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α-CYCLIZATION OF TERTIARY AMINES. PART 3. CAPTODATIVE OR PUSH-PULL ENAMINES FORM PYRROLINES, PYRROLIZIDINES AND THEIR RING HOMOLOGUES WITH DIMETHYL ACETYLENEDICARBOXYLATE IN A HIGHLY DIASTEREOSELECTIVE REACTION

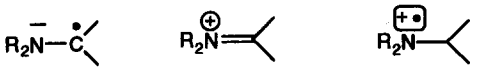
Benoît De Boeck, Shuiping Jiang, Zdenek Janousek and Heinz G. Viehe*

Laboratoire de Chimie Organique, Université Catholique de Louvain, Place L. Pasteur, 1; B-1348 Louvain-la-Neuve, Belgium

Dedicated to Professor Léon Ghosez on the occasion of his 60th birthday.

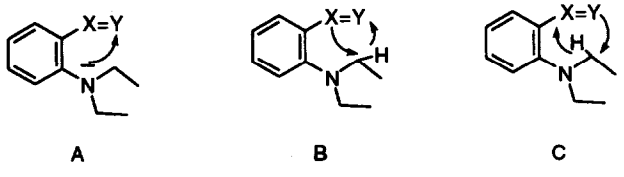
Abstract : The title one-pot reaction occurs through a sequence of [2+2] cycloaddition, ring opening to dienamines and formation of a 1,5-dipole by [1,6] hydrogen-shift. This intermediate may cyclize or, in sterically suitable cases and at lower temperatures, lead to isolable N-vinyl enamines by proton transfer.

Most reactions of tertiary alkylamines in the alpha position require oxidation to either radicals, radical cations[1] or to iminium salts[2] (Scheme 1).



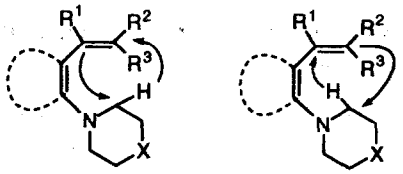
Scheme 1

Compounds with electrophilic multiple bonds may be the oxidants[3]. Numerous intramolecular oxidations of tertiary amines by polar double bonds have been carried out to generate 1,5- or 1,6-dipoles leading to useful heterocyclizations (Scheme 2, B and C). These reactions may compete with N-alkylation (Scheme 2, A). The term "Tertiary Amino Effect" has been coined by H.Suschitzky and O. Meth-Cohn for this type of reactions[4] (Scheme 2).



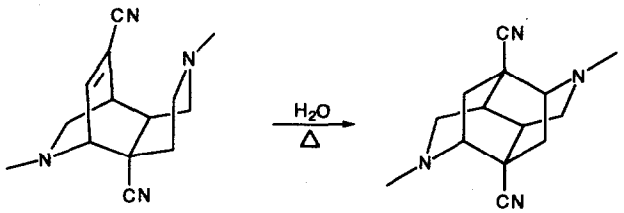
Scheme 2

D.Reinhoudt and W.Verboom[5] have elaborated and largely extended this principle mainly to o-vinylanilines or to dienamines with favorable geometry (Scheme 3).



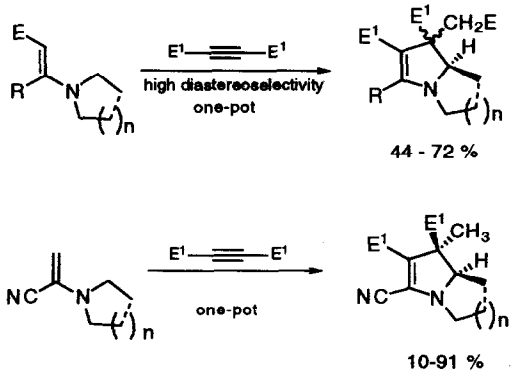
Scheme 3

The literature shows that the proximity of an acrylonitrile moiety to the tertiary amine permits hydride (or hydrogen) transfer through space and no conjugated diene framework is required for this reaction[6] (Scheme 4).



Scheme 4

Based on these reports and our own results[7,8] we have called such reactions "α-Cyclization of Tertiary Amines" (α-CTA). We report now on this reaction type by comparing captodative (cd) and push-pull (pp) enamines (2-(N,N-dialkylamino)acrylonitriles and 3-(N,N-dialkylamino)acrylate esters, respectively) according to Scheme 5. Whereas enamines are generally known to produce [2+2] cycloadducts which undergo cycloreversion to give dienes[9], the subsequent α-CTA is hardly known[10].



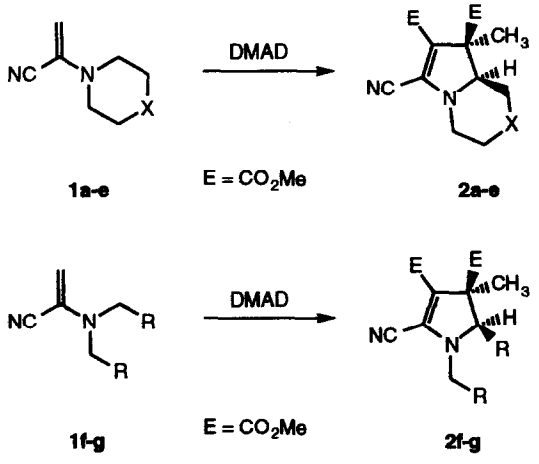
n = 1, 2, 3, 4,
N,N-dimethylamino and N,N-diethylamino
R = H, Me, Ph
E = CO_2Me, CO_2Et; E^1 = CO_2Me

Scheme 5

RESULTS AND DISCUSSION

I. Reactions of cd enamines with dimethyl acetylenedicarboxylate (DMAD)

Refluxing 2-cycloalkylaminoacrylonitriles **1a-e** in acetonitrile in the presence of dimethyl acetylenedicarboxylate (DMAD) produces annulated pyrrolines **2a-e** in medium to high yields, and with high diastereoselectivity (Scheme 6 and Table 1). Acyclic derivatives like 2-(N,N-diethylamino) and 2-(N,N-dimethylamino)acrylonitrile **1f** and **1g** lead to substituted pyrrolines **2f** and **2g**.



Scheme 6

2-dialkylamino acrylonitrile	Product	X	Yield (%)	Reaction conditions	Stereochemistry
1a	**2a**	-	37	B	trans
1b	**2b**	CH_2	40	B (20 h)	trans
1c	**2c**	$(CH_2)_2$	85	B	trans
1d	**2d**	$(CH_2)_3$	90	B	trans
1d	**2d**	$(CH_2)_3$	62	A	trans
1e	**2e**	O	10	C	trans
1f	**2f**	R = H	42	C	-
1g	**2g**	$R = CH_3$	91	B	trans*

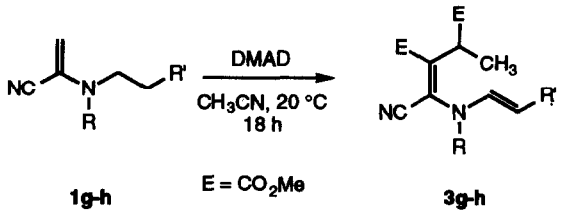
A : CH_3CN, 20 °C, 18 h; B : CH_3CN, 80 °C, 3 h; C : 1. CH_3CN, 80 °C, 3 h 2. DMSO, 130 °C, 4 h

* the same nomenclature as in the bicyclic compounds is applied (i. e. the carbomethoxy group trans to the bridgehead hydrogen)

Table 1 : Reactions of 2-(N,N-dialkylamino)acrylonitriles with DMAD

While **1g** yields a cycloadduct in refluxing acetonitrile, an interesting formal H_2-transfer reaction occurs at room temperature with 2-(N,N-diethylamino) and 2-[(N-methyl-N-phenylethyl)amino]acrylonitriles

1g and **1h** in the presence of DMAD (Scheme 7 and Table 2). The N-vinyl enamine **3g** obtained from 2-(N,N-diethylamino)acrylonitrile has been characterised by its ^1H and ^{13}C NMR as well as IR spectra but could not be properly purified because of its facile hydrolysis.



