be established by a multiplet at 4.83-4.92 ppm (**5A**) or 5.15 ppm (**5C**) in the ^{1}H NMR spectrum and a doublet at 54.8-55.5 ppm (**5A**) or 56.8 ppm (**5C**) in the



5, 7-13
15, 16 R

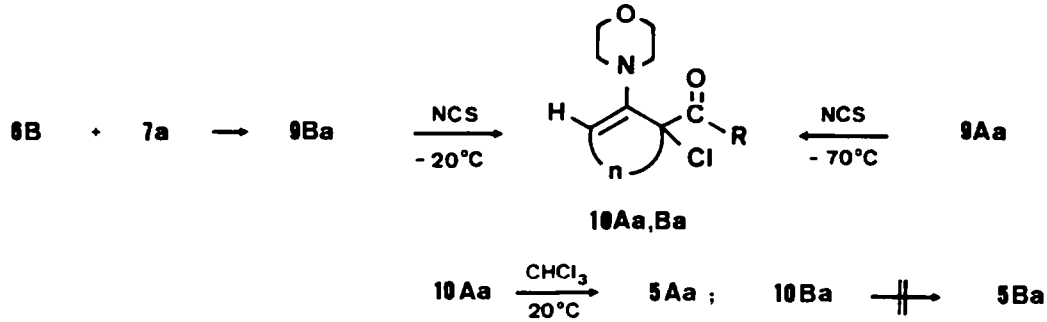
a	C_6H_5	**b**	4-CH_3-C_6H_4
c	4-Cl-C_6H_4	**d**	4-NO_2-C_6H_4
e	CH_3	**f**	CH_2-C_6H_5

1-6, 8-13, 15, 16, 28, 29: **A** $(CH_2)_3$ **B** $(CH_2)_4$ **C** $(CH_2)_9$



^{13}C NMR spectrum. The observed values of the coupling constant $^{1}J_{CH}$ = 146-153 Hz for the doublet are characteristic of an adjacent chlorine group[13]; these values exclude the existence of an isomeric compound (presence of an CHCOR-moiety, Cl at the CC-double bond).

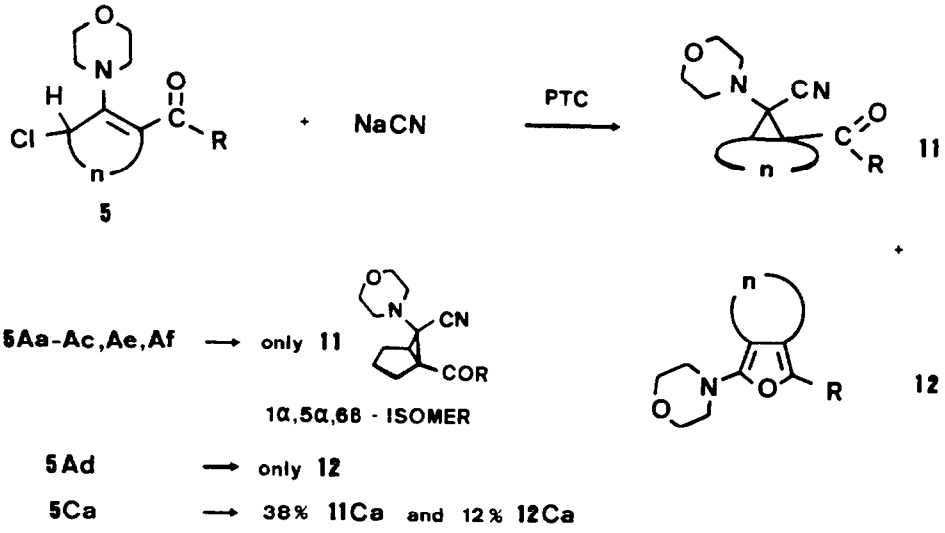
Analogous chlorination of the seven-membered system **9B** with NCS at 0°C led to a nonconjugated chloroenamine **10Ba** instead of the expected conjugated species **5Ba**. A purer product **10Ba** (53% yield) was obtained by running the chlorination reaction at -20°C. The nonconjugated chloroallyl group is indicated in the ^{13}C NMR spectrum by two singlets at 151.5 ppm and 84.1 ppm and one doublet at 120.5 ppm. Similarily pure **10Aa** was accessible in 41% yield from the chlorination of **9Aa** with NCS at -70°C (^{13}C NMR of the chloroallyl moiety: singlets at 146.3 ppm and 79.0 ppm, doublet at 109.6 ppm). Thus far **10Ba** could not be converted into the conjugated isomer **5Ba**. **10Ba** proved to be stable for a longer period even in boiling dichloromethane solution. **10Aa**, however, isomerized into **5Aa** in a chloroform solution upon standing at room temperature for 24 h.



Direct NCS-chlorination transforms a nonconjugated acylenamine **8** into chloroenamine **5** and a conjugated enamine **9** into chloroenamine **10**. **8**, thereby, is much more reactive than **9**. Benzoylated chloroenamine **5A** was formed to a higher extend from a mixture **8A/9A** than **8**, its direct precursor, was present in this mixture. This requires at least one isomerization process which could take place at the stage of the starting materials **8/9** or the products **5/10**. An equilibrium at the side of the starting materials was assumed for the explanation of the reaction of **8A/9A** with azodicarboxylate generating products exclusively derived from **8A**.[12] An isomerization at the product side was observed to be the reason for the formation of a seven-membered carbamoylated chloroenamine **4B**.[2] The chlorination of **8Aa** at different temperatures leading either to **5Aa** or to **10Aa** and a subsequent slow transformation of **10Aa** into **5Aa** demonstrate that both isomerization processes can be effective for acylated six-membered enamines. In the case of the seven-membered ring an isomerization process seems to be difficult as well for **10** as for **9**.

AMINOCYCLOPROPYLKETONES 11 AND AMINOFURANS 12

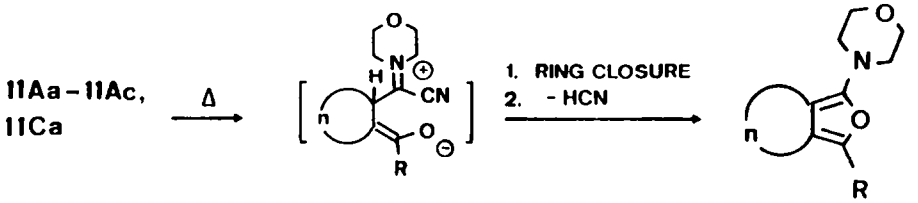
Reaction of the acylated chloroenamines **5Aa-5Ac, 5Ae** and **5Af** with cyanide gave aminobicyclohexylketones **11Aa-11Ac, 11Ae** and **11Af** in 46-70% yield. Acetonitrile - water (1:1) or ether - water (9:1) as a solvent in the presence of methyltrioctylammonium chloride as a phase transfer catalyst proved to be the best conditions for the cyclopropane formation. The cyclopropane moiety in **11A** is established by the ^{13}C NMR spectrum indicating two singlets (δ = 48-54 ppm) and one doublet (δ = 39-40 ppm, $^{1}J_{CH}$ = 170-173 Hz) in the expected regions.

