Pergamon

Tetrahedron 54 (1998) 513–520

TETRAHEDRON

THE INTERMEDIATE OF "α-CYCLISATION‡ OF TERTIARY AMINES" AS A VINYL-1,3-DIPOLE #.

Benoît De Boeck and Heinz G. Viehe*

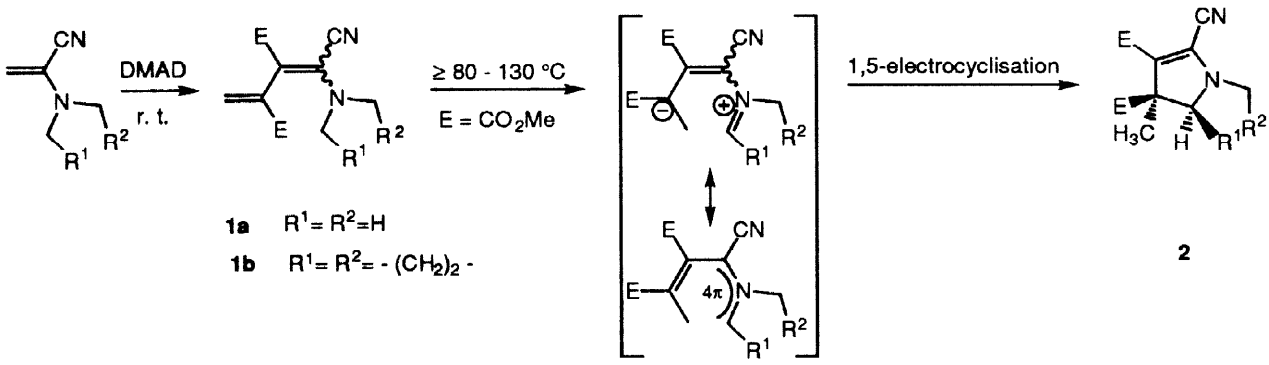
Laboratoire de Chimie Organique, Université Catholique de Louvain, Place L. Pasteur, 1, 1348 Louvain-la-Neuve, Belgium

#Dedicated to Dieter SEEBACH at the occasion of his 60th anniversary

Received 28 July 1997; accepted 31 October 1997

Abstract : Captodative α-cyano-enamines react at room temperature with DMAD *via* [2+2] cycloaddition and cycloreversion to dienamines **1**. These can be isolated or cyclise above 80-130°C. At these temperatures, they can also react as vinyl-1,3-dipoles as shown by cycloaddition to acrylonitrile or N-phenyl-maleimide.

Both captodative (cd) and push-pull (pp) enamines undergo "α-Cyclisation of Tertiary Amines"[1] on heating above 80°C with dimethyl acetylenedicarboxylate (DMAD) to pyrroline derivatives. Although they differ in reactivity (vide infra), both cd and pp α-cyano-enamines at room temperature yield isolable dienamines **1a** and **1b** being obtained from cd enamines. Refluxing in acetonitrile (for **1b**) or heating at 130°C in DMSO (for **1a**), these undergo a 1,6-H shift followed by electrocyclisation of the intermediate 1,5-dipoles to pyrroline derivatives **2a** and **2b** (scheme 1).[1a]



scheme 1

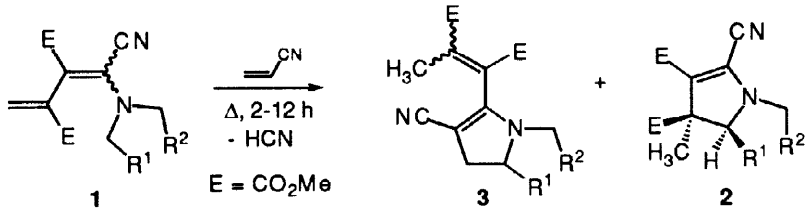
* Fax : 32(10) 47 27 88

0040-4020/98/$19.00
PII: S0040-4020(97)10302-7

1,5-Dipoles and vinyl-1,3-dipoles are two resonance forms of the same chemical entity and both their 1,5-electrocyclisations[2] and cycloadditions[2h,3] are known. Vinyl azomethine ylides are one class of compound capable of undergoing these two main pathways : 1,5-electrocyclisation to 2-pyrrolines, or 1,3-dipolar cycloaddition if a dipolarophile is present. Other pathways such as rearrangement through a 1,6-H shift[1a,2e,3b], or intramolecular nucleophilic addition[2h,4], are also possible.