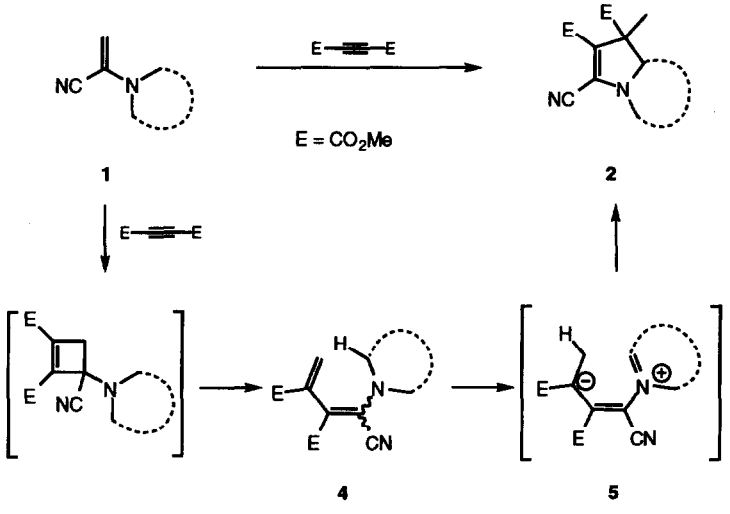
Scheme 7

2-dialkylamino acrylonitrile	Product	R	R'	Yield (%)
1g	**3g**	Et	H	quantitative*
1h	**3h**	Me	Ph	67

* by ^1H NMR

Table 2 : Reactions of acyclic 2-(N,N-dialkylamino)acrylonitriles with DMAD at room temperature

The initial steps of the α-CTA reaction, [2+2] cycloaddition and cycloreversion to a dienamine, occur at room temperature for all cd enamines in this series. The intermediate cis- and trans- dienamines **4** have not been isolated but were characterised in the crude mixture by ^1H NMR (δ, ppm = ~5.3; ~5.8; ~6.4; ~6.5; J ≈ 0.8 Hz). In the cases **1a-e** with cyclic amino substituents, after refluxing in acetonitrile, the hydrogen transfer occurs leading to a 1,5-dipole **5** which then undergoes cyclization to annulated pyrrolines **2a-f** (Scheme 8).



Scheme 8

Probably because of favorable geometry in **4**, cyclization of the acrylonitrile **1d** carrying an eight-membered amine ring already takes place at room temperature while all the other acrylonitrile derivatives need heating.

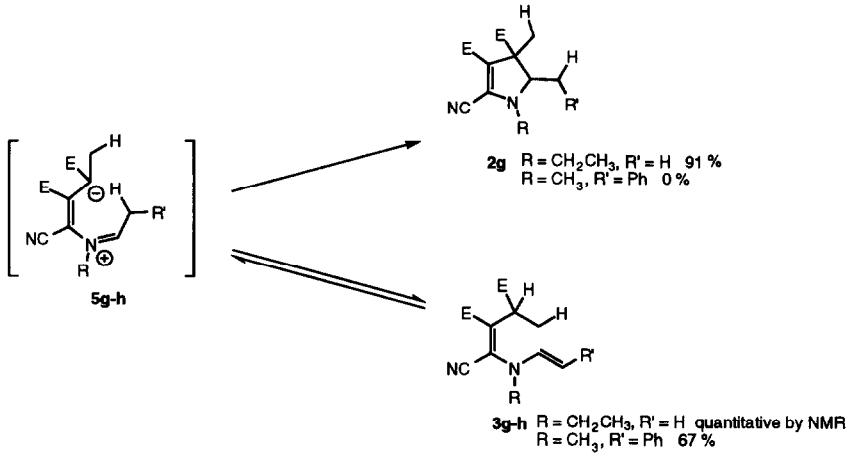
Compared with its 2-piperidino analogue **1b**, 2-morpholino acrylonitrile **1e** produces the expected bicyclic compound only under forcing conditions. Thus, the corresponding dienamines **4e** are detected in the ^1H NMR spectrum of the crude mixture, the cyclization occurring with very low yield (Scheme 6 and Table 1) but only upon heating in DMSO at 130 °C for four hours.

2-(N,N-Dimethylamino)acrylonitrile **1f**, at room temperature, furnishes dienes **4f**, while **1g** produces the N-vinyl enamine **3g**. Both **1f** and **1g** cyclize by heating in acetonitrile (Scheme 6 and Table 1).

While the expected pyrroline **2g** is formed in refluxing acetonitrile, the same reaction at room temperature yields the N-vinyl enamine **3g** as the only product (Scheme 7) characterised by ^1H and ^{13}C NMR as well as IR spectra. Using as the starting material the 2-[(N-methyl-N-phenylethyl)amino]acrylonitrile **1h** yields the N-(2-styryl) enamine **3h** (Scheme 7 and Table 2) which is so stable that it does not cyclize in acetonitrile at 80 °C.

These results could be explained via the 1,5-dipolar intermediates **5g-h** which may follow two possible pathways (Scheme 9) : either cyclization occurs to the expected pyrroline such as **2g**; or transprotonation leads to the observed N-vinyl enamines **3g-h**. Heating the N-vinyl enamine **3g** reverts the reaction and produces the pyrroline **2g** (Scheme 9).

In dry acetonitrile, the proton transfer from the 1,5-dipolar intermediate must be intramolecular. The comparison between 2-(N,N-diethylamino)acrylonitrile **1g** and the perhydroazocine derivative **1d** is interesting. Both react at room temperature but, for apparently sterical reasons, **5g** is transprotonated while **5d** cyclizes.



Scheme 9

The stereochemistry of the products has been assigned by comparison based on the ^{1}H and ^{13}C characteristic peaks of the trans-pyrrolizidine **2a** for which structure has been proven by X-ray analysis[11].

In the bicyclic compounds **2a-e** and **2g**, the coupling constant $^{3}J_{C\text{-}H}$ of 5.6-7.8 Hz between C^{b} and H^{a} is indicative of a cis relationship (Figure 1). Moreover, in the NOE difference spectra of the pyrroline **2g**, irradiation of H^{a} results in a 18 % intensity enhancement of H^{b}.

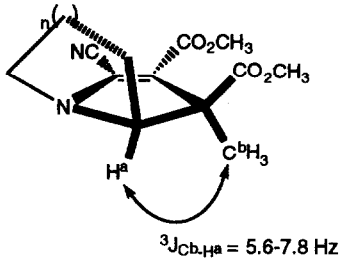


Figure 1 : Relative stereochemistry of the products **2a-e** and **2g**

Examination of the possible conformations of the 1,5-dipolar intermediate **5a-g** (Figure 2) can explain this stereochemistry. The cyclization may arise by a disrotatory concerted 1,5-dipolar process[12]. The two possible conformations **5a-g (A)** and **5a-g (B)** of the 1,5-dipole are in equilibrium but the more favored ones are **5a-g (A)** where the steric interactions are minimised. Equilibration of **5a-g (A)** and **5a-g (B)** is favored by the cyano group, which stabilises the negative charge in the 1,5-dipolar intermediate, thus giving it a longer lifetime. **5a-g (A)** gives the observed trans product by disrotatory cyclization.

The next part compares the results for cd enamines with those for pp enamines.

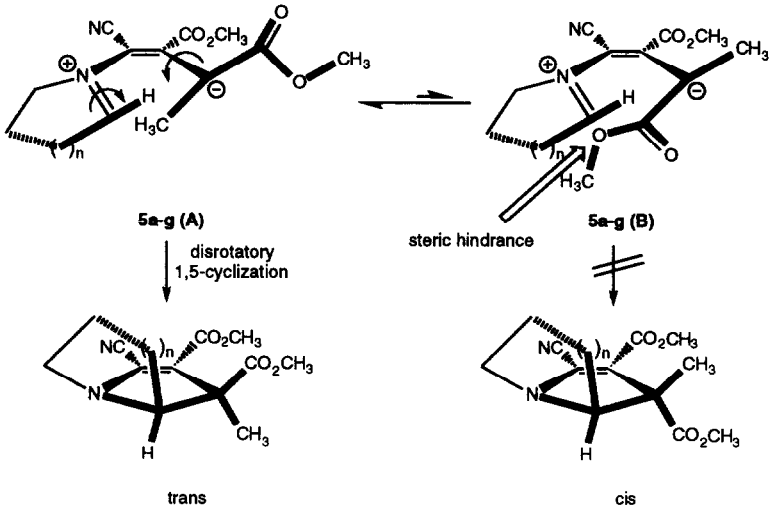
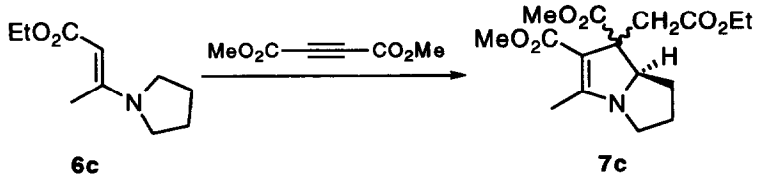


Figure 2 : Conformations of the 1,5-dipolar intermediate before the cyclization

II. Reactions of pp enamines with dimethyl acetylenedicarboxylate

Heating of 3-pyrrolidinoacrylate **6c** with DMAD in DMSO under different conditions gave results summarized in Scheme 10 and Table 3.