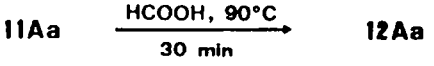


Morpholine ^{1}H NMR signals of an ABXY-type (**11Ae, 11Af**) or of an ABXY-type with beginning coalescence (**11Aa-11Ac**) ($CDCl_3$) give the information about the uniform endo-morpholino configuration of the obtained aminobicyclohexylketones (assignment of configuration by this method is described in ref. [4,14-17]). Temperature dependency of the ^{1}H NMR - OCH_2-signals was studied for **11Aa** and **11Ae** in $C_6D_5NO_2$ (**11Aa**: H_{X1} = 3.71 ppm, H_{X2} = 3.66 ppm, $^{2}J_{AB}$ = $^{3}J_{AB}$ = 10 Hz; H_{Y1}/H_{Y2} = 3.92 ppm, 3.98 ppm, $^{2}J_{AB}$ = 10 Hz; T_c = 333 K; **11Ae**: H_{X1} = 3.26 ppm, H_{X2} = 3.31 ppm, $^{2}J_{AB}$ = $^{3}J_{AB}$ = 11 Hz; H_{Y1}/H_{Y2} = 3.56 ppm, $^{2}J_{AB}$ = 11 Hz; T_c = 368 K). $\Delta G^{\ddagger}$-values of 68.1-69.3 kJ/mol (**11Aa**) and 75.8-76.3 kJ/mol (**11Ae**) were calculated for the morpholine dynamics using the well known approximation formula[18] as described in ref.[4]; these values unequivocally are characteristic of a morpholino moiety in the endo-position of a bicyclohexyl system.[4,15]

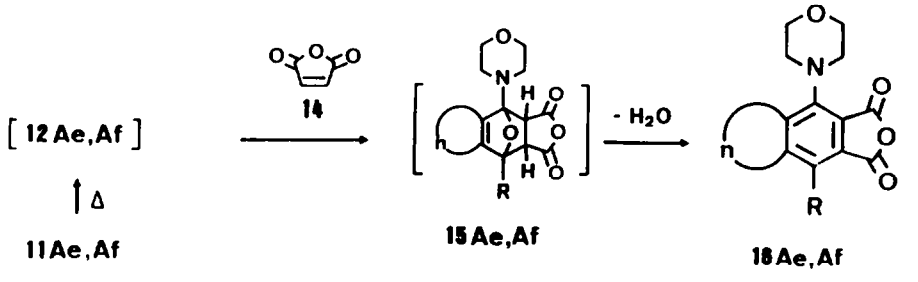
Aminofuran **12Ca** (12% yield) was obtained from the analogous treatment of benzoylated chloroenamine **5Ca** with cyanide besides the expected aminocyclopropylketone **11Ca** (38% yield). Again the ^{13}C NMR signals at 47.1 (s), 46.0 (s) and 32.4 (d, $^{2}J_{CH}$ = 160 Hz) are significant of the cyclopropane moiety in **11Ca**; the configuration of the bicyclic ketone **11Ca**, however, is not clear

(see ref.[2,3]). In the case of the nitrobenzoyl chloroenamine **5Ad** an aminofuran **12Ad** was the sole reaction product (55% yield) which was isolated. A decomposition of aminocyclopropylketones **11** is expected to be the origin of the aminofurans **12**. Thus aminofurans **12** indeed were accessible in 44–71% yield by heating the arylsubstituted bicyclic derivatives **11Aa–11Ac** or **11Ca** to 160°C for 3 h. The formation of **12** from **11** can be understood as a homoenamine type reaction[19] or a heterovinyl cyclopropane rearrangement[20]. In each case **13** should be the intermediate of the thermal decomposition of **11**.



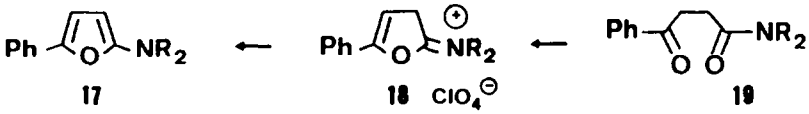


Ring closure and elimination of HCN are the subsequent steps on the way to the aminofurans **12**. Decomposition of **11Aa** to aminofuran **12Aa** (77% yield) also could be achieved by heating in formic acid. The opening of the cyclopropane ring is facilitated by increasing acceptor strenght of the carbonyl group (e.g. nitrophenyl moiety in the non isolable **11Ad**). Heating the alkylsubstituted cyclopropylketones **11Ae** and **11Af** in boiling formic acid or without a solvent gave no isolable furan derivatives. It could be demonstrated that **12Ae** and **12Af** are not obtained due to less thermal stability of alkylsubstituted aminofurans. Decomposition of **11Ae** and **11Af** in the presence of maleic anhydride led to annulated aminophthalic anhydrides **16Ae** and **16Af** which stem from a Diels-Alder reaction of **12Ae/12Af** with **14** as a trapping reagent. **15** as the

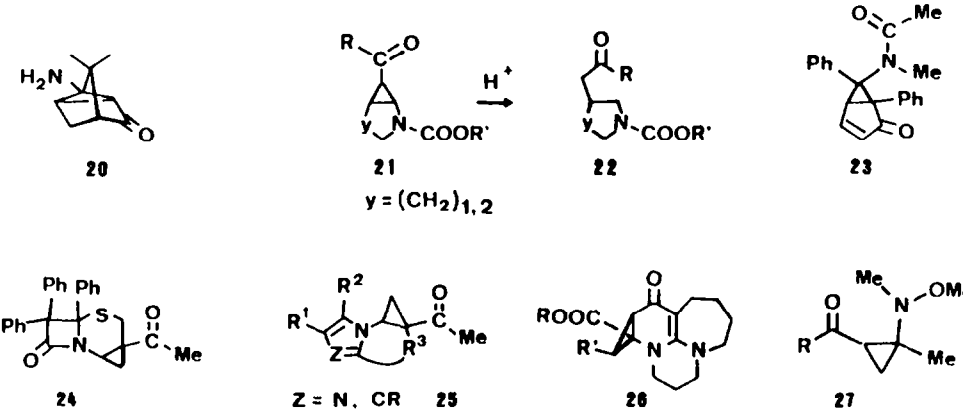


primary product is not stable under the reaction conditions; a cleavage of the N,O-acetal function and elimination of water led to **16Ae** and **16Af** as the isolable products. Analogously a Diels-Alder product **16Ac** was accessible by heating maleic anhydride (**14**) either with aminocyclopropylketone **11Ac** (→ 48% yield) or aminofuran **12Ac** (→ 61% yield). In the former case a decomposition of **11Ac** to **12Ac** took place prior to the cycloaddition reaction with **14**. ^{1}H NMR and ^{13}C NMR data clearly demonstrate the aminophthalic anhydride constitution **16** of the Diels-Alder products. Diels-Alder reactions with furans as dienes are well known. An aminophthalic anhydride derivative, similar to **16**, was reported to be the result of a Diels-Alder reaction of **14** with aminofuran **17**.[21]

Simple arylsubstituted dialkylaminofurans **17** could be synthesized by deprotonation of iminium salts **18** which were obtained from tertiary amides of ß-aroylpropionic acids **19**, acetic anhydride and perchloric acid.[21] The aryl moiety in **19** is essential for the success of this synthesis, alkyl substituted aminofurans could not be prepared by this procedure.[21]