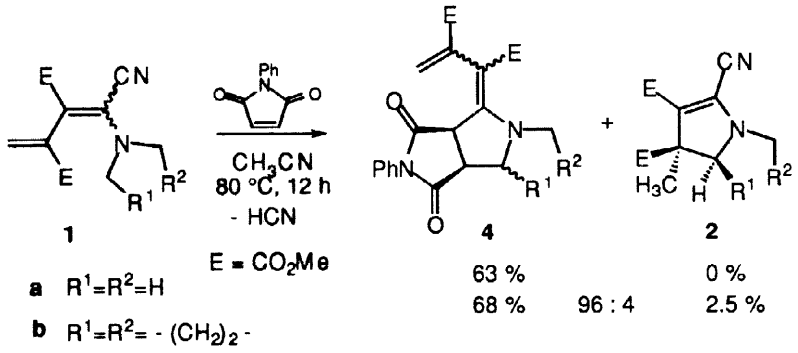
We now report that the "α-Cyclisation of Tertiary Amines" occurs *via* a vinyl azomethine ylide intermediate, and both 1,5-electrocyclisation and 1,3-dipolar cycloaddition take place if a dipolarophile is present.

Thus, in refluxing acrylonitrile, dienamine **1a** leads to the 2-vinyl-pyrroline **3a** with a yield of 91% through a 1,3-dipolar cycloaddition followed by elimination of HCN from the postulated initial cycloadduct (scheme 2). The corresponding pyrrolidino-substituted diene **1b** affords, in analogous conditions, a mixture of the cycloadduct **3b** and of the pyrrolizidine **2b** resulting from α-cyclisation (scheme 2).



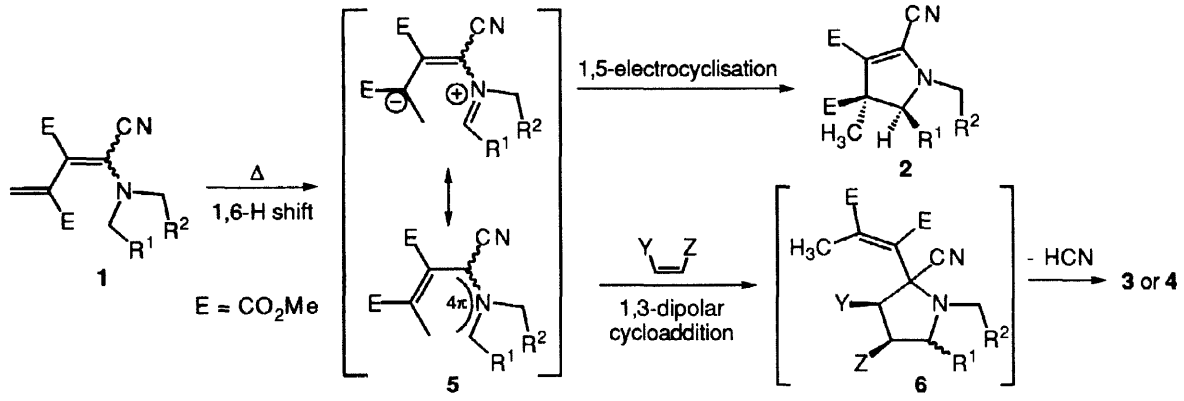
scheme 2

With N-phenyl-maleimide in refluxing acetonitrile, compound **1a** leads exclusively to the formation of the propenylidene-substituted cycloadduct **4a** (scheme 3). Again, analogous conditions applied to the dienamine **1b** lead to a mixture of cycloadducts **4b**, in which the stereochemistry of the double bond is still not yet established, along with a small amount of the pyrrolizidine **2b** (scheme 3).