6c **7c**

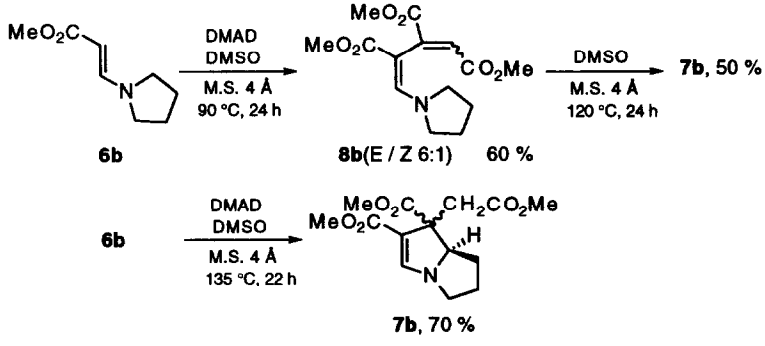
Scheme 10

Entry	Solvent	Temperature (° C)	Reaction time (h)	Molecular sieves 4 Å	Yield* (%)
1	DMSO	80-90	24	-	29
2	DMSO	80-90	24	+	72
3	DMSO/H_2O 6/1	135	24	+	70

* isolated yield after flash chromatography

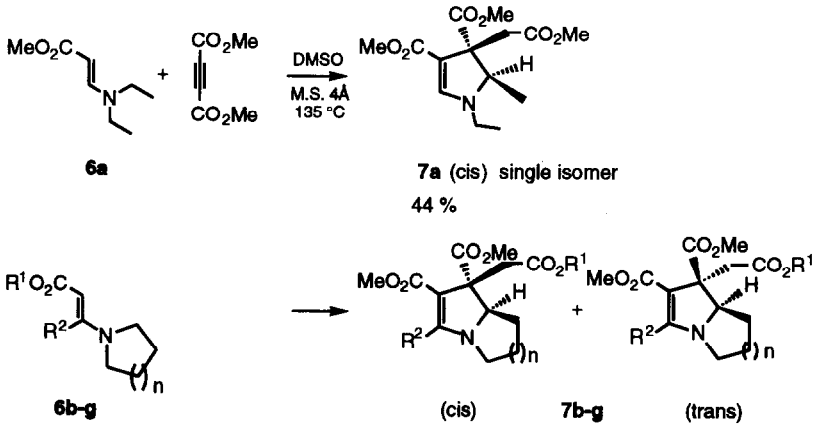
Table 3

Table 3 indicates that the best conditions are those of the entry 2. Initially, molecular sieves 4 Å were added for drying, but surprisingly the yield was increased dramatically from 29 to 72 %. The role of molecular sieves in this reaction remains to be explained. Entry 3 shows that the presence of water has no influence on the yield. The temperature variations are important as shows the comparison between **6b** and **6c**. When **6b**, with less favorable geometry than **6c**, reacts with DMAD at 90°C, only the non-cyclized diene product **8b**(E) and (Z) is obtained in a ratio of 6:1 (Scheme 11). In the ^1H NMR spectra two signals were observed at 6.80 and 5.49 ppm which are characteristic of the (E) and (Z) isomers of the diene **8b**. Increasing the temperature to 120°C resulted in a 50% conversion of diene **8b** to **7b**. Further rising the temperature to 135°C gave the bicyclic product **7b** in 70% yield.



Scheme 11

After optimisation of the reaction conditions, the α-CTA was extended to other 3-(N,N-dialkylamino)acrylates carrying not only the common five- and six-membered rings (**6b**, **6c**, **6d**, **6e**) but also those with larger rings (**6f**, **6g**). In all cases the cyclized products **7a-g** were isolated mostly in good yields (Scheme 12 and Table 4).



Scheme 12

Entry	Substrate	n	R^1	R^2	Products (ratio)	Yield (%)
1	**6b**	1	Me	H	**7b** (cis : trans) (6 : 94)	70
2	**6c**	1	Et	Me	**7c** (cis : trans) (36 : 64)	72
3	**6d**	1	Et	Ph	**7d** (cis) single isomer	67
4	**6e**	2	Me	H	**7e** (cis : trans) (44 : 56)	64
5	**6f**	3	Me	H	**7f** (trans) single isomer	52
6	**6g**	4	Me	H	**7g** (trans) single isomer	59

Table 4

The assignment of the stereochemistry of the products is based on the ^1H NMR and ^{13}C NMR spectral analysis with the confirmation by X-ray diffraction analysis in the case of **7d**. In the ^1H NMR spectra of the single diastereoisomer **7f**, the narrow AB signals of the CH_2E group at 3.03, 2.87 ppm (AB, J = -15.3 and -15.4 Hz) indicate the CH_2E group is opposite to the perhydroazepine ring and is cis to the bridgehead hydrogen NCH, resulting in a long range coupling in the ^{13}C NMR spectra. The coupling constant $^3J_{C\text{-}H}$ for the CH_2E group is 7 Hz. In the ^1H NOE difference spectra, irradiation of the NCH resulted in a great 20 % enhancement of intensities for CH_2E and ester OCH_3, respectively (Figure 3).

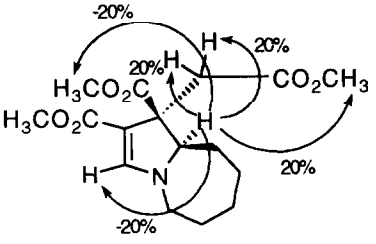


Figure 3 : Intensities enhancements in ^1H NOE spectrum of **7f**

These results confirm that the $CH_2CO_2CH_3$ group is cis to the bridghead NCH, i.e. trans to the perhydroazepine ring.

In contrast with the single trans isomer **7f**, the ^1H NMR spectra of the single isomers **7a** and **7d** show broad absorptions at 3.90, 2.68 (AB, J = -17.6 and -17.6 Hz) and at 3.99, 2.76 ppm (AB, J = -17.8 and -17.7 Hz). Taking into account the absence of coupling constant ^3J of the CH_2E group in the ^{13}C NMR spectra we can conclude that the CH_2E side chain is cis to the 2-methyl group in **7a** and cis to the pyrrolidine ring in **7d**, respectively. The X-ray diffraction analysis[11] of **7d** confirms this cis relationship.

The major diastereoisomer of **7c**(trans) gives a strong narrow AB signal at 3.11, 2.75 ppm (AB, J = -15 and -15 Hz) and the minor isomer **7c**(cis) exhibits weak broad signals at 3.89, 2,54 ppm (AB, J = -17.9 and -17.8 Hz). In the ^{13}C NMR spectra of the **7c**(trans) isomer the coupling constant ^3J between CH_2E and the NCH is 6.4 Hz. In contrast, ^3J in the **7c**(cis) isomer is not observed. The ratio of the two diastereoisomers is calculated by comparing the integrals of the NCH hydrogen in the ^1H NMR spectrum. The NCH proton in the cis isomer exhibits a relatively low field chemical shift at 4.48-4.40 ppm (dd, J = 5 and 4.8 Hz) due to the deshielding by the cis carbomethoxy group. On the other hand, the hydrogen of the NCH in the trans isomer gives absorption at 4.39-4.31 ppm (dd, J = 5.9 and 5.7 Hz). Analysis of the ^1H NMR and ^{13}C NMR spectra enabled us to assign the stereochemistry for all products (Table 4).

The high diastereoselectivity of the cyclization shows that sterically well-defined intermediates are involved. The stereochemistry of the two newly formed contiguous asymmetric carbons by the carbocyclizations of the 1,5-dipoles depends not only on the interaction between the CH_2E group and the amino rings, but also on those between the CH_2E and the group R on the double bond (Figure 4). This competition between the two factors determines the diastereoisomeric ratios.

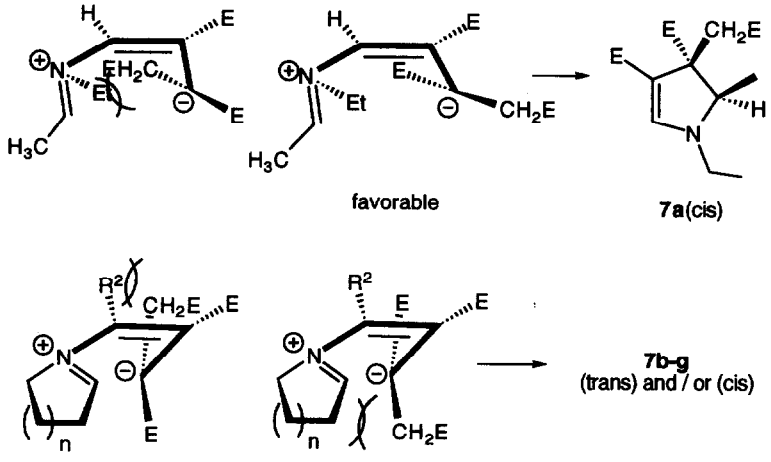


Figure 4

When the group R^2 is hydrogen, the role of the amino ring size is significant. Only one diastereoisomer is obtained if a larger amino ring is present (entries 5 and 6). The presence of a smaller CH_2CN function instead of CH_2E decreases the selectivity[7]. Entries 1, 2, 3 illustrate the influence of the R^2 group located on the double bond. Its bulk interacts with that of the CH_2E moiety. Thus with R^2 = phenyl, the single isomer **7d**(cis) is formed. In the case of **7a** the steric interactions between the CH_2E group and the ethyl group favors the single isomer **7a**(cis).