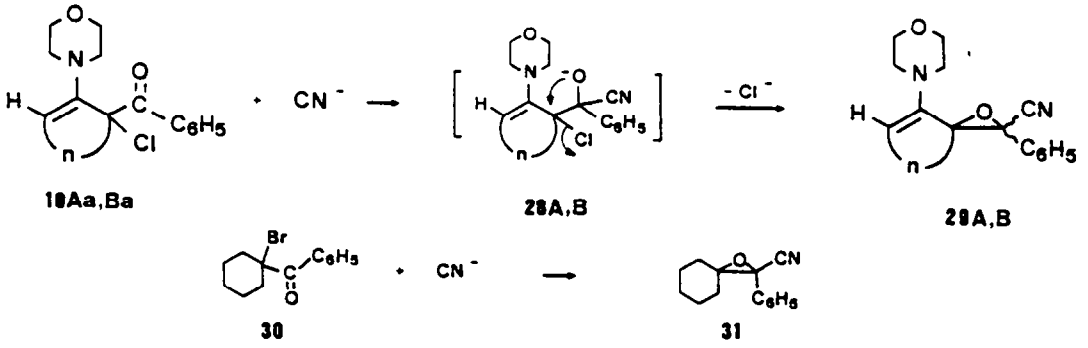
The sequence **6** → **5** → **11** → **12** represents a new way to aminocyclopropylketones **11** and to aminofurans **12**. Only very few aminocyclopropylketones thus far have been reported in the literature; with one exception these compounds represent no real push-pull substituted cyclopropanes due to a deactivation of the amino moiety [e.g. **20**[22] (exception, but a very special compound), **21**[23,24] (N-deactivation by an ester moiety), **23**[25] and **24**[26] (N-deactivation by an acyl group), **25** (N-deactivation by incorporation of the nitrogen atom into a pyrrole-[27], an imidazole-[28,29] or an indole-[30] unit); **26**[31] (a vinylogous amide



rather than an aminocyclopropylketone)]. **21** gave rise to a ring opening reaction in the presence of acid to produce isomerized ketones **22**[23,24]. No aminofuran formation is observed in contrast to our investigations. N-Alkoxyaminocyclopropylketones **27** are described in a recent publication; the ^{13}C NMR data given, however, are not in accordance with the proposed type of compounds.[32]

EPOXYENAMINES 29

The nonconjugated acylated chloroenamines **10** principally should produce the same bicyclic ketones **11** upon interaction with cyanide as their conjugated counterpart **5**. Epoxyenamines **29A,B**, however, were formed from sodium cyanide and chloroenamines **10Aa** and **10Ba** in water instead of the expected cyclopropyl ketones **11Aa** and **10Ba**. Better yields of **29** were obtained by running the reaction in dichloromethane and by using tetraethylammonium cyanide. The resulting epoxyenamines **29** (**29A**: 67% yield; **29B**: 70% yield) proved to be



a mixture of two diastereomeric compounds. In both cases a pure isomer was accessible by crystallization from ether (**29A**: 20% yield; **29B**: 31% yield). The ^{13}C NMR spectra are in accordance with the functional groups in **29A,B** [pure isomers: CC-double bond: **29A**: 143.7 (s), 119.8 (d); **29B**: 146.8 (s), 108.7 (d); oxirane: **29A**: 69.5 (s), 57.2 (s); **29B**: 71.2 (s), 58.4 (s)]. An additional set of ^{13}C NMR signals was observed for the second diastereomeric compound in the crude reaction products.

29 should be derived from an attack of the cyanide to the carbonyl group of **10a** leading to intermediate **28**. The latter gives **29** by a subsequent nucleophilic substitution of chloride. The formation of **29** from **10** parallels to the reaction of bromoketone **30** with cyanide generating epoxide **31**.[33] The different carbonyl activities of the two isomeric chloroenamines explain the varying reaction behaviour: **10** possesses a ketone carbonyl function which easily adds

cyanide at the carbonyl group to give an epoxide. Contrarily, the vinylogous carboxamide **5** do not add cyanide at the carbonyl moiety; this allows the formation of a cyclopropane species **10** by a 1,3-ring closure reaction.

EXPERIMENTAL

^1H NMR and ^{13}C NMR spectra were recorded with a Bruker AM 400 or - if not otherwise noted - a Bruker WP 200 spectrometer (TMS as internal standard). IR spectra were measured on a Perkin-Elmer 397 Infrared Spectrophotometer. Melting points are uncorrected. Microanalyses were performed with a Perkin-Elmer 240 Elemental Analyzer. N_2 as inert gas and anhydrous solvents were used for the acylation and the chlorination reactions.

(2-Morpholino-1-cyclohepten-1-yl)-phenyl-methanone (**9Ba**): **9Ba** was prepared according to a general procedure[8] from 9.06 g (50 mmol) of enamine **6B**, 9.35 mL (55 mmol) of ethyldiisopropylamine and 5.8 mL (50 mmol) of benzoyl chloride (**7a**) in dichloromethane (40 mL) at 0°C. Stirring at 20°C for 2 h, working up as usual and distillation in a Kugelrohr apparatus at 178-184°C/ 0.03 mbar gave 8.7 g (61%) **9Ba** as an yellow oil. IR (film, cm^{-1}) 1630, 1580 (C=O, C=C); ^1H NMR ($CDCl_3$, 400 MHz) δ 1.50-1.79 (m, 6H), 2.37-2.49 (m, 4H), 2.58-2.68 (m, 4H), 3.70-3.78 (m, 4H), 7.30-7.50 (m, 3H), 7.70 (d, 2H); ^{13}C NMR ($CDCl_3$) δ 199.0 (s), 160.4 (s), 140.5 (s), 131.4 (d), 128.6 (d), 128.1 (d), 123.6 (s), 66.8 (t), 50.9 (t), 31.9 (t), 30.5 (t), 30.1 (t), 27.4 (t), 25.9 (t). Anal. Calcd for $C_{18}H_{23}NO_2$: C, 75.76; H, 8.12; N, 4.91. Found: C, 75.1; H, 7.93; N, 4.7.

(3-Chloro-2-morpholino-1-cyclohexen-1-yl)-phenyl-methanones 5Aa-5Ad - General Procedure: A solution of acid chloride **7** (45 mmol; **7a**: 6.32 g; **7b**: 6.95 g; **7c**; 7.88g; **7d**: 8.35 g) in chloroform (10 mL) was dropped at 0°C within 10 min to a mixture of enamine **6A** (7.53 g, 45 mmol) and triethylamine (10.0 g, 100 mmol) in chloroform (10 mL). Stirring was continued for 2 h at 20°C, then the solvent was evaporated. Extraction of the residue with ether (30 mL), filtration, washing of the residue with ether (3 x 5 mL) and evaporation of the combined ether solutions gave crude benzoylated enamines **8Aa-8Ad/ 9Aa-9Ad**. N-Chlorosuccinimide (6.00 g, 45 mmol) in acetonitrile (50 mL) was added to a solution of the crude acylated enamine **8A** in acetonitrile (50 mL) at 0°C within 15 min. After additional stirring at 20°C for 2 h and removal of the solvent the residue was triturated with a mixture of 70 mL of H_2O and 30 mL of ether. In the case of **5Aa** and **5Ac** the water phase was separated and extracted with ether (2 x 20 mL). Concentration of the dried, combined ether solutions to 30 mL and storing at -18°C for 16 h gave crystalline chloroenamines **5Aa** and **5Ac** which were recrystallized from ether (20 mL). A similar procedure was used for **5Ab** and **5Ad**; here, however, a portion of the chloroenamine could be obtained as a white solid by suction prior to the separation of the ether - water mixture.