scheme 3

The mechanism of these processes is proposed in scheme 4. The first step of the α-cyclisation is a 1,6-H shift[5]. In the presence of a dipolarophile, the vinyl 1,3-dipole **5** undergoes 1,5-electrocyclisation to 2-pyrroline derivatives (α-cyclisation), and 1,3-dipolar cycloaddition leading to 2-vinyl-pyrrolines or 2-propenylidene-pyrrolines by spontaneous elimination of HCN from the postulated initial cycloadduct **6**.



scheme 4

For the "α-Cyclisation of Tertiary Amines", this report is the first showing competition between the two pathways. 1,5-Electrocyclisation and 1,3-dipolar cycloaddition appear as comparable in rate, a potent dipolarophile such as N-phenyl-maleimide favoring the latter process.

Substitution on the vinyl azomethine ylides has an important influence on their fate.[2a,d,3,6] Electron-withdrawing groups slow their 1,5-electrocyclisation and 1,3-dipolar cycloaddition is favored when a dipolarophile is present. Furthermore, in our case, the substituents influence the regiochemistry.

The regiochemistry of the cycloaddition with acrylonitrile is opposite to the one generally observed for 1,3-dipoles[7] and predicted by FMO theory.[8] AM1 calculations[9] performed on **5a** show that taking into account the $HOMO_{dipole}$ and the $LUMO_{acrylonitrile}$ does not predict the observed regiochemistry. Besides steric accessibility, the easiest explanation for this observation would be that the dipolar character is less important than the 1,3-diradical nature in this vinyl-captodative system.[10]

In summary, we have shown that in the appropriate conditions, the 1,5-dipole intermediate of the "α-Cyclisation of Tertiary Amines" can be diverted from its normal cyclisation pathway and can react as a vinyl-1,3-dipole giving access to a variety of highly substituted pyrrolizidines with biological potential.[11]

ACKNOWLEDGEMENTS

The authors are grateful to the "Actions de Recherches Concertées" (ARC) and the Fonds National de la Recherche Scientifique (Belgium) for financial support.

EXPERIMENTAL PART

General. The ^1H NMR spectra were recorded on a Gemini-200 (200 MHz) and on a Gemini-300 (300 MHz) spectrometers. The ^{13}C NMR spectra were recorded on a Gemini-200 (50 MHz) and on a Gemini-300 (75 MHz) spectrometers (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; b, broad. In the ^{13}C data, the capital letter indicates the $^{1}J_{C-H}$ coupling and the small letter indicates the $^{2}J_{C-H}$ or $^{3}J_{C-H}$ coupling. IR and mass spectra were recorded on a Nicolet-205 and Finnigan-Mat TSQ-70 apparatus, respectively. Melting points were determined with a Leitz Wetzlar microscope and are uncorrected. Elemental analysis were carried out by Dr A Stones at the University College London, London, UK.

Acetonitrile and dichloromethane 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).

2-(N,N-Dialkylamino)acrylonitriles were prepared[12] in medium to high yields by addition of amines to α-chloro acrylonitrile followed by elimination and rearrangement. They were distilled before use.