ACKNOWLEDGEMENTS

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EXPERIMENTAL PART

General

The ^1H NMR spectra were recorded on a Gemini-200 (200 MHz) and on a Gemini-300 (300 MHz) spectrometer. The ^{13}C NMR spectra were recorded on a Gemini-200 (50 MHz) and on a Gemini-300 (75 MHz) spectrometer (δ are given in ppm and J are given in Hz). The samples were dissolved in $CDCl_3$ with tetramethylsilane (TMS) as internal standard. The following abbreviations are used : S, s, singlet; D, d, doublet; T, t, triplet; Q, q, quartet; m, multiplet. IR and mass spectra were recorded on a Nicolet-205 and

Varian-445SEI apparatus, respectively. Melting points were determined in capillaries and are uncorrected. Elemental analysis were carried out by Dr A. Stones at the University College London, London, UK.

Dimethyl acetylenedicarboxylate (Janssen) was used without further purification. Acetonitrile and DMSO were distilled on calcium hydride prior to use. All reactions were carried out under inert atmosphere. Column chromatography was performed with Merck Silica Gel 60 (70-230 mesh ASTM).

Synthesis of enamines

All the enamines we used are easily synthesized by known procedures. 3-(N,N-Dialkylamino)acrylic esters are prepared by addition of the corresponding amines to propiolate esters. 2-(N,N-Dialkylamino)acrylonitriles **1a-h** are prepared[13] in medium to high yields by addition of amines to α-chloro acrylonitrile followed by elimination and rearrangement.

Reactions of α-dialkylamino acrylonitriles with DMAD

General procedure A

One equivalent of DMAD in 5 ml of acetonitrile is added to a solution of ~4 mmole of 2-(N,N-dialkylamino)acrylonitrile dissolved in 25 ml of acetonitrile, in a dry apparatus under Argon atmosphere. The solution soon turns to green and after a few hours to orange. After stirring for 18 hours, the solvent is evaporated under reduced pressure and the residual oil is purified by column chromatography over silica gel (eluent : ethyl acetate/light petroleum ether 1/4).

General procedure B

One equivalent of DMAD in 5 ml of acetonitrile is added to a solution of ~4 mmole of 2-(N,N-dialkylamino)acrylonitrile dissolved in 25 ml of acetonitrile, in a dry apparatus under Argon atmosphere. The solution is refluxed for 3 hours and soon turns to green then orange. After cooling, the solvent is evaporated under reduced pressure and the residual oil is purified by column chromatography over silica gel (eluent : ethyl acetate/light petroleum ether 1/4).

General procedure C

One equivalent of DMAD in 5 ml of acetonitrile is added to a solution of ~4 mmole of 2-(N,N-dialkylamino)acrylonitrile dissolved in 25 ml of acetonitrile, in a dry apparatus under Argon atmosphere. The solution is refluxed for 3 hours and soon turns to green then orange. After cooling, the solvent is evaporated under reduced pressure. 25 ml of DMSO are added to the residual oil and this solution is heated at 130 °C for 4 hours. After cooling, 50 ml of water is added and the solution is extracted four times with 50 ml of diethyl ether. The combined organic layers are washed with 50 ml of brine and dried on magnesium sulfate. After evaporation of the solvent under reduced pressure, the residual oil is purified by column chromatography over silica gel (eluent : ethyl acetate/light petroleum ether 1/4).

*Reaction of 2-pyrrolidinoacrylonitrile **1a** with DMAD*

General procedure B, starting from 500 mg (4.1 mmole) of **1a** and 580 mg (4.1 mmole) of DMAD, affords **2a** (400 mg; 37 %) as colorless crystals which are recrystallised in ethyl acetate (m. p. : 110 °C). IR (cm^{-1}, KBr) : 3017, 2992, 2953, 2889, 2236 (CN), 1735 (C=O), 1690 (C=C), 1599, 1573; ^1H NMR (δ, ppm) : 3.77 (3 H, s, $OC\underline{H}_3$), ~3.72 (1 H, hidden by methyl groups at 3.71 and 3.77, $NC\underline{H}$), 3.71 (3 H, s, $OC\underline{H}_3$), 3.5 - 3.2 (2 H, m, $NC\underline{H}_2$-), 2.2 - 1.6 (4 H, m, -$C\underline{H}_2$-$C\underline{H}_2$-), 1.58 (3 H, s, $C(E)C\underline{H}_3$); ^{13}C NMR (δ, ppm) : 171.46 (Sm, $C(CH_3)$-$\underline{C}$=O), 162.44 (Sm, =C-$\underline{C}$=O), 132.24 (Sm, =$\underline{C}$(E)C), 120.83 (Sm, -$\underline{C}$N), 111.44 (S, =$\underline{C}$(CN)N), 75.72 (Dm, J = 146.8 Hz, $N\underline{C}H$), 53.66 (Sm, $\underline{C}(E)CH_3$), 51.94 (Q, J = 147.5 Hz, $O\underline{C}H_3$), 51.28 (Q, J = 147.3 Hz, $O\underline{C}H_3$), 48.64 (Tm, J = 143.3 Hz, N-$\underline{C}H_2$-), 26.94 (Tm, J = 121.5 Hz, -$\underline{C}H_2$-), 24.52 (Tm, J = 128.2 Hz, -$\underline{C}H_2$-), 23.46 (Qd, ^1J = 130.3 Hz, ^3J = 7.56 Hz, $C(E)\underline{C}H_3$); MS m/e : 264.1 (M^+), 205.1 (100 %, M^+ - CO_2CH_3), 173.1 (M^+ - CO_2CH_3- CH_3OH), 161.1, 146.1 (M^+ - CO_2CH_3- CH_3OH - HCN); Anal. Calcd. for $C_{13}H_{16}N_2O_4$ (264.30) : C : 59.08 %; H : 6.10 %; N : 10.59 %; Found : C : 59.10 %; H : 6.22 %; N : 10.53 %

*Reaction of 2-piperidinoacrylonitrile **1b** with DMAD*

General procedure B (refluxing for 20 hours), starting from 540 mg (4 mmole) of **1b** and 560 mg (4 mmole) of DMAD, affords **2b** (450 mg; 40 %) as a pale yellow oil; IR (cm^{-1}, neat) : 2950, 2859, 2241 (CN), 1735 (C=O), 1697 (C=C), 1582; ^1H NMR (δ, ppm) : 3.75 (3 H, s, $OC\underline{H}_3$), ~3.74 (1 H, hidden by methyl groups at 3.70 and 3.75, $NC\underline{H}_2$-), 3.70 (3 H, s, $OC\underline{H}_3$), 3.21 (1 H, dd, J = 11.2 Hz and 3.4 Hz, $NC\underline{H}$), 2.92 (1 H, td, J = 12.4 Hz and 3.5 Hz, $NC\underline{H}_2$-), 1.53 (3 H, s, $C(E)C\underline{H}_3$), 2.0 - 1.2 (6 H, m, -$C\underline{H}_2$-$C\underline{H}_2$-$C\underline{H}_2$-); ^{13}C NMR (δ, ppm) : 171.83 (Sm, $C(CH_3)$-$\underline{C}$=O), 163.34 (Sq, J = 3.8 Hz, =C-$\underline{C}$=O), 130.65 (Sm, =$\underline{C}$(E)C), 115.56 (Sm, $\underline{C}$N), 110.34 (S, =$\underline{C}$(CN)N), 72.36 (Dm, J = 140.9 Hz, $N\underline{C}H$), 55.23 (Sm, $\underline{C}(E)CH_3$), 51.96 (Q, J = 147.4 Hz, $O\underline{C}H_3$), 51.02 (Q, J = 147.0 Hz, $O\underline{C}H_3$), 46.22 (Tm, J = 138.2 Hz, N-$\underline{C}H_2$-), 26.25 (Tm, J = 126.2 Hz, -$\underline{C}H_2$-), 24.92 (Tm, J = 130.8 Hz, -$\underline{C}H_2$-), 23.21 (Tm, J = 128.8 Hz, -$\underline{C}H_2$-), 22.49 (Qd, ^1J = 129.8 Hz, ^3J = 7.1 Hz, $C(E)\underline{C}H_3$); MS m/e : 278.1 (M^+), 219.1 (100 %, M^+ - CO_2CH_3), 187.1 (M^+ - CO_2CH_3 - CH_3OH), 175.1, 160.1 (M^+ - CO_2CH_3- CH_3OH - HCN), 82.9