(3-Chloro-2-morpholino-1-cyclohexen-1-yl)-phenyl-methanone (**5Aa**): Yield: 5.02 g (37%); mp 116°C; IR (KBr, cm^{-1}) 1640, 1600 (C=O, C=C); ^1H NMR ($CDCl_3$) δ 1.69-2.38 (m, 5H), 2.57-2.70 (m, 1H), 2.70-2.95 (m, 4H), 2.98-3.28 (m, 4H), 4.90 (m_c, 1H), 7.30-7.60 (m, 3H), 7.76 (d, 2H); ^{13}C NMR ($CDCl_3$) δ 199.7 (s), 149.0 (s), 138.4 (s), 132.7 (d), 128.7 (d), 128.4 (d), 126.0 (s), 66.5 (t), 55.0 (d, $^1J_{CH}$ = 146 Hz), 50.9 (t), 33.0 (t), 27.1 (t), 16.8 (t). Anal. Calcd for $C_{17}H_{20}ClNO_2$: C, 66.77; H, 6.59; N, 4.58. Found:C, 66.9; H, 6.61; N, 4.7.

(3-Chloro-2-morpholino-1-cyclohexen-1-yl)-(4-methyl-phenyl)-methanone (**5Ab**): Yield: 7.63 g (53%); mp 151°C; IR (KBr, cm^{-1}) 1650, 1610 (C=O, C=C); ^1H NMR ($CDCl_3$) δ 1.70-2.35 (m, 5H), 2.41 (s, 3H), 2.56-2.97 (m, 5H), 3.05-3.31 (m, 4H), 4.90 (m_c, 1H), 7.20, 7.23, 7.66, 7.70 (AA'XX'-system, 4H); ^{13}C NMR ($CDCl_3$) δ 199.5 (s), 148.1 (s), 135.6 (s), 129.5 (s), 129.2 (d), 129.0 (d), 126.3 (s), 66.6 (t), 55.0 (d, $^1J_{CH}$ = 151 Hz), 50.8 (t), 33.1 (t), 27.2 (t), 21.7 (q), 16.8 (t). Anal. Calcd for $C_{18}H_{22}ClNO_2$: C, 67.60; H, 6.93; N, 4.38. Found: C, 67.7; H, 6.93; N, 4.5.

(3-Chloro-2-morpholino-1-cyclohexen-1-yl)-(4-chlorophenyl)-methanone (**5Ac**): Yield: 8.88 g (58%); mp 128°C decomp.; IR (KBr, cm^{-1}) 1650, 1590 (C=O, C=C); ^1H NMR ($CDCl_3$) δ 1.73-2.38 (m, 5H), 2.58-2.78 (m, 1H), 2.79-2.99 (m, 4H), 3.10-3.33 (m, 4H), 4.90 (m_c, 1H), 7.38, 7.43, 7.70, 7.75 (AA'XX'-system, 4H); ^{13}C NMR ($CDCl_3$) δ 198.5 (s), 149.6 (s), 138.9 (s), 136.9 (s), 130.3 (d), 128.9 (d), 125.4 (s), 66.6 (t), 54.8 (d, $^1J_{CH}$ = 151 Hz), 51.0 (t), 33.0 (t), 27.0 (t), 16.8 (t). Anal. Calcd for $C_{17}H_{19}Cl_2NO_2$: C, 60.01; H, 5.63; N, 4.12. Found: C, 59.8; H, 5.61; N, 4.3.

(3-Chloro-2-morpholino-1-cyclohexen-1-yl)-(4-nitrophenyl)-methanone (**5Ad**): Yield: 9.31 g (59%); mp 123°C; IR (KBr, cm^{-1}) 1630, 1600 (C=O, C=C), 1520 (NO_2); ^1H NMR ($CDCl_3$) δ 1.75-2.43 (m, 5H), 2.62-2.97 (m, 5H), 3.01-3.32 (m, 4H), 4.92 (m_c, 1H), 7.87, 7.92, 8.26, 8.31 (AA'XX'-system, 4H); ^{13}C NMR ($CDCl_3$) δ 197.2 (s), 152.3 (s), 149.4 (s), 144.3 (s), 129.4 (d), 123.7 (d), 124.0 (s), 66.3 (t), 54.7 (d, $^1J_{CH}$ = 153 Hz), 51.2 (t), 32.9 (t), 26.9 (t), 16.7 (t). Anal. Calcd for $C_{17}H_{19}ClN_2O_4$: C, 58.21; H, 5.46; N, 7.99. Found: C, 57.8; H, 5.33; N, 7.7.

(3-Chloro-2-morpholino-1-cyclohexen-1-yl)-ethanones 5Ae and 5Af - General Procedure: A solution of acid chloride **7** (50 mmol; **7e**: 3.92 g; **7f**: 7.73 g) in dichloromethane (20 mL) was dropped at 0°C within 15 min to a mixture of enamine **6A** (8.30 g, 50 mmol) and ethyldiisopropylamine (9.35 mL, 55 mmol) in dichloromethane (20 mL). Stirring was continued for 3 h at 20°C, then N-chlorosuccinimide (5.32 g, 40 mmol) was added at 0°C under vigorous stirring in small portions to the solution. After 30 min at 0°C the solvent was removed and the residue was extracted with ether (250 mL). Washing of the ether layer with water (3 x 75 mL), drying and concentration of the ether solutuion to 30 mL and storing at -20°C for 16 h gave chloroenamines **5Ae** and **5Af** which were recrystallized from ether (60 mL).

1-(3-Chloro-2-morpholino-1-cyclohexen-1-yl)-ethanone (**5Ae**): Yield: 4.68 g (38%); mp 56°C decomp.; IR (KBr, cm^{-1}) 1695, 1640 (C=O, C=C); ^1H NMR ($CDCl_3$) δ 1.65-2.28 (m, 5H), 2.36 (s, 3H), 2.51-2.70 (m, 1H), 2.89-3.23 (m, 4H), 3.56-3.87 (m, 4H), 4.92 (m_c, 1H); ^{13}C NMR ($CDCl_3$) δ 203.1 (s), 150.2 (s), 125.3 (s), 66.8 (t), 55.5 (d, $^1J_{CH}$ = 151 Hz), 51.7 (t), 32.7 (t), 29.3 (q), 26.4 (t), 16.5 (t). Anal. Calcd for $C_{12}H_{18}ClNO_2$: C, 59.14; H, 7.44; N, 5.75. Found: C, 58.8; H, 7.22; N, 5.7.

1-(3-Chloro-2-morpholino-1-cyclohexen-1-yl)-2-phenyl-ethanone (**5Af**): Yield: 7.84 g (49%); mp 98°C; IR (KBr, cm^{-1}) 1690, 1640 (C=O, C=C); ^1H NMR ($CDCl_3$) δ 1.50-2.23 (m, 6H), 2.32-2.55 (m, 1H), 2.86-3.16 (m, 4H), 3.59-3.80 (m, 4H), 3.93 (H_A), 4.13 (H_B) (AB-system, J_{AB} = 14.8 Hz, 2H), 4.83 (m_c, 1H), 7.09-7.48 (m, 5H); ^{13}C NMR ($CDCl_3$) δ 204.4 (s), 148.0 (s), 134.9 (s), 129.5 (d), 128.5 (d), 127.7 (s), 126.8 (d), 67.0 (t), 54.9 (d, $^1J_{CH}$ = 152 Hz), 51.7 (t), 48.7 (t), 32.7 (t), 27.3 (t), 16.6 (t). Anal. Calcd for $C_{18}H_{22}ClNO_2$: C, 67.60; H, 6.93; N, 4.38. Found: C, 67.6; H, 6.81; N, 4.4.