Synthesis of 2-dimethylamino-3,4-dicarbomethoxy-penta-2,4-dienenitrile 1a. In a dry apparatus under argon atmosphere, DMAD (710mg, 5.0mmoles) was added to a solution of 2-dimethylamino-acrylonitrile (480mg, 5.0mmoles) in 25ml of dichloromethane. This solution was refluxed for 12 hours. After cooling, the solvent was evaporated under reduced pressure. Column chromatography of the residual oil over silica gel (dichloromethane) afforded 380mg (32%) of an equimolar mixture of *(E)* and *(Z)* isomers of **1a** as a pale yellow oil; **IR** (cm^{-1}, neat): 2953, 2227 (CN), 2205, 1726 (C=O), 1703 (C=O), 1573 (C=C),1436, 1402; **^{1}H** (δ, ppm): 2.93 (6 H, s, NCH_3), 3.03 (6 H, s, NCH_3), 3.68 (3 H, s, OCH_3), 3.73 (3 H, s, OCH_3), 3.76 (3 H, s, OCH_3), 3.77 (3 H, s, OCH_3), 5.30 (1 H, d, J = 1.8 Hz, $NC=CC=CH_2$), 5.85 (1 H, d, J = 1.1 Hz, $NC=CC=CH_2$), 6.46 (1 H, d, J = 1.1 Hz, $NC=CC=CH_2$), 6.48 (1 H, d, J = 1.3 Hz, $NC=CC=CH_2$); **^{13}C** (δ, ppm): 43.03 (Q, J = 139.0 Hz, NCH_3), 43.06 (Q, J = 138.8 Hz, NCH_3), 43.16 (Q, J = 139.2 Hz, NCH_3), 43.19 (Q, J = 139.2 Hz, NCH_3), 51.57 (Q, J = 147.0 Hz, OCH_3), 51.66 (Q, J = 147.0 Hz, OCH_3), 51.96 (Q, J= 147.2 Hz, OCH_3), 52.03 (Q, J = 147.3 Hz, OCH_3), 108.86 (S, $NC=CC=CH_2$), 109.46 (S, $NC=CC=CH_2$), 113.27 (S, CN), 113.32 (S, CN), 127.23 (T, J = 162.0 Hz, $NC=CC=CH_2$), 130.69 (T, J = 162.2 Hz, $NC=CC=CH_2$), 131.52 (Sm, $NC=CC=CH_2$), 131.71 (Sm, $NC=CC=CH_2$), 135.36 (S, $NC=CC=CH_2$), 137.10 (S, $NC=CC=CH_2$), 164.50 (Sq, J = 4.0 Hz, CO_2CH_3), 165.99 (Sm, CO_2CH_3), 166.26 (Sm, CO_2CH_3), 166.29 (Sm, CO_2CH_3); **MS** m/e : 238.0 ($M^{\cdot+}$), 223.1 ($M^{\cdot+}$ - CH_3^+), 206.1 ($M^{\cdot+}$ - $CH_3OH^{\cdot+}$), 191.1 (100%, $M^{\cdot+}$ - $CH_3OH^{\cdot+}$ - $CH_3OH_2^+$), 179.1, 156.2, 147.1 ($M^{\cdot+}$ - $CH_3OH^{\cdot+}$ - $CH_3OH_2^+$ - $(CH_3)_2N^+$), 128.1, 119.1, 86.0, 84.0, 58.1, 49.0; Anal. Calcd. for $C_{11}H_{14}N_2O_4$ (238.24): C: 55.46%, H: 5.92%, N: 11.76%; found: C: 55.18%, H: 5.91%, N: 10.99%.

Reaction of 2-dimethylamino-3,4-dicarbomethoxy-penta-2,4-dienenitrile 1a with acrylonitrile. Synthesis of 3a. In a dry apparatus under argon atmosphere, 2-dimethylamino-3,4-dicarbomethoxy-penta-2,4-dienenitrile **1a** (210mg, 0.88mmoles) was dissolved into 5ml of acrylonitrile. This solution was refluxed for 12 hours. After cooling, excess acrylonitrile was evaporated under reduced pressure. Column chromatography of the residual oil over silica gel (diethyl ether) afforded 210mg (91%) of **3a** as an orange oil; **IR** (cm^{-1}, neat): 2954, 2861, 2852, 2188 (CN), 1736 (C=O), 1731 (C=O), 1694, 1649, 1582 (C=C),1437; **^{1}H** (δ, ppm): 2.09 (3 H, s, $CH_3C=C$), 2.66 (3 H, s, NCH_3), 2.83 (2 H, t, J = 10.3 Hz, NCH_2CH_2), 3.49 (2 H, t, J = 10.1 Hz, NCH_2CH_2), 3.79 (3 H, s, OCH_3), 3.84 (3 H, s, OCH_3); **^{13}C** (δ, ppm): 17.91 (Q, J = 130.7 Hz,