*Reaction of 2-(1-azacycloheptyl)acrylonitrile **1c** with DMAD*

General procedure B, starting from 540 mg (3.6 mmole) of **1c** and 510 mg (3.6 mmole) of DMAD, affords **2c** (890 mg; 85 %) as a pale yellow oil; IR (cm^{-1}, neat) : 2941, 2933, 2874, 2860, 2238 (CN), 1736 (C=O), 1685 (C=C), 1591; ^1H NMR (δ, ppm) : 3.74 (3 H, s, $OC\underline{H}_3$), 3.68 (3 H, s, $OC\underline{H}_3$), 3.68 - 3.58 (1 H, m, $NC\underline{H}_2$-), 3.55 (1 H, dd, J = 8.8 Hz and 3.0 Hz, $NC\underline{H}$), 3.40 - 3.30 (1 H, m, $NC\underline{H}_2$-), 1.51 (3 H, s, $C(E)C\underline{H}_3$), 1.90 - 1.30 (8 H, m, -$C\underline{H}_2$-$C\underline{H}_2$-$C\underline{H}_2$-$C\underline{H}_2$-); ^{13}C NMR (δ, ppm) : 172.24 (Sm, $C(CH_3)$-$\underline{C}$=O), 163.22 (Sq, J = 3.9 Hz, =C-$\underline{C}$=O), 131.49 (Sm, =$\underline{C}$(E)C), 114.64 (Sm, $\underline{C}$N), 110.81 (S, =$\underline{C}$(CN)N), 74.55 (Dm, J = 143.4 Hz, $N\underline{C}H$), 56.17 (Sm, $\underline{C}(E)CH_3$), 51.95 (Q, J = 147.3 Hz, $O\underline{C}H_3$), 50.93 (Q, J = 146.9 Hz, $O\underline{C}H_3$), 48.13 (Tm, J = 137.4 Hz, N-$\underline{C}H_2$-), 30.36 (Tm, J = 125.4 Hz, -$\underline{C}H_2$-), 27.97 (Tm, J = ~124 Hz, -$\underline{C}H_2$-), 27.31 (Tm, J = 126.9 Hz, -$\underline{C}H_2$-), 26.29 (Tm, J = 128.7 Hz, -$\underline{C}H_2$-), 24.00 (Qd, ^1J = 129.8 Hz, ^3J =

7.8 Hz, C(E)$\underline{C}H_3$); MS m/e : 292.3 (M^+), 233.1 (M^+ - CO_2CH_3), 201.1 (M^+ - CO_2CH_3 - CH_3OH), 189.1, 86.9, 84.9, 82.9 (100 %)

Reaction of 2-(1-azacyclooctyl)acrylonitrile ***1d*** *with DMAD*

General procedure B, starting from 330 mg (2 mmole) of **1d** and 280 mg (2 mmole) of DMAD, affords **2d** (550 mg; 90 %) as a pale yellow oil which solidifies slowly (pale yellow crystals, m. p. : 69-77 °C).

General procedure A, starting from 130 mg (0.8 mmole) of **1d** and 110 mg (0.8 mmole) of DMAD, affords **2d** (150 mg; 62 %); IR (cm^{-1}, KBr) : 2982, 2937, 2853, 2243 (CN), 1739 (C=O), 1691 (C=C), 1594, 1482; ^1H NMR (δ, ppm) : 3.87 - 3.75 (1 H, m, NC$\underline{H}_2$-), 3.75 (3 H, s, OC$\underline{H}_3$), 3.69 (3 H, s, OC$\underline{H}_3$), 3.33 (1 H, dd, J = 8.6 Hz and 3.8 Hz, NC$\underline{H}$), 3.08 (1 H, m, NC$\underline{H}_2$-), 1.58 (3 H, s, C(E)C$\underline{H}_3$), 2.0 - 1.4 (10 H, m, -C$\underline{H}_2$-C$\underline{H}_2$-C$\underline{H}_2$-C$\underline{H}_2$-C$\underline{H}_2$-); ^{13}C NMR (δ, ppm) : 172.46 (Sm, C(CH_3)-$\underline{C}$=O), 163.22 (Sm, =C-$\underline{C}$=O), 132.35 (Sm, =$\underline{C}$(E)C), 115.47 (Sm, $\underline{C}$N), 111.00 (S, =$\underline{C}$(CN)N), 75.76 (Dm, J = ~143 Hz, N$\underline{C}$H), 56.28 (Sm, $\underline{C}$(E)CH_3), 52.05 (Q, J = 147.3 Hz, O$\underline{C}H_3$), 51.09 (Q, J = 147.0 Hz, O$\underline{C}H_3$), 48.42 (Tm, J = 137.2 Hz, N-$\underline{C}H_2$-), 28.08 (Tm, J = 126.2 Hz, -$\underline{C}H_2$-), 27.46 (Tm, J = 126.0 Hz, -$\underline{C}H_2$-), 26.77 (Tm, J = 126.5 Hz, -$\underline{C}H_2$-), 24.46 (Qd, ^1J = 129.7 Hz, ^3J = 7.5 Hz, C(E)$\underline{C}H_3$), 23.67 (Tm, J = ~125 Hz, -$\underline{C}H_2$-), 22.31 (Tm, J = 125.1 Hz, -$\underline{C}H_2$-); MS m/e : 306.2 (M^+), 247.2 (100 %, M^+ - CO_2CH_3), 215.1 (M^+ - CO_2CH_3- CH_3OH), 203.2; Anal. Calcd. for $C_{16}H_{22}N_2O_4$ (306.36) : C : 62.73 %; H : 7.24 %; N : 9.14 %; Found : C : 62.89 %; H : 7.27 %; N : 8.99 %

Reaction of 2-morpholinoacrylonitrile ***1e*** *with DMAD*

General procedure C, starting from 500 mg (3.6 mmole) of **1e** and 510 mg (3.6 mmole) of DMAD, affords **2e** (100 mg; 10 %) as colorless crystals which are recrystallised in ethyl acetate (m. p. : 123,5 °C); IR (cm^{-1}, KBr) : 2993, 2950, 2912, 2875, 2858, 2242 (CN), 1790, 1735 (C=O), 1688 (C=C), 1577; ^1H NMR (δ, ppm) : , 3.89 - 3.78 (1 H, m, -C$\underline{H}_2$- or NC$\underline{H}$), 3.71 (3 H, s, OC$\underline{H}_3$), ~3.65 (1 H, hidden by methyl groups at 3.66 and 3.71, -C$\underline{H}_2$- or NC$\underline{H}$), 3.66 (3 H, s, OC$\underline{H}_3$), 3.56 - 3.16 (5 H, m, -C$\underline{H}_2$- and/or NC$\underline{H}$), 1.50 (3 H, s, C(E)C$\underline{H}_3$); ^{13}C NMR (δ, ppm) : 170.99 (Sm, C(CH_3)-$\underline{C}$=O), 162.77 (Sq, J = 4.0 Hz, =C-$\underline{C}$=O), 129.58 (Sm, =$\underline{C}$(E)C), 117.32 (S, $\underline{C}$N), 110.03 (S, =$\underline{C}$(CN)N), 69.37 (Dq, J = 148.0 Hz and 4.9 Hz, N$\underline{C}$H), 66.88 (Tm, J = 144.0, -$\underline{C}H_2$-O), 66.48 (Tm, J = 145.6 Hz, -$\underline{C}H_2$-O), 53.79 (S, $\underline{C}$(E)CH_3), 52.34 (Q, J = 147.6 Hz, O$\underline{C}H_3$), 51.38 (Q, J = 147.3 Hz, O$\underline{C}H_3$), 45.65 (Tt, J = 138.6 Hz and 4.0 Hz, N-$\underline{C}H_2$-), 22.20 (Qd, ^1J = 130.5 Hz and ^3J = 6.3 Hz, C(E)$\underline{C}H_3$); MS m/e : 280.0 (M^+), 221.1 (100 %, M^+ - CO_2CH_3), 191.0 (M^+ - CO_2CH_3- CH_2O), 189.0 (M^+ - CO_2CH_3- CH_3OH), 177.0 (M^+ - CO_2CH_3 - C_2H_4O), 159.0 (M^+ - CO_2CH_3- CH_2O - CH_3OH), 149.0, 131.0, 59.0; Anal. Calcd. for $C_{13}H_{16}N_2O_5$ (280.28) : C : 55.71 %; H : 5.75 %; N : 9.99 %; Found : C : 55.93 %; H : 5.75 %; N : 9.96 %