(3-Chloro-2-morpholino-1-cycododecen-1-yl)-phenyl-methanone (**5Ca**): **5Ca** was obtained from enamine **6C** (12.57 g, 50 mmol), ethyldiisopropylamine (9.35 mL, 55 mmol), benzoyl chloride (**7a**) (7.02 g, 50 mmol), N-chlorosuccinimide (5.34 g, 40 mmol) in dichloromethane (40 mL) according to the procedure for the preparation of **5Ae/5Af**. Yield: 12.17 g (62%); mp 96°C decomp.; IR (KBr, cm^{-1}) 1640, 1615 (C=O, C=C); ^1H NMR ($CDCl_3$, 400 MHz) δ 1.20-1.88 (m, 13H), 2.13-2.21 (m, 2H), 2.31-2.36 (m, 1H), 2.47-2.53 (m, 1H), 2.91-3.00 (m, 4H), 3.06-3.13 (m, 4H), 5.15 (m_c, 1H), 7.42-7.54 (m, 3H), 7.90 (d, 2H); ^{13}C NMR ($CDCl_3$) δ 198.5 (s), 148.1 (s), 138.3 (s), 135.2 (s), 132.4 (d), 128.4 (d), 128.1 (d), 66.4 (t), 56.8 (d, $^1J_{CH}$ = 147 Hz), 52.3 (t), 33.4 (t), 27.1 (t), 26.2 (t), 26.1 (t), 23.3 (t), 23.2 (t), 22.9 (t), 21.4 (t), 20.2 (t). Anal. Calcd for $C_{23}H_{32}ClNO_2$: C, 70.84; H, 8.27; N, 3.59. Found: C, 70.5; H, 8.26; N, 3.9.

(3-Chloro-2-morpholino-1-cycloalken-3-yl)-phenyl-methanones 10Aa and 10Ba - General Procedure: N-Chlorosuccinimide (2.66 g, 20 mmol) was added in small portions to a stirred solution of 20 mmol of acylenamine (**8Aa/9Aa**: 5.45 g; **9Ba**: 5.71 g) in dichloromethane (20 mL) at -70°C (for **8Aa/9Aa**) or -20°C (for **9Ba**). Continuous stirring for 1 h at this temperature, removal of the solvent at -20°C and working up as described for **5Ae/5Af** gave chloroenamines **10**.

(3-Chloro-2-morpholino-1-cyclohexen-3-yl)-phenyl-methanone (**10Aa**): Yield: 2.51 g (41%); mp 84°C, decomp.; IR (KBr, cm^{-1}) 1675 (C=O), 1610 (C=C); ^1H NMR ($CDCl_3$, 400 MHz) δ 1.80-1.95 (m, 1H), 2.07-2.33 (m, 2H), 2.39-2.72 (m, 5H), 3.14-3.49 (m, 6H), 5.14 (m_c, 1H), 7.39 (t, 2H), 7.51 (t, 1H), 7.86 (d, 2H); ^{13}C NMR ($CDCl_3$) δ 195.2 (s), 146.3 (s), 135.6 (s), 132.5 (d), 129.1 (d), 128.3 (d), 109.6 (d), 79.0 (s), 66.7 (t), 50.6 (t), 38.3 (t), 24.2 (t), 18.6 (t). Anal. Calcd for $C_{17}H_{20}ClNO_2$: C, 66.77; H, 6.59; N, 4.58. Found: C, 66.6; H, 6.50; N, 4.5.

3-Chloro-2-morpholino-1-cyclohepten-3-yl)-phenyl-methanone (**10Ba**): Yield: 3.39 g (53%); mp 116°C, decomp.; IR (KBr, cm^{-1}) 1685 (C=O), 1630 (C=C); ^1H NMR ($CDCl_3$, 400 MHz) δ 1.58-1.73 (m, 1H), 1.73-1.94 (m, 2H), 1.94-2.21 (m, 2H), 2.21-2.53 (m, 4H), 2.53-2.69 (m, 1H), 3.07-3.26 (m, 4H), 3.26-3.40 (m, 2H), 5.45 (t, 1H), 7.29-7.49 (m, 3H), 7.84 (d, 2H); ^{13}C NMR ($CDCl_3$) δ 193.1 (s), 151.5 (s), 136.2 (s), 132.1 (d), 129.5 (d), 128.1 (d), 120.5 (d), 84.1 (s), 66.8 (t), 52.5 (t), 39.0 (t), 26.4 (t), 26.3 (t), 25.9 (t). Anal. Calcd for $C_{18}H_{22}ClNO_2$: C, 67.60; H, 6.93; N, 4.38. Found: C, 67.7; H, 6.91; N, 4.6.

Bicyclic Alkanones 11Aa-11Ac, 11Ae and 11Af - General Procedure: A mixture of acylated chloroenamine **5** (10 mmol; **5Aa**: 3.06 g; **5Ab**: 3.20 g; **5Ac**: 3.40 g; **5Af**: 3.20 g), sodium cyanide (0.49 g, 10 mmol), methyltrioctylammonium chloride (0.1 mL, 0.22 mmol), water (60 mL) and acetonitrile (60 mL) was vigorously stirred at 20°C for 16 h. The reaction of **5Ae** (2.44 g, 10 mmol) analogously was run in an ether (45 mL) - water (5 mL) mixture instead of acetonitrile - water. Addition of ether (60 mL), separation of the ether phase, extraction of the water by ether (2 x 30 mL) and evaporation of the combined ether solutions gave crude **11A** which was purified by recrystallization.

1α,5α,6ß-1-Benzoyl-6-morpholino-bicyclo[3.1.0]hexane-6-carbonitrile (**11Aa**): Crystallized from ether; yield: 1.66 g (56%); mp 111°C; IR (KBr, cm^{-1}) 2240 (C-N), 1670 (C=O); ^1H NMR ($CDCl_3$) δ 1.85-2.46 (m, 6H), 2.50-2.77 (m, 3H), 2.77-3.05 (m, 2H), 3.53-3.78 (m, 2H), 3.82-4.05 (m, 2H), 7.40-7.68 (m, 3H), 7.90 (d, 2H); ^{13}C NMR ($CDCl_3$) δ 197.3 (s), 135.8 (s), 133.7 (d), 129.0 (d), 128.8 (d), 115.3 (s), 66.8 (t), 51.7 (s), 50.7 (t), 50.4 (t), 48.2 (s), 40.4 (d, $^1J_{CH}$ = 170 Hz), 30.1 (t), 27.2 (t), 25.5 (t). Anal. Calcd for $C_{18}H_{20}N_2O_2$: C, 72.95; H, 6.80; N, 9.45. Found: C, 72.9; H, 6.77; N, 9.3.

1α,5α,6ß-1-(4-Methylbenzoyl)-6-morpholino-bicyclo[3.1.0]hexane-6-carbonitrile (**11Ab**): Crystallized from ether - pentane (1:1); yield 1.74 g (56%); mp 88°C; IR (KBr, cm^{-1}) 2230 (C-N), 1670 (C=O); ^1H NMR ($CDCl_3$) δ 1.80-2.13 (m), 2,13-2.48 (m), 2.38 (s) (9 H), 2.48-3.00 (m, 5H), 3.50-3.75 (m, 2H), 3.75--4.00 (m, 2H), 7.24, 7.28, 7.75, 7.79 (AA'XX'-system, 4H); ^{13}C NMR ($CDCl_3$) δ 199.5 (s), 144.5 (s), 133.7 (s), 129.6 (d), 129.2 (d), 115.3 (s), 66.9 (t), 52.0 (s), 51.0 (t), 50.8 (t), 47.9 (s), 40.1 (d, $^1J_{CH}$ = 170 Hz), 30.4 (t), 27.5 (t), 25.8 (t), 21.6 (q). Anal. Calcd for $C_{19}H_{22}N_2O_2$: C, 73.52; H, 7.14; N, 9.03. Found: C, 73.3; H, 7.17; N, 9.0.