$\underline{C}H_3C{=}C$), 28.42 (T, J = 133.6 Hz, $NCH_2\underline{C}H_2$), 34.99 (Q, J = 137.4 Hz, $N\underline{C}H_3$), 52.47 (Q, J = 147.9 Hz, OCH_3), 52.55 (Q, J = 148.0 Hz, OCH_3), 53.98 (T, J = 142.0 Hz, $N\underline{C}H_2CH_2$), 79.09 (Sm, C=$\underline{C}$CN), 118.68 (S, $\underline{C}N$), 123.31 (Sq, J ~ 5 Hz, $CH_3\underline{C}{=}C$), 145.76 (St, J = 7.2 Hz, $\underline{C}{=}CCN$), 158.08 (Sm, $CH_3C{=}\underline{C}$), 163.83 (Sm, $\underline{C}O_2CH_3$), 168.09 (Sm, $\underline{C}O_2CH_3$); **MS** m/e : 264.1 ($M^{\cdot+}$), 232.0 ($M^{\cdot+}$ - $CH_3OH^{\cdot+}$), 215.1, 187.1, 155.7 (100%), 128.0; Anal. Calcd. for $C_{13}H_{16}N_2O_4$ (264.28): C: 59.08%, H: 6.10%, N: 10.60%; found: C: 58.53%, H: 5.93%, N: 10.41%.

Reaction of 2-pyrrolidino-3,4-dicarbomethoxy-penta-2,4-dienenitrile 1b with acrylonitrile. Synthesis of 3b and 2b. In a dry apparatus under argon atmosphere, DMAD (1.0g, 6.9mmoles) diluted in 5ml of CH_2Cl_2 was added to 2-pyrrolidino-acrylonitrile (850mg, 6.9mmoles) in 10ml of CH_2Cl_2. This solution was refluxed for 1.5 hour. After cooling, the solvent was evaporated under reduced pressure. To the resulting oil (a 70/30 mixture of *E/Z* or *Z/E* isomers of 2-pyrrolidino-3,4-dicarbomethoxy-penta-2,4-dienenitrile **1b**) were added 10ml of acrylonitrile. After refluxing for 2 hours, excess acrylonitrile was evaporated under reduced pressure and column chromatography of the residual oil over silica gel (diethyl ether) afforded 140mg (8%) of **2b** (described elsewhere[1a]) and 970mg (49%) of **3b** (two isomers) as colourless crystals recrystallised from chloroforme/hexane 1:4 (m. p. : 89.0-90.0 °C); **IR** (cm^{-1}, KBr): 2971, 2955, 2930, 2202 (CN), 1730 (C=O), 1711 (C=O), 1634 (C=C), 1594 (C=C), 1444, 1368, 1284, 1272, 1200; **^{1}H** (δ, ppm): 1.80 (2 H, q, J = 7.8 Hz, $NCH_2CH_2C\underline{H}_2$), 1.80-2.00 (2 H, m, $NCH_2C\underline{H}_2CH_2$), 2.12 (3 H, s, $C\underline{H}_3C{=}C$), 2.71 (1 H, dd, J = 15.2 Hz and 3.8 Hz, $NC{=}C(CN)C\underline{H}_2CH$), 2.99 (1 H, dd, J = 15.3 Hz and 10.8 Hz, $NC{=}C(CN)C\underline{H}_2CH$), 3.00-3.15 (2 H, m, $NC\underline{H}_2CH_2CH_2$), 3.80 (3 H, s, $OC\underline{H}_3$), 3.81 (3 H, s, $OC\underline{H}_3$), 3.80-4.00 (1 H, m, $NC{=}C(CN)CH_2C\underline{H}$); **^{13}C** (δ, ppm, minor isomer between brackets): 17.59 (17.19) (Q, J = 130.0 Hz, $\underline{C}H_3C{=}C$), 24.58 (24.14) (Tm, J ~ 133 Hz, $NCH_2CH_2\underline{C}H_2$), 31.10 (30.80) (Tm, J ~ 131 Hz, $NCH_2\underline{C}H_2CH_2$), 34.22 (Td, J = 136.2 Hz and 5.2 Hz, $NC{=}C(CN)\underline{C}H_2CH$), 48.26 (47.57) (Tm, J ~ 137 Hz, $N\underline{C}H_2CH_2CH_2$), 52.41 (Q, J = 147.7 Hz, $O\underline{C}H_3$), 52.57 (Q, J = 147.7 Hz, $O\underline{C}H_3$), 64.13 (Dm, J = 147.6 Hz, $NC{=}C(CN)CH_2\underline{C}H$), 85.15 (82.47) (Sm, $NC{=}\underline{C}(CN)CH_2CH$), 117.56 (S, $\underline{C}N$), 128.52 (125.20) (Sm, $CH_3C{=}\underline{C}$), 140.22 (144.80) (Sm, $N\underline{C}{=}C(CN)CH_2CH$), 158.96 (Sm, $CH_3\underline{C}{=}C$), 165.29 (Sm, $\underline{C}O_2CH_3$), 167.14 (Sm, $\underline{C}O_2CH_3$); **MS** m/e : 290.3 ($M^{\cdot+}$, 100%), 275.3 ($M^{\cdot+}$ - CH_3^+), 259.3 ($M^{\cdot+}$ - CH_3O^+), 231.3 ($M^{\cdot+}$ - $CO_2^{\cdot+}$ - CH_3^+), 199.2 ($M^{\cdot+}$ - $CO_2^{\cdot+}$ - CH_3^+ - $CH_3OH^{\cdot+}$), 172.3 ($M^{\cdot+}$ - $CO_2^{\cdot+}$ - CH_3^+ - $CH_3OH^{\cdot+}$ - $HCN^{\cdot+}$), 143.2, 44.0; Anal. Calcd. for $C_{15}H_{18}N_2O_4$ (290.32): C: 62.06%, H: 6.25%, N: 9.65%; found: C: 62.17%, H: 6.31%, N: 9.71%.