Reaction of 2-(N,N-dimethylamino)acrylonitrile ***1f*** *with DMAD*

General procedure C, starting from 192 mg (2 mmole) of **1f** and 284 mg (2 mmole) of DMAD, affords **2f** (200 mg; 42 %) as a pale yellow oil; IR (cm^{-1}, neat) : 2996, 2975, 2954, 2904, 2243 (CN), 1740 (C=O), 1690 (C=C), 1587; ^1H NMR (δ, ppm) : 3.75 (3 H, s, OC$\underline{H}_3$), 3.74 (3 H, s, OC$\underline{H}_3$), 3.70 (1 H, d, J = 10.6 Hz, NC$\underline{H}_2$-), 3.31 (1 H, d, J = 10.6 Hz, NC$\underline{H}_2$-), 2.95 (3 H, s, NC$\underline{H}_3$), 1.50 (3 H, s, C(E)C$\underline{H}_3$); ^{13}C NMR (δ,

ppm) : 173.94 (Sm, $C(CH_3)$-$\underline{C}$=O), 162.76 (Sq, J = 4.0 Hz, =C-$\underline{C}$=O), 132.00 (Sm, =$\underline{C}$(E)C), 117.19 (Sm, $\underline{C}$N), 110.50 (S, =$\underline{C}$(CN)N), 65.44 (Tm, J = 142.1 Hz, N-$\underline{C}H_2$-), 52.66 (Q, J = 147.5 Hz, O$\underline{C}H_3$), 51.92 (Sq, J = 3.6 Hz, $\underline{C}$(E)CH_3), 51.23 (Q, J = 147.1 Hz, O$\underline{C}H_3$), 35.68 (Q, J = 138.6 Hz, N-$\underline{C}H_3$), 21.77 (Qt, ^{1}J = 130.3 and ^{3}J = 6.4 Hz, C(E)$\underline{C}H_3$); MS m/e : 238.1 (M^+), 179.1 (100 %, M^+ - CO_2CH_3), 147.0 (M^+ - CO_2CH_3 - CH_3OH), 135.1, 120.0, 118.9; Anal. Calcd. for $C_{11}H_{14}N_2O_4$ (238.24) : C : 55.46 %; H : 5.92 %; N : 11.76 %; Found : C : 55.37 %; H : 6.18 %; N : 11.63 %

Reaction of 2-(N,N-diethylamino)acrylonitrile ***1g*** *with DMAD*

General procedure B, starting from 500 mg (4 mmole) of **1g** and 580 mg (4.1 mmole) of DMAD, affords **2g** (970 mg; 91 %) as a colorless oil; IR (cm^{-1}, neat) : 2984, 2953, 2241 (CN), 1738 (C=O), 1700 (C=C), 1589; ^{1}H NMR (δ, ppm) : 3.95 (1 H, q, J = 6.7 Hz, NC$\underline{H}CH_3$), 3.75 (3 H, s, OC$\underline{H}_3$), 3.73 (3 H, s, OC$\underline{H}_3$), 3.47 (1 H, dq, J = 14.7 Hz and 7.3 Hz, NC$\underline{H}_2CH_3$), 3.21 (1 H, dq, J = 14.0 Hz and 7.0 Hz, NC$\underline{H}_2CH_3$), 1.28 (3 H, s, C(E)C$\underline{H}_3$), 1.21 (3 H, d, J = 6.8 Hz, NCHC$\underline{H}_3$), 1.17 (3 H, t, J = 7.1 Hz, $NCH_2C\underline{H}_3$); ^{13}C NMR (δ, ppm) : 173.97 (Sm, $C(CH_3)$-$\underline{C}$=O), 162.63 (Sq, J = 4.0 Hz, =C-$\underline{C}$=O), 130.78 (Sm, =$\underline{C}$(E)C), 117.82 (Sm, $\underline{C}$N), 110.60 (S, =$\underline{C}$(CN)N), 64.51 (Dm, J = 140.0 Hz, N$\underline{C}$H), 54.80 (Sq, J = 4.0 Hz, $\underline{C}$(E)CH_3), 52.53 (Q, J = 147.3 Hz, O$\underline{C}H_3$), 51.17 (Q, J = 147.1 Hz, O$\underline{C}H_3$), 40.14 (Tq, ^{1}J = 138.2 Hz and ^{3}J = 4.1 Hz, N$\underline{C}H_2CH_3$), 14.31 (Qd, ^{1}J = 129.8 and ^{3}J = 5.6 Hz, C(E)$\underline{C}H_3$), 12.36 (Qt, ^{1}J = 127.3 Hz and ^{3}J = 2.7 Hz, $NCH_2\underline{C}H_3$), 11.72 (Q, J = 127.1 Hz, NCH$\underline{C}H_3$); MS m/e : 266.2 (M^+), 207.2 (100 %, M^+ - CO_2CH_3), 175.1 (M^+ - CO_2CH_3 - CH_3OH), 163.2, 147.8; Anal. Calcd. for $C_{13}H_{18}N_2O_4$ (266.29) : C : 58.63 %; H : 6.81 %; N : 10.51 %; Found : 58.06 %; H : 6.73 %; N : 10.18 %

Reaction of 2-(N,N-diethylamino)acrylonitrile ***1g*** *with DMAD*

General procedure A, starting from 500 mg (4 mmole) of **1g** and 580 mg (4.1 mmole) of DMAD,. After this reaction, the solvent must imperatively be evaporated under reduced pressure without any heating and the product must be kept under inert atmosphere. The reaction affords **3g** as an orange oil (quantitative yield as determined by ^{1}H NMR); IR (cm^{-1}, neat) : 2982, 2954, 2230 (CN), 1744 (C=O), 1731 (C=O), 1593, 1435; ^{1}H NMR (δ, ppm) : 6.10 (1 H, dd, J = 15.4 Hz and 8.9 Hz, NC$\underline{H}$=CH_2), 4.26 (1 H, dd, J = 15.5 Hz and 1.4 Hz, NCH=C$\underline{H}_2$), 4.22 (1 H, dd, J = 8.8 Hz and 1.6 Hz, NCH=C$\underline{H}_2$), 3.84 (3 H, s, OC$\underline{H}_3$), ~3.75 (1 H, m, NC$\underline{H}_2CH_3$), 3.69 (3 H, s, OC$\underline{H}_3$), 3.51 (1 H, q, J = 7.2 Hz, C$\underline{H}$(E)CH_3), 3.50-3.10 (1 H, m, NC$\underline{H}_2CH_3$), 1.38 (3 H, d, J = 7.1 Hz, CH(E)C$\underline{H}_3$), 1.21 (3 H, t, J = 7.2 Hz, $NCH_2C\underline{H}_3$); ^{13}C NMR (δ, ppm) : 171.87 (Sm, $CH(CH_3)$-$\underline{C}$=O), 164.28 (Sm, =C-$\underline{C}$=O), 138.10 (Dt, J = 171.7 Hz and 3.8 Hz, N$\underline{C}$H=CH_2), 134.87 (Sm, =$\underline{C}$(E)C), 125.73 (Sm, =$\underline{C}$(CN)N), 113.21 (S, $\underline{C}$N), 89.91 (DDd, J = 163.5 Hz, 156.6 Hz and 3.2 Hz, NCH=$\underline{C}H_2$), 52.14 (Q, J = 148.1 Hz, O$\underline{C}H_3$), 52.07 (Q, J = 147.2 Hz, O$\underline{C}H_3$), 44.04 (Tt, J = 138.1 Hz and 4.4 Hz, N$\underline{C}H_2CH_3$), 38.88 (Dq, ^{1}J = 126.9 Hz and ^{3}J = 4.2 Hz, $\underline{C}$H(E)CH_3), 15.35 (Qd, ^{1}J = 130.3 Hz and ^{3}J = 5.6 Hz, CH(E)$\underline{C}H_3$), 12.66 (Qm, J = 127.3 Hz, $NCH_2\underline{C}H_3$)