1α,5α,6ß-1-(4-Chlorophenyl)-6-morpholino-bicyclo[3.1.0]hexane-6-carbonitrile (**11Ac**): Crystallized from ether; yield: 1.52 g (46%); mp 128°C; IR (KBr, cm^{-1}) 2220 (C-N), 1660 (C=O); ^1H NMR ($CDCl_3$) δ 1.83-2.13 (m, 3H), 2.13-2.46 (m, 3H), 2.50-3.00 (m, 5H), 3.45-3.70 (m, 2H), 3.77-4.02 (m, 2H), 7.41, 7.45, 7.77, 7.81 (AA'XX'-system, 4H); ^{13}C NMR ($CDCl_3$) δ 195.3 (s), 139.9 (s), 134.5 (s), 130.4 (d), 129.2 (d), 115.0 (s), 66.8 (t), 51.8 (s), 51.0 (t), 50.8 (t), 48.3 (s), 40.3 (d, $^1J_{CH}$ = 173 Hz), 30.2 (t), 27.5 (t), 25.8 (t). Anal. Calcd for $C_{18}H_{19}ClN_2O_2$: C, 65.35; H, 5.79; N, 8.47. Found: C, 65.1; H, 5.84; N, 8.5.

1α,5α,6ß-1-Acetyl-6-morpholino-bicyclo[3.1.0]hexane-6-carbonitrile (**11Ae**): Crystallized from ether; yield: 1.63 g (70%); mp 101°C; IR (KBr, cm^{-1}) 2205 (C N), 1700 (C=O); ^1H NMR ($CDCl_3$) δ 1.78-2.25 (m, 6H), 2.33 (s, 3H), 2.44--2.50 (m, 1H), 2.55 (H_{A1}, $^2J_{HH}$ = 11 Hz, 1H), 2.60 (H_{A2}, $^2J_{HH}$ = 11 Hz, 1H), 2.74 (H_{B1}, H_{B2}, $^2J_{HH}$ = $^3J_{HH}$ = 11 Hz), 3.55 (H_{X1}, $^2J_{HH}$ = $^3J_{HH}$ = 11Hz, 1H), 3.58 (H_{X2}, $^2J_{HH}$ = $^3J_{HH}$ = 11 Hz, 1H), 3.86 (H_{Y1}, H_{Y2}, $^2J_{HH}$ = 11 Hz); ^{13}C NMR ($CDCl_3$) δ 203.0 (s), 114.2 (s), 66.6 (t), 53.5 (s), 51.0 (t), 50.4 (t), 49.6 (s), 39.7 (d, $^1J_{CH}$ = 172 Hz), 28.9 (q), 27.7 (t), 26.5 (t), 25.8 (t). Anal. Calcd for $C_{13}H_{18}N_2O_2$: C, 66.64; H, 7.74; N, 11.96. Found: C, 66.7; H, 7.78; N, 12.0.

1α,5α,6β-6-Morpholino-1-(phenylacetyl)-bicyclo[3.1.0]hexane-6-carbonitrile (**11Af**): Crystallized from ether; yield: 1.46 g (47%); mp 95°C; IR (KBr, cm^{-1}) 2215 (C-N), 1705 (C=O); ^1H NMR ($CDCl_3$) δ 1.50 (d, 1H), 1.70-2.12 (m, 5H), 2.21-2.56 (H_{A1}, H_{B1}, H_{B2}, m, 4H), 2.63 (H_{A2}, $^2J_{AB}$ = $^3J_{AB}$ = 10 Hz, 1H), 3.34 (H_{X1}, $^2J_{AB}$ = $^3J_{AB}$ = 10 Hz, 1H), 3.45 (H_{X2}, $^2J_{AB}$ = $^3J_{AB}$ = 10 Hz, 1H), 3.61 (H_{Y1}, $^2J_{AB}$ = 10 Hz, 1H), 3.79 (H_{Y2}, $^2J_{AB}$ = 10 Hz, 1H), 3.86 (H_M), 3.95 (H_N) (AB-system, $^2J_{AB}$ = 15 Hz, 2H), 7.16-7.42 (m 5H); ^{13}C NMR ($CDCl_3$) δ 202.8 (s), 133.3 (s), 129.9 (d), 128.9 (d), 127.3 (d), 114.1 (s), 66.6 (t), 66.4 (t), 52.8 (s), 50.4 (s), 49.7 (t), 48.7 (t), 39.3 (d, $^1J_{CH}$ = 171 Hz), 27.5 (t), 26.5 (t), 25.3 (t), 21.4 (t). Anal. Calcd for $C_{19}H_{22}N_2O_2$: C, 73.53; H, 7.14; N, 9.03. Found: C, 73.5; H, 7.11; N, 9.1.

Reaction of Chloroenamine 5Ad with Cyanide - *4-[5,6-Dihydro-3-(4-nitrophenyl)-4H-cyclopenta[c]furan-1-yl]-morpholine* (**12Ad**): Crude **12Ad** was obtained from **5Ad** (3.15 g, 10 mmol) according to the general procedure for the reaction of cyanide with chloroenamines **5A**. Washing with water (300 mL) and crystallization from ether gave deep red crystals of **12Ad**. Yield: 1.72 g (55%); mp 210°C; IR (KBr, cm^{-1}) 1500 (NO_2); ^1H NMR ($CDCl_3$) δ 2.40 (2H), 2.65 (2H), 2.70 (2H) (AA'BB'CC'-system), 3.23-3.37 (4H), 3.75-3.88 (4H) (AA'XX'-system), 7.27, 7.31, 8.05, 8.09 (AA'XX'-system); ^{13}C NMR ($CDCl_3$) δ 150.8 (s), 143.3 (s), 139.5 (s), 137.4 (s), 134.0 (s), 124.7 (d), 121.1 (d), 110.6 (s), 66.3 (t), 47.6 (t), 31.8 (t), 25.7 (t), 24.4 (t). Anal. Calcd for $C_{17}H_{18}N_2O_4$: C, 64.96; H, 5.77; N, 8.91. Found: C, 64.6; H, 5.79; N, 9.3.

Reaction of Chloroenamine 5Ca with Cyanide: A mixture of acylated chloroenamine **5Ca** (3.90 g, 10 mmol), sodium cyanide (0.49 g, 10 mmol), methyltrioctylammonium chloride (0.1 mL, 0.22 mmol), water (60 mL) and acetonitrile (60 mL) was vigorously stirred at 20°C for 16 h. Addition of ether (60 mL), separation of the ether phase, extraction of the water by ether (2 x 30 mL), concentration of the combined ether solutions to 20 mL and storage at -20°C for 16 h gave **11Ca**. **12Ca** could be obtained by further concentration of the filtrate. **11Ca** and **12Ca** were recrystallized from ether.

1-Benzoyl-12-morpholino-bicyclo[9.1.0]dodecane-12-carbonitrile (**11Ca**): Yield: 1.45 g (38%); mp 169°C; IR (KBr, cm^{-1}) 2205 (C-N), 1665 (C=O); ^1H NMR ($CDCl_3$, 400 MHz) δ 1.02-1.86 (m, 17H), 2.18-2.30 (m, 2H), 2.67-2.90 (m, 4H), 3.66-3.92 (m, 4H), 7.43-7.61 (m, 3H), 7.85 (d, 2H); ^{13}C NMR ($CDCl_3$) δ 198.4 (s), 137.0 (s), 132.9 (d), 128.9 (d), 128.5 (d), 116.3 (s), 66.8 (t), 51.2 (t), 47.1 (s), 46.0 (s), 32.4 (d, $^1J_{CH}$ = 160 Hz), 26.7 (t), 26.6 (t), 25.1 (t), 24.7 (t), 23.6 (t), 22.2 (t), 21.5 (t), 21.4 (t), 20.8 (t): Anal. Calcd for $C_{24}H_{32}N_2O_2$: C, 75.75; H, 8.48; N, 7.36. Found: C, 75.3; H, 8.40; N, 7.6.