Reaction of 2-dimethylamino-3,4-dicarbomethoxy-penta-2,4-dienenitrile 1a with N-phenylmaleimide. Synthesis of 4a. In a dry apparatus under argon atmosphere, N-phenyl-maleimide (170mg, 1.0 mmole) was added to 2-dimethylamino-3,4-dicarbomethoxy-penta-2,4-dienenitrile **1a** (150mg, 0.62mmoles) in 5ml of acetonitrile. This solution was refluxed for 12 hours. After cooling, the solvent was evaporated under reduced pressure and the residual oil was precipitated in ethyl acetate. Filtration and washing of the precipitate with diethyl ether afforded 150mg (63%) of **4a** as pale yellow crystals recrystallised from chloroforme/hexane 1:1 (m.p. : 197.0-198.0°C); **IR** (cm^{-1}, KBr): 3007, 2952, 2943, 1785, 1720 (C=C), 1687 (NC=O), 1617 (C=C), 1584, 1499, 1432, 1380, 1290, 1274, 1213, 1193, 1171; **^{1}H** (δ, ppm): 2.76 (3 H, s, $N\underline{C}H_3$), 3.69 (3 H, s, $OC\underline{H}_3$), ~3.7 (1 H, masked by OCH_3, $NCH_2C\underline{H}$), 3.76 (3 H, s,

OCH_3), 3.84 (1 H, sb, NCH_2CH), 3.87 (1 H, d, J = 3.6 Hz, NCH_2CH), 5.30 (1 H, d, J = 1.8 Hz, $NC=CC=CH_2$), 5.92 (1 H, d, J = 9.2 Hz, $NC(=C)CH$), 6.41 (1 H, d, J = 1.8 Hz, $NC=CC=CH_2$), 7.2-7.5 (5 H, m, arom. H); ^{13}C (δ, ppm): 38.87 (Q, J = 138.6 Hz, NCH_3), 39.85 (Db, J = 145.8 Hz, NCH_2CH), 50.50 (Db, J = 146.5 Hz, $NC(=C)CH$), 51.40 (Q, J = 146.2 Hz, OCH_3), 52.22 (Q, J = 147.0 Hz, OCH_3), 57.95 (Tm, J = 145.4 Hz, NCH_2CH), 95.17 (St, J = 8.2 Hz, $NC=CC=CH_2$), 126.32 (Dt, J = 164.0 Hz and 6.2 Hz, arom. CH), 127.25 (T, J = 160.7 Hz, $NC=CC=CH_2$), 128.75 (Dt, J = 161.8 Hz and 7.2 Hz, arom. CH), 128.12 (Dd, J = 162.5 Hz and 7.7 Hz, arom. CH), 131.60 (Sm, arom. CN(CO)), 136.60 (Sb, $NC=CC=CH_2$), 153.85 (St, J = 2.3 Hz, $NC=CC=CH_2$), 168.00 (Sm, CO_2CH_3), 169.20 (St, J = 3.7 Hz, CO_2CH_3), 172.40 (Sdd, J = 7.4 Hz and 4.4 Hz, NCO), 176.00 (Sm, NCO); **MS** m/e : 384.2 ($M^{\cdot+}$, 100%), 325.2 ($M^{\cdot+}$ - $CO_2^{\cdot+}$ - CH_3^+), 293.1 ($M^{\cdot+}$ - $CO_2^{\cdot+}$ - CH_3^+ - $CH_3OH^{\cdot+}$), 266.4 ($M^{\cdot+}$ - 2 x [$CO_2^{\cdot+}$ + CH_3^+]), 118.0; Anal. Calcd. for $C_{20}H_{20}N_2O_6$ (384.39): C: 62.49%, H: 5.24%, N: 7.29%; found: C: 62.45%, H: 5.33%, N: 7.11%.