Reaction of 2-[(N-methyl-N-phenylethyl)amino]acrylonitrile with DMAD

General procedure A, starting from 210 mg (1.12 mmole) of **1h** and 160 mg (1.12 mmole) of DMAD, affords **3h** (250 mg; 67 %) as a red oil which solidifies slowly (m. p. : 78.5 - 83.5 °C); IR (cm^{-1}, neat) : 3060, 3025, 2998, 2952, 2844, 2220 (CN), 1747 (C=O), 1725 (C=O), 1671, 1639, 1586; ^1H NMR (δ, ppm) : 7.13 - 7.32 (5 H, m, arom. C<u>H</u>), 6.91 (1 H, d, J = 14.1 Hz, NC<u>H</u>=CHPh), 5.78 (1 H, d, J = 14.4 Hz, NCH=C<u>H</u>Ph), 3.85 (3, s, OC<u>H</u>$_3$), ~3.72 (1 H, hidden by the methyl group at 3.72, C<u>H</u>(E)CH$_3$), 3.72 (3 H, s, OC<u>H</u>$_3$), 3.22 (3 H, s, NC<u>H</u>$_3$), 1.39 (3 H, d, J = 6.8 Hz, CH(E)C<u>H</u>$_3$); ^{13}C NMR (δ, ppm) : 171.67 (Sm, CH(CH$_3$)-<u>C</u>=O), 164.10 (Sm, =C-<u>C</u>=O), 136.10 (Sm, NCH=CH<u>C</u>), 133.84 (Dm, J = 169.5 Hz, N<u>C</u>H=CHPh), 131.36 (Sm, =<u>C</u>(E)C), 128.21 (Dd, J = 159.3 Hz and 6.3 Hz, arom. =<u>C</u>H), 126.87 (Sm, =<u>C</u>(CN)N), 125.47 (Dm, J = ~142.0 Hz, arom. =<u>C</u>H), 124.42 (Dm, J = 157.3 Hz, arom. =<u>C</u>H), 113.18 (S, <u>C</u>N), 108.14 (D, J = 153.6 Hz, NCH=<u>C</u>HPh), 52.86 (Q, J = 148.9 Hz, O<u>C</u>H$_3$), 51.82 (Qd, J = 147.3 Hz and 2.6 Hz, O<u>C</u>H$_3$), 38.75 (Dq, ^{1}J = 126.6 Hz and ^{3}J = 4.2 Hz, <u>C</u>H(E)CH$_3$), 36.60 (Qd, J = 139.7 Hz and 4.2 Hz, N<u>C</u>H$_3$), 15.51 (Qd, ^{1}J = 130.3 Hz and ^{3}J = 5.6 Hz, CH(E)<u>C</u>H$_3$); MS m/e : 327.8 (M^+), 226.8 (M^+ - PhCCH), 225.8 (M^+ - PhCCH - H), 187.2, 186.3, 166.9 (100 %, M^+ - PhCCH - H - CH_3OH - CO), 135.3, 95.0, 84.9, 82.9; Anal. Calcd. for $C_{18}H_{20}N_2O_4$ (328.37) : C : 65.84 %; H : 6.14 %; N : 8.53 %; Found : C : 65.41 %; H : 6.01 %; N : 8.55 %

Reactions of 3-(N,N-dialkylamino)acrylates with DMAD

*Trimethyl 1-pyrrolidino-butadiene-2,3,4-tricarboxylate **8b**(Z) and (E)*

150 mg of DMAD in 3 ml of DMSO (tech.) are added dropwise to a solution of methyl 3-pyrrolidinoacrylate (160 mg) in 4 ml of DMSO in the presence of 4 g of molecular sieves (4 Å) at room temperature. The mixture is heated at 90 °C for 24 h. Then 20 ml of ethyl acetate are added and the mixture is filtered through celite and washed with water and brine. The organic phase is dried over magnesium sulfate. After removal of the solvent, flash chromatography of the residue (silica gel, hexane/ethyl acetate 5/4) furnished 180 mg (60%) of **8b** as yellow oil; ^1H NMR (δ, ppm): 7.89 (s, 1 H, =C<u>H</u>N, trans), 7.78 (s, 1 H, =C<u>H</u>N, cis), 6.8 (s, 1 H, =C<u>H</u>E, trans), 5.49 (s, 1 H, =C<u>H</u>E, cis), 3.82, 3.71, 3.68 (3 x s, 9 H, OC<u>H</u>$_3$, trans), 3.83, 3.76, 3.69 (3 x s, 9 H, OC<u>H</u>$_3$, cis), 3.24 (m, 4 H, N(C<u>H</u>$_2$)$_2$), 1.91 (m, 4 H, -C<u>H</u>$_2$C<u>H</u>$_2$-)

General procedure for the reactions between 3-(N,N-dialkylamino)acrylates and DMAD

A solution of DMAD (1.2 mmol) in 3 ml of DMSO (tech.) is added dropwise to a solution of 3-(N,N-dialkylamino)acrylates (1 mmol) in 4 ml of DMSO in the presence of 4 g of molecular sieves (4 Å) at room temperature. The mixture is stirred for 22 hours at 135°C, cooled and 20 ml of ethyl acetate are added and the mixture is filtered through celite and washed with water and brine. The organic layer is dried over magnesium sulfate. After removal of the solvent, flash chromatography of the residue (silica gel, hexane / ethyl acetate 5/4) afforded pure products.

*N-Ethyl-3-(carbomethoxymethyl)-3,4-bis-(carbomethoxy)-4,5-dehydro-2-methyl-pyrrolidine **7a**(cis)*

131 mg (44 %) of light yellow oil; IR (cm^{-1}, neat) : 2945, 1734, 1675, 1576, 1435, 1170; ^1H NMR (δ, ppm) : 7.18 (s, 1 H, =CHN), 4.54-4.44 (dd, J = 6.7 and 6.7 Hz, 1 H, NCH), 3.90, 2.68 (AB, J = -17.6 and -17.6 Hz, 2 H, CH_2E), 3.71, 3.66, 3.64 (3 x s, 9 H, OCH_3), 3.3-3.18 (dq, J = 7 and 1.3 Hz, 2 H, NCH_2CH_3), 1.29-1.22 (t, J = 7.2 Hz, 3 H, NCH_2CH_3), 1.13, 1.1 (d, J = 6.6 Hz, 3 H, CH_3); ^{13}C NMR (δ, ppm) : 174.32, 173.08, 165.56 (3 x s, C=O), 150.88 (d, J = 176.1 Hz, =CHN), 97.24 (s, =C(E)), 64.15 (d, J = 147.1 Hz, NCH), 55.55 (s, $C(E)CH_2E$), 52.38, 51.66, 50.15 (3 x q, J = 147, 146.9 and 145.8 Hz, OCH_3), 41.5 (t, J = 138.2 Hz, NCH_2), 34.67 (t, J = 132.3 Hz, CH_2E), 13.9 (q, J = 127.2 Hz, CH_3), 13.05 (q, J = 127 Hz, CH_3); M.S. : m/e 299.4 (M^+), 180.1 (100 %)

*Dimethyl 2,3-dehydro-1-(carbomethoxymethyl)-*1H*-pyrrolizidine-1,2-dicarboxylate **7b**(cis) and (trans)*

210 mg (70 %) of light yellow oil; IR (cm^{-1}, neat) : 2950, 1735, 1680, 1593, 1440, 1140; ^1H NMR (δ, ppm): 7.1 (s, 1 H, =CHN, cis), 7.08 (s, 1 H, =CHN, trans), 4.59-4.51 (dd, J = 5.4 Hz, 1 H, NCH, cis), 4.47-4.39 (dd, J = 6.4 Hz, 1 H, NCH, trans), 3.75, 3.71, 3.69, 3.66, 3.65 (5 x s, 9 H, OCH_3), 3.24 (m, 2 H, NCH_2), 3.15, 2.74 (AB, J = -15.2 and -15.2 Hz, 2 H, CH_2E, trans), 2.55 (d, AB, J = -18Hz, H_α of CH_2E, cis), 1.85 (m, 4H, $-CH_2CH_2-$); ^{13}C NMR 171.95, 165.1 (2 x s, C=O), 155.3 (d, =CHN, cis), 153.39 (d, J = 174.2 Hz, =CHN, trans), 107.78 (s, =C(E)), 73.32 (d, J = 148.1 Hz, NCH), 55.83 (s, $C(E)CH_2E$), 52.07, 51.42, 50.45 (3 x q, J = 147.3, 146.8 and 146.1 Hz, OCH_3), 48.27 (t, J = 141.9 Hz, NCH_2), 39.73 (t, ^1J = 134.3 Hz, ^3J = 6.4 Hz, CH_2E, trans), 27.43, 25.48 (2 x t, J = 132 and 134.1 Hz, $-CH_2CH_2-$); M.S.: m/e 297.2 (M^+), 178.1 (100 %)

Dimethyl 2,3-dehydro-1-(carbethoxymethyl)-3-methyl- 1H*-pyrrolizidine-1,2-dicarboxylate **7c**(cis) and (trans)*

230 mg (72 %) of light yellow oil. IR (cm^{-1}, neat) : 2952, 1732, 1674, 1583, 1435, 1140; ^1H NMR (δ, ppm) : 4.48-4.4 (dd, J = 5 and 4.8 Hz, 1 H, NCH, cis), 4.39-4.31 (dd, J = 5.9 and 5.7 Hz, 1 H, NCH, trans), 4.18-4.08 (q, J = 7.1 Hz, 2 H, OCH_2CH_3), 3.89, 2.54 (AB, J = -17.9 and -17.8 Hz, 2 H, CH_2E, cis), 3.72, 3.68, 3.65 (3 x s, 9 H, OCH_3), 3.34-3.2 (m, 2 H, NCH_2), 3.11, 2.75 (AB, J = -15 and -15 Hz, 2 H, CH_2E, trans), 2.21 (s, 3 H, CH_3), 2.0-1.39 (m, 4 H, $-CH_2CH_2-$), 1.3-1.21 (2 x t, J = 7.1 and 7.1 Hz, 3 H, OCH_2CH_3); ^{13}C NMR (δ, ppm) : 175.4, 173, 172.5, 166.2, 164.4, 163.5 (6 x s, C=O), 171.9 (s, $=C(CH_3)N$), 103.2, 101.8 (2 x s, =C(E)), 71.9, 71.8 (2 x d, J = 157.9 and 157.9 Hz, NCH), 60.5, 60.4 (2 x t, J = 147.3 and 147.1 Hz, OCH_2CH_3), 55.7, 53.8 (2 x s, $C(E)CH_2E$), 52.3, 51.9, 50.2 (3 x q, OCH_3), 45.9 (t, J = 133.8 Hz, NCH_2), 40.8 (t, ^1J = 130.2 Hz, ^3J = 6.4 Hz, CH_2E, trans), 37.5 (t, J = 129.3 Hz, CH_2E, cis), 27.8, 26.9, 25.8, 22.6 (4 x t, $-CH_2CH_2-$), 14.3, 14.2 (2 x q, J = 129.2 Hz, OCH_2CH_3). M.S. : m/e 325.3 (M^+), 206.1 (100 %)