4-(5,6,7,8,9,10,11,12-Octahydro-3-phenyl-4H-cycloundeca[c]furan-1-yl)-morpholine (**12Ca**): Yield: 0.42 g (12%); mp 111°C; ^1H NMR ($CDCl_3$, 400 MHz) δ 1.15--1.85 (m, 14H), 2.39 (t, 2H), 2.63 (t, 2H), 3.05-3.16 (4H), 3.74-3.90 (4H) (AA'XX'-system), 7.19 (t, 1H), 7.35 (t, 2H), 7.58 (d, 2H); ^{13}C NMR ($CDCl_3$) δ 152.7 (s), 142.1 (s), 132.3 (s), 128.4 (d), 125.8 (d), 124.7 (d), 123.8 (s), 112.5 (s), 67.2 (t), 50.9 (t), 27.0 (t), 26.5 (t), 26.2 (t), 25.6 (t), 24.9 (t), 24.2 (t), 23.6 (t), 23.5 (t), 21.1 (t). Anal. Calcd for $C_{23}H_{31}NO_2$: C, 78.15; H, 8.84; N, 3.96. Found: C, 78.0; H, 8.78; N, 3.8.

Thermolysis of the Aminocyclopropylketones 11 - General Procedure: Aminocyclopropylketone **11** (5.0 mmol, **11Aa**: 1.48g; **11Ab**: 1.55 g; **11Ac**: 1.66 g; **11Ca**: 1.90 g) was heated in an N_2-atmosphere to 160°C for 3 h. Distillation in a Kugelrohr apparatus and recrystallization from ether gave pure furans **12**.

4-(5,6-Dihydro-3-phenyl-4H-cyclopenta[c]furan-1-yl)-morpholine (**12Aa**): Distilled at 163-170°C/0.001 mbar; yield: 0.96 g (71%); mp 97°C; ^1H NMR ($CDCl_3$) δ 2.36 (2H), 2.61 (2H), 2.73 (2H) (AA'BB'CC'-system), 3.20-3.25 (4H), 3.78-3.82 (4H) (AA'XX'-system), 7.05 (t, 1H), 7.27 (t, 2H), 7.41 (d, 1H); ^{13}C NMR ($CDCl_3$) δ 148.5 (s), 136.0 (s), 132.3 (s), 132.2 (s), 128.8 (d), 124.9 (d), 122.4 (d), 110.4 (s), 66.5 (t), 48.8 (t), 32.1 (t), 25.1 (t), 24.1 (t). Anal. Calcd for $C_{17}H_{19}NO_2$: C, 75.81; H, 7.11; N, 5.20. Found: C, 75.8; H, 7.08; N, 5.4.

4-[5,6-Dihydro-3-(4-methylphenyl)-4H-cyclopenta[c]furan-1-yl]-morpholine (**12Ab**): Distilled at 164-166°C/0.001 mbar; yield: 0.84 g (59%); ^1H NMR

($CDCl_3$) δ 2.30 (s, 3H), 2.35 (2H), 2.65 (2H), 2.73 (2H) (AA'BB'CC'-system), 3.10-3.30 (4H), 3.65-3.90 (4H) (AA'XX'-system), 7.10, 7.15, 7.33, 7.37 (AA'XX'-system); ^{13}C NMR ($CDCl_3$) δ 148.2 (s), 136.3 (s), 134.7 (s), 134.6 (s), 131.3 (s), 129.5 (d), 122.5 (d), 110.5 (s), 66.6 (t), 49.0 (t), 32.3 (t), 25.1 (t), 24.1 (t), 21.2 (q). Anal. Calcd for $C_{18}H_{21}NO_2$: C, 76.30; H, 7.47; N, 4.94. Found: C, 76.1; H, 7.38; N, 5.1.

4-[3-(4-Chlorophenyl)-5,6-dihydro-4H-cyclopenta[c]furan-1-yl]-morpholine (**12Ac**): Distilled at 175-183°C; yield: 0.66 g (44%); ^1H NMR ($CDCl_3$) δ 2.32 (2H), 2.60 (4H) (AA'BB'CC'-system), 3.15-3.35 (4H), 3.75-3.95 (4H) (AA'XX'--system), 7.15, 7.18, 7.23, 7.26 (AA'BB'-system, 4H); ^{13}C NMR ($CDCl_3$) δ 158.9 (s), 148.8 (s), 134.9 (s), 133.0 (s), 131.7 (s), 128.9 (d), 123.5 (d), 110.3 (s), 66.5 (t), 48.6 (t), 32.1 (t), 25.1 (t), 24.1 (t). Anal. Calcd for $C_{17}H_{18}ClNO_2$: C, 67.21; H, 5.97; N, 4.61. Found: C, 67.1; H, 5.96; N, 4.9.

4-(5,6,7,8,9,10,11,12-Octahydro-3-phenyl-4H-cycloundeca[c]furan-1-yl)-morpholine (**12Ca**): Yield: 1.15 g (65%); mp 111°C; in the ^1H NMR spectrum identical with the product obtained directly from the reaction of **4Ca** with cyanide.

Decomposition of 11(3)a in Formic Acid - *4-(5,6-Dihydro-3-phenyl-4H-cyclopenta[c]furan-1-yl)-morpholine* (**12Aa**): Aminocyclopropylketone **11Aa** (0.30 g, 1.0 mmol) was heated to 90°C for 30 min in 1 mL of formic acid. Removal of the formic acid in vacuo, addition of ether (10 mL), extraction with saturated aqueous Na_2CO_3-solution, removal of the solvent and recrystallization from methanol gave pure **12Aa**. Yield 0.21 g (77%); mp 97°C; in the ^1H NMR and the ^{13}C NMR spectra identical with the product from the thermolysis of **11Aa**.

Diels-Alder Reactions with Maleic Anhydride (14): A mixture of maleic anhydride (**14**) (0.20 g, 2.0 mmol) and aminocyclopropylketone **11** (2.0 mmol, **11Ac**: 0.66 g; **11Ae**: 0.47 g; **11Af**: 0.62 g) or furan **12Ac** (0.60 g, 2.0 mmol) was heated for 1 h (**11Ac**, **12Ac**: 160°C; **11Ae**, **11Af**: 120°C). Addition of methanol (1 mL) to the cooled reaction product, storing at 20°C for 16 h and isolation of the resulting crystals by suction gave pure Diels-Alder compounds **16**.

3,5,6,7-Tetrahydro-4-morpholino-8-(4-chlorophenyl)-1H-cyclopenta[e]isobenzofuran-1,3-dione (**16Ac**): Yield: 0.37 g (48%) from **11Ac**, 0.47 g (61%) from **12Ac**; mp 170°C; IR (KBr, cm^{-1}): 1815, 1790, 1745 (C=O); ^1H NMR ($CDCl_3$) δ 2.14 (2H), 2.78 (2H), 3.14 (2H) (AA'BB'CC'-system), 3.38-3.56 (4H), 3.82-4.00 (4H) (AA'XX'-system), 7.18, 7.28, 7.40, 7.50 (AA'XX'-system, 4H); ^{13}C NMR ($CDCl_3$) δ 162.7 (s), 161.8 (s), 156.2 (s), 147.1 (s), 146.4 (s), 134.5 (s), 133.3 (s), 131.3 (s), 130.9 (d), 128.6 (d), 128.5 (s), 119.1 (s), 67.7 (t), 51.5 (t), 33.8 (t), 32.9 (t), 26.0 (t). Anal. Cald for $C_{21}H_{18}ClNO_4$: C, 65.71; H, 4.73; N, 3.65. Found: C, 65.8; H, 4.83; N, 3.6.