Reaction of 2-pyrrolidino-3,4-dicarbomethoxy-penta-2,4-dienenitrile 1b with N-phenylmaleimide. Synthesis of 4b and 2b. In a dry apparatus under argon atmosphere, DMAD (850mg, 6.0mmoles) diluted in 5ml of CH_2Cl_2 was added to 2-pyrrolidino-acrylonitrile (730mg, 6.0mmoles) in 10ml of CH_2Cl_2. This solution was refluxed for 1.5 hour. After cooling, the solvent was evaporated under reduced pressure. To the resulting oil (a 70/30 mixture of *E/Z* or *Z/E* isomers of 2-pyrrolidino-3,4-dicarbomethoxy-penta-2,4-dienenitrile **1b**) were added 1.0g (5.8mmoles) of N-phenyl-maleimide and 10ml of acetonitrile. This solution was refluxed for 12 hours. After cooling, the solvent was evaporated under reduced pressure and column chromatography of the residual oil over silica gel (eluent : ethyl acetate/ light petroleum ether 1:1) afforded 40mg (2.5%) of **2b** (described elsewhere[1a]) and 1.63g (68%) of **4b** (two isomers) as colourless crystals recrystallised from dichloromethane/methanol 1:3 (m. p. : 177.0-178.5 °C); **IR** (cm^{-1}, KBr): 3112, 3002, 2948, 1784 (N-C=O), 1725 (conj. C=O), 1720 (conj. C=O), 1686 (N-C=O), 1656 (C=C), 1619 (C=C), 1578, 1498, 1382, 1297; **^1H** (δ, ppm): 1.23-1.38 (1 H, m, $NCH_2CH_2CH_2$), 1.51-1.65 (1 H, m, $NCH_2CH_2CH_2$), 1.92-2.24 (5 H, m, $NCH_2CH_2CH_2$), 2.31 (1 H, ddd, J= 11.8 Hz, 5.7 Hz and 5.7 Hz, $NCH_2CH_2CH_2$), 2.71 (1 H, ddd, J = 10.8 Hz, 10.4 Hz and 7.7 Hz, $NCH_2CH_2CH_2$), 3.00 (1 H, ddd, J= 11.0 Hz, 8.4 Hz and 8.4 Hz, $NCH_2CH_2CH_2$), 3.22 (2 H, dd, J= 9.5 Hz and 10.3 Hz, $NCH_2CH_2CH_2$), 3.45 (1 H, dd, J= 9.6 Hz and 5.2 Hz, NCHCH), 3.65 (1 H, masked by OCH_3, NCHCH), 3.66 (6 H, s, OCH_3), 3.75 (3 H, s, OCH_3), 3.76 (3 H, s, OCH_3), 4.06 (1 H, ddd, J = 10.4 Hz, 5.2 Hz and 5.2 Hz, NCHCH), 4.20 (1 H, ddd, J= 11.4 Hz, 10.4 Hz and 4.6 Hz, NCHCH), 5.41 (1 H, d, J = 1.7 Hz, $NC=CC=CH_2$), 5.53 (1 H, d, J= 1.8 Hz, $NC=CC=CH_2$), 5.69 (1 H, d, J = 8.6 Hz, $NC(=C)CH$), 6.17 (1 H, d, J = 9.6 Hz, $NC(=C)CH$), 6.40 (1 H, d, J = 1.7 Hz, $NC=CC=CH_2$), 6.42 (1 H, d, J = 1.8 Hz, $NC=CC=CH_2$), 7.20-7.50 (10 H, m, arom. H); ^{13}C (δ, ppm): 26.88 (Tm, J = 134.2 Hz, $NCH_2CH_2CH_2$), 27.08 (Tm, J =132.4 Hz, $NCH_2CH_2CH_2$), 27.95 (Tm, J = 133.6 Hz, $NCH_2CH_2CH_2$), 32.46 (Tm, J = 132.0 Hz, $NCH_2CH_2CH_2$), 41.21 (Dd, J = 144.4 Hz and 3.2 Hz, NCHCH), 46.05 (Dm, J = 144.4 Hz, NCHCH), 48.91 (Tm, J = 144.0 Hz, $NCH_2CH_2CH_2$), 50.11 (Tm, J = 144.2 Hz, $NCH_2CH_2CH_2$), 51.28 (Q, J = 145.6 Hz, OCH_3), 51.28 (Q, J = 145.6 Hz, OCH_3), 52.12 (Q, J = 145.7 Hz, OCH_3), 52.17 (Q, J = 146.8 Hz, OCH_3), 52.86 (D, J = 146.41 Hz, $NC(=C)CH$), 53.92 (D, J = 144.4 Hz, $NC(=C)CH$), 67.23 (Dm, J = 151.6 Hz, NCHCH), 69.65 (Dm, J = 143.6 Hz, NCHCH), 96.94 (Sdd, J = 10.4 Hz and 5.2 Hz, $NC=CC=CH_2$), 98.20 (Sdd, J = 9.2 Hz and 5.6 Hz, $NC=CC=CH_2$), 126.32 (Dt, J = 162.4 Hz and 6.4 Hz, arom. CH), 126.41 (Dt, J = 164.4 Hz and 5.6 Hz, arom. CH), 126.53 (T, J = 161.2 Hz,