Dimethyl 2,3-dehydro-1-(carbethoxymethyl)-3-phenyl- 1H*-pyrrolizidine-1,2-dicarboxylate **7d**(cis)*

260 mg (67 %) of white solide, m.p. 93-94°C; IR (cm^{-1}, KBr) : 2925, 2361, 1729, 1670, 1550; ^1H NMR (δ, ppm): 7.39 (s, 5 H, Ph), 4.6-4.53 (dd, J = 4.4 and 5.1 Hz, 1 H, NCH), 4.21-4.11 (q, J = 7.3 and 7.2 Hz, 2 H, OCH_2CH_3), 3.99, 2.76 (AB, J = -17.8 and -17.7 Hz, 2 H, CH_2E), 3.74, 3.46 (2 x s, 6 H, OCH_3), 3.15, 2.88 (2 x m, 2 H, NCH_2), 1.85-1.58 (m, 4 H, $-CH_2CH_2-$), 1.32-1.25 (t, J = 7.2 and 7 Hz, 3 H, OCH_2CH_3); ^{13}C

NMR (δ, ppm) : 174.98, 172.29, 165.61 (3 x s, C=O), 165.97 (s, =C(Ph)N), 132.51 (s, arom.), 129.39, 129.14, 127.67 (3 x d, J = 158.5, 158.5 and 73.3 Hz, arom.), 71.62 (d, J = 149.2, NCH), 60.37 (t, J = 147.3 Hz, OCH_2CH_3), 54.87 (s, C(E)CH_2E), 52.43, 50.1 (2 x q, J = 147.1 and 146.1 Hz, OCH_3), 47.95 (t, J = 139.9 Hz, NCH_2), 37.79 (t, J = 129.7 Hz, CH_2E), 29.02, 24.44 (2 x t, J = 129.1 and 131.4 Hz, -CH_2CH_2-), 14.12 (q, J = 126.9 Hz, OCH_2CH_3). M.S. : m/e 387.2 (M^+), 268.1 (100 %); Anal. Calcd. for $C_{21}H_{25}NO_6$ (387.50) : C : 65.10 %; H : 6.50 %; N : 3.62 %; Found : C : 64.59 %; H : 6.63 %; N: 3.41%

*Dimethyl 2,3-dehydro-1-(carbomethoxymethyl)-*1H*-indolizidine-1,2-dicarboxylate* ***7e*** *(cis) and (trans)*

200 mg (64 %) of light yellow oil; IR (cm^{-1}, neat) : 2950, 1732, 1682, 1575, 1434; ^{1}H NMR (δ, ppm) : 7.16 (s, 1 H, =CHN, cis), 7.15 (s, 1 H, =CHN, trans), 4.3-4.23 (m, J = 5.2 Hz, 1 H, NCH, cis), 4.11-4.04 (m, J = 3.3 Hz, 1 H, NCH, trans), 3.86, 2.65 (AB, J = -17.5 and -17.6 Hz, 2 H, CH_2E, cis), 3.73, 3.72, 3.68, 3.66, 3.64 (5 x s, 9 H, OCH_3), 3.55-3.03 (m, 2 H, NCH_2), 3.07, 2.84 (AB, J = -15.2 and -15.2 Hz, 2 H, CH_2E, trans), 1.92-1.47 (m, 6 H, -$CH_2CH_2CH_2$-); ^{13}C NMR (δ, ppm) : 174.1, 172.92, 172.36, 172.07, 165.83, 165.46 (6 x s, C=O), 151.4, 150.4 (2 x d, J = 176.6 and 176.6 Hz, =CHN), 99.89, 98.06 (2 x s, =C(E)), 68.83, 68.68 (2 x d, J = 143.9 and 143.9 Hz, NCH), 57.14, 55.31 (2 x s, C(E)CH_2E), 52.39, 52.03, 51.6, 51.33, 50.2, 50.1 (6 x q, OCH_3), 47.93, 47.54 (2 x t, NCH_2), 39.4 (t, ^{1}J = 131 Hz, ^{3}J = 6.8 Hz, CH_2E, trans), 34.6 (t, J = 130.7 Hz, CH_2E, cis), 27.31, 26.36, 25.8, 25.68, 23.56, 23.38 (6 x t, -$CH_2CH_2CH_2$-); M.S. : m/e 311.2 (M^+), 192.1 (100 %)

*Dimethyl Δ-2,3-dehydro-1-(carbomethoxymethyl)-*1H*-pyrrolidino-[1,2-a]-perhydroazepine-1,2-dicarboxylate* ***7f*** *(trans)*

170 mg (52 %) of light yellow oil; IR (cm^{-1}, neat): 2950, 1730, 1680, 1590, 1435; ^{1}H NMR (δ, ppm) : 7.17 (s, 1 H, =CHN), 4.35-4.29 (dd, J = 2.9 and 3 Hz, 1 H, NCH), 3.7, 3.67, 3.64 (3 x s, 9 H, OCH_3), 3.88 (m, 2 H, NCH_2), 3.03, 2.87 (AB, J = -15.3 and -15.4 Hz, 2 H, CH_2E), 1.74-1.47 (m, 8 H, -$CH_2CH_2CH_2CH_2$-); Irradiation of the proton (NCH) at 4.35-4.29 ppm resulted in an enhancement of 20 % at 3.64 ppm (OCH_3), at 3.08-2.82 ppm (CH_2E) and a negative effect of 20 % at 7.17 ppm (=CHN) and 3.7 ppm (OCH_3); ^{13}C NMR (δ, ppm) : 172.89, 172.13, 165.59 (3 x s, C=O), 152.19 (d, J = 175.3 Hz, =CHN), 100.69 (s, =C(E)), 71.32 (d, J = 148.7 Hz, NCH), 58.62 (s, C(E)CH_2E), 52.07, 51.35, 50.27 (3 x q, J = 147.3, 146.7 and 145.9 Hz, OCH_3), 49.46 (t, J = 137.9 Hz, NCH_2), 40.24 (t, ^{1}J = 132.5 Hz, ^{3}J = 7 Hz, CH_2E), 31.73, 28.25, 27.7, 27.05 (4 x t, -$CH_2CH_2CH_2CH_2$-); M.S. : m/e 325.2 (M^+), 206.1 (100 %)

*Dimethyl Δ-2,3-dehydro-1-(carbomethoxymethyl)-*1H*-pyrrolidino-[1,2-a]-perhydroazocine* ***7g*** *(trans)*

200 mg (59 %) of light yellow oil; IR (cm-1, neat) : 2948, 1732, 1681, 1598, 1431, 1188; ^{1}H NMR (d, ppm) : 7.14 (s, 1 H, =CHN), 4.19-4.11 (dd, J = 3 Hz, 1 H, NCH), 3.7, 3.66, 3.64 (3 x s, 9 H, OCH_3), 3.58-3.07 (m, 2 H, NCH_2), 2.94 (s, 2 H, CH_2E), 1.74-1.57 (m, 10 H, -$CH_2CH_2CH_2CH_2CH_2$-); ^{13}C NMR (d, ppm) : 173.04, 172.04, 165.6 (3 x s, C=O), 153.13 (d, J = 175.7 Hz, =CHN), 101.11 (s, =C(E)), 71.99 (d, J = 149.3 Hz, NCH), 58.76 (s, C(E)CH_2E), 52.07, 51.33, 50.29 (3 x q, J = 147.2, 146.7 and 145.8 Hz,

$O\underline{C}H_3$), 49.26 (t, J = 136.3 Hz, $N\underline{C}H_2$), 40.25 (t, ^1J = 132.3 Hz, ^3J = 7.2 Hz, $\underline{C}H_2E$), 28.82, 28.35, 27.18, 24.23, 23.22 (5 x t, $-\underline{C}H_2\underline{C}H_2\underline{C}H_2\underline{C}H_2\underline{C}H_2-$); M.S. : m/e 339.2 ($M^+$), 220.2 (100 %)

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