3,5,6,7-Tetrahydro-8-methyl-4-morpholino-1H-cyclopenta[e]isobenzofuran-1,3-dione (**16Ae**): Yield: 0.22 g (38%); mp 175°C; IR (KBr, cm^{-1}): 1815, 1780, 1750 (C=O); ^1H NMR ($CDCl_3$) δ 2.19 (2H), 2.93 (2H), 3.08 (2H) (AA'BB'CC'--system), 2.50 (s, 3H), 3.26-3.41 (4H), 3.80-3.94 (4H) (AA'XX'-system); ^{13}C NMR ($CDCl_3$) δ 164.1 (s), 161.9 (s), 156.7 (s), 146.1 (s), 146.0 (s), 130.0 (s), 128.6 (s), 119.0 (s), 67.7 (t), 51.4 (t), 33.5 (t), 31.6 (t), 25.0 (t), 14.1 (q). Anal. Calcd for $C_{16}H_{17}NO_4$: C, 66.89; H, 5.96; N, 4.88. Found: C, 66.3; H, 5.98; N, 4.8.

8-Benzyl-3,5,6,7-tetrahydro-4-morpholino-1H-cyclopenta[e]isobenzofuran-1,3-dione (**16Af**): Yield: 0.30 g (42%); mp 171°C; IR (KBr, cm^{-1}): 1810, 1780, 1740 (C=O); ^1H NMR ($CDCl_3$, 400 MHz) δ 2.14 (2H), 2.86 (2H), 3.05 (2H) (AA'BB'CC'-system), 3.34-3.40 (4H), 3.83-3.91 (4H) (AA'XX'-system), 4.40 (s, 2H), 7.10-7.28 (m, 5H); ^{13}C NMR ($CDCl_3$) δ 164.1 (s), 161.7 (s), 156.9 (s), 146.6 (s), 146.5 (s), 138.7 (s), 132.2 (s), 129.0 (s), 128.6 (d), 126.5 (d), 119.1 (s), 67.8 (t), 51.6 (t), 33.9 (t), 33.6 (t), 32.1 (t), 25.4 (t). Anal. Calcd for $C_{22}H_{21}NO_4$: C, 72.71; H, 5.82; N, 3.85. Found: C, 72.5; H, 5.90; N, 3.9.

Reaction of Chloroenamines 10Aa and 10Ba with Tetraethylammonium Cyanide - General Procedure: A solution of chloroenamine **10a** (2.0 mmol, **10Aa**: 0.63 g; **10Ba**: 0.64 g) and tetraethylammonium cyanide (0.51 g, 3.0 mmol) in dichloromethane (15 mL) was stirred at 20°C for 16 h. Extraction with water (3 x 10

mL), evaporation of the dichloromethane and distillation of the residue in a Kugelrohr apparatus in vacuo gave **29** as a mixture of two isomers. Crystallization from ether afforded a pure isomer.

4-Morpholino-2-phenyl-1-oxa-spiro[2,5]-4-octene-2-carbonitrile (**29A**): Yield: Mixture of isomers: 0.40 g (67%), colorless oil distilled at 162-166°C/0.0001 mbar; pure isomer: 0.12 g (20%), mp 174°C.

Pure isomer: IR (KBr, cm^{-1}): 2205 (C-N), 1630 (C=C); ^1H NMR ($CDCl_3$, 400 MHz) δ 1.13-1.24 (m, 1H), 1.37-1.53 (m, 1H), 1.57-1.68 (m, 1H), 1.71-1.84 (m, 1H), 2.13-2.32 (m, 2H), 2.57-2.68 (m, 2H), 3.09-3.23 (m, 2H), 3.75-3.92 (m, 4H), 5.55 (m_c, 1H), 7.35-7.52 (m, 5H); ^{13}C NMR ($CDCl_3$) δ 143.7 (s), 132.4 (s), 128.9 (d), 128.4 (d), 126.4 (d), 119.8 (d), 118.1 (s), 69.5 (s), 66.5 (t), 57.2 (s), 52.1 (t), 26.2 (t), 24.4 (t), 20.6 (t).

Characteristic signals of the second isomer: ^1H NMR ($CDCl_3$, 400 MHz) δ 1.81--2.12 (m, 6H), 2.69-2.79 (m, 2H), 2.83-2.95 (m, 2H), 5.18 (m_c, 1H); ^{13}C NMR ($CDCl_3$) δ 142.9 (s), 129.1 (s), 128.8 (d), 128.1 (d), 126.7 (d). 118.4 (d), 117.8 (s), 68.4 (s), 66.2 (t), 58.1 (s), 51.0 (t), 31.0 (t), 24.5 (t), 22.0 (t).

Anal. Calcd for $C_{18}H_{20}N_2O_2$: C, 72.95; H, 6.80; N, 9.45. Found for the pure isomer: C, 73.1; H, 6.80; N, 9.6. Found for the mixture of isomers: C, 72.3; H, 6.80; N, 9.4.

4-Morpholino-2-phenyl-1-oxa-spiro[2,6]-4-nonene-2-carbonitrile (**29B**): Yield: Mixture of isomers: 0.434 g (70%), colorless oil distilled at 180-183°C/0.04 mbar; pure isomer: 0.19 g (31%), mp 95°C;

Pure isomer: IR (KBr, cm^{-1}): 2320 (C-N), 1620 (C=C); ^1H NMR ($CDCl_3$, 400 MHz) δ 1.18-1.32 (m, 1H), 1.62-1.82 (m, 2H), 1.92-2.30 (m, 7H), 2.78-2.90 (m, 2H), 3.59-3.68 (m, 2H), 3.68-3.77 (m, 2H), 4.60 (m_c, 1H), 7.29 (m_c, 3H), 7.58 (m_c, 2H); ^{13}C NMR ($CDCl_3$) δ 146.8 (s), 130.9 (s), 129.2 (d), 127.8 (d), 126.5 (d), 118.1 (s), 108.7 (d), 71.2 (s), 66.8 (t), 58.4 (s), 49.0 (t), 35.0 (t), 27.4 (t), 26.5 (t), 25.4 (t).

Characteristic signals of the second isomer: ^1H NMR ($CDCl_3$, 400 MHz) δ 0.82--0.98 (m, 1H), 1.30-1.48 (m, 2H), 1.48-1.60 (m, 1H), 2.54-2.65 (m, 2H), 2.88-2.99 (m, 2H), 5.08 (m_c, 1H), 7.35 (m_c, 3H), 7.49 (m_c, 2H); ^{13}C NMR ($CDCl_3$) δ 149.3 (s), 131.5 (s), 129.4 (d), 128.7 (d), 126.7 (d), 117.4 (s), 109.3 (d), 70.5 (s), 66.9 (t), 59.4 (s), 50.0 (t), 30.3 (t), 26.3 (t), 25.8 (t), 25.0 (t).

Anal. Calcd for $C_{19}H_{22}N_2O_2$: C, 73.52; H, 7.14; N, 9.03. Found for the pure isomer: C, 73.5; H, 7.24; N, 9.1. Found for the mixture of isomers: C, 72.8; H, 7.20; N, 8.9.

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