NC=CC=$\underline{C}H_2$), 127.83 (T, J = 160.0 Hz, NC=CC=$\underline{C}H_2$), 128.62 (Dt, J = 161.6 Hz and 7.6 Hz, arom. $\underline{C}H$), 129.03 (Dd, J = 162.0 Hz and 7.6 Hz, arom. $\underline{C}H$), 131.82 (Sm, NC=$C\underline{C}$=CH_2), 131.92 (Sm, NC=$C\underline{C}$=CH_2), 137.18 (S, arom. $\underline{C}N(CO)$), 137.24 (S, arom. $\underline{C}N(CO)$), 152.42 (Sm, N$\underline{C}$=CC=CH_2), 154.33 (Sm, N$\underline{C}$=CC=CH_2), 167.95 (Sm, $\underline{C}O_2CH_3$), 168.05 (Sm, $\underline{C}O_2CH_3$), 168.25 (Sm, $\underline{C}O_2CH_3$), 168.80 (Sq, J = 4.1 Hz, $\underline{C}O_2CH_3$), 172.18 (St , J = 7.0 Hz, N$\underline{C}$O), 172.60 (St, J = 6.8 Hz, N$\underline{C}$O), 174.49 (Sm, N$\underline{C}$O), 175.27 (Sm, N$\underline{C}$O); **MS** m/e : 410.6($M^{\cdot+}$), 350.4 ($M^{\cdot+}$ - $CH_3OH^{\cdot+}$ - $CO^{\cdot+}$), 322.4 (100%, $M^{\cdot+}$ - $CH_3OH^{\cdot+}$ - 2 x $CO^{\cdot+}$), 262.3, 204.6, 144.3, 44.1; Anal. Calcd. for $C_{22}H_{22}N_2O_6$ (410.43): C: 64.38%, H: 5.40%, N: 6.83%; found : C: 64.09%, H: 5.28%, N: 6.63%

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‡ Part 5. For previous work, see ref. 4a and references therein

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