

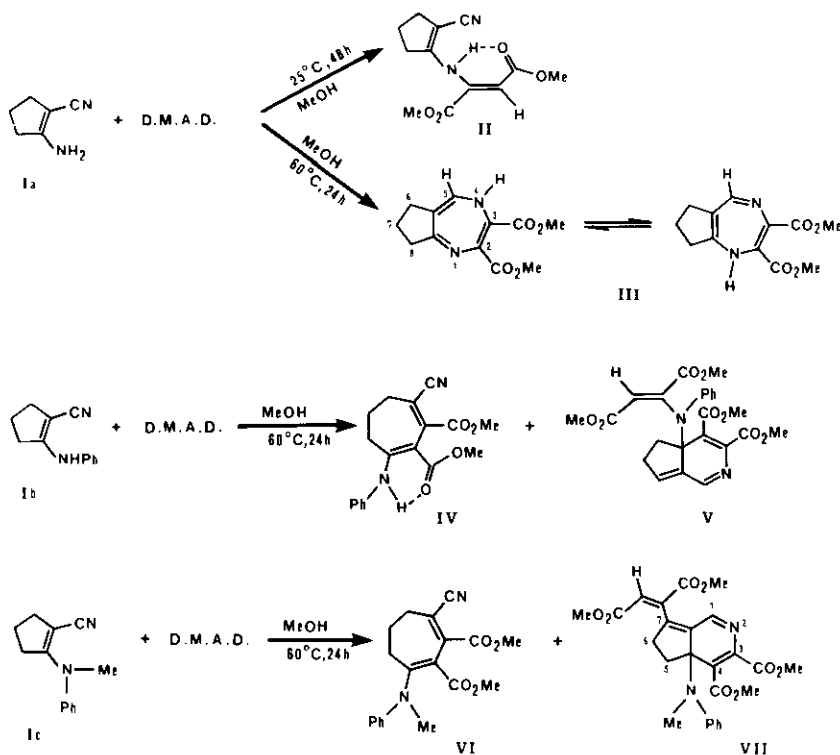
N-SUBSTITUTED 2-AMINOCYANOCYCLOPENTENES REACTIVITY WITH DIMETHYLACETYLENE-DICARBOXYLATE

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Abstract - 2-Aminocyanocyclopentene and its N-phenylamino and N-methyl-N-phenyl-2-aminocyanocyclopentene derivatives react in good yields with dimethyl acetylenedicarboxylate, leading to cycloheptadiene derivatives through ring expansions and/or condensed ring heterocycles via cycloaddition mechanisms.

Related to the general studies undertaken several years ago in our laboratory on enamionitriles¹, we wish to report in this paper some results concerning N-substituted 2-aminocyanocyclopentenes (Ia, Ib, Ic) reactivity. Up to the present time, this class of compounds seems to be unstudied, and the compounds obtained by reaction with dimethyl acetylenedicarboxylate (DMAD) show interesting structures.



SCHEME I

2-Aminocyanocyclopentene reactivity (compound Ia)

2-Aminocyanocyclopentene reacts slowly, in methanolic solution, with DMAD. Nature of formed products depends on reaction temperature, only one product is obtained in each case :

- At 25°C, we observed the formation of dimethyl-2-cyanocyclopentenyl-N-aminofumarate (II), which is the classical Michael adduct². A six membered chelation between the ester carbonyl and the amino groups, is observed by ir spectrometry, which ascertains the fumaroyl geometry.
- Through a refluxing methanolic solution, 2,3-dicarbomethoxy[b]cyclopenta-1,4-diazepine (III) is obtained.

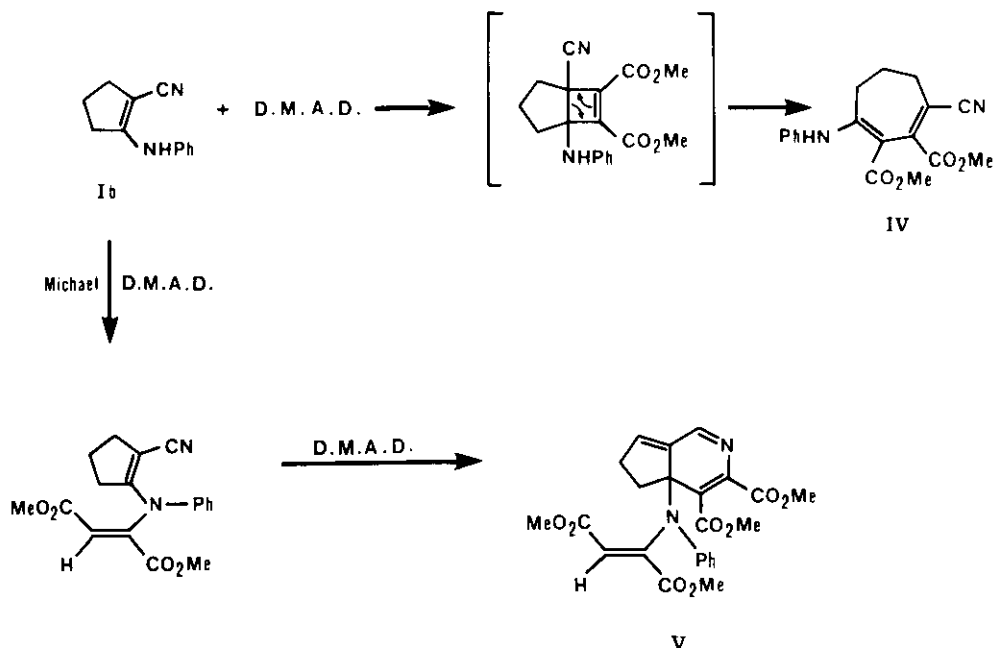
2-(N-phenylamino)-cyanocyclopentene reactivity (compound Ib)

This N-substituted enamine reacts with DMAD in methanolic solution, giving two products :

4-anilino-2,3-dicarbomethoxy-1-cyano-1,3-cycloheptadiene (IV) and 4a-N-dimethoxyfumaroylanilino-4a(H)-3,4-dicarbomethoxy[c]cyclopentenopyridine (V).

Formation of compound (IV) results from 1-2 addition of one DMAD molecule on compound (Ib) via a cyclobutene intermediary followed by cycle expansion. This kind of insertion upon enamines has been described several times³⁻⁴.

Formation of compound (V) needs two molecules of DMAD. The first step consists in a Michael addition of (Ib) on DMAD, giving an adduct identified by VPC/MS, which reacts on a second molecule of DMAD to yield compound (V).



SCHEME II

2-(N-Methyl-N-phenylamino)-cyanocyclopentene reactivity (compound Ic).

This compound reacts slowly on DMAD in refluxing methanol, yielding two products :

4-(N-Methyl-N-phenylamino)-2,3-dicarbomethoxy-1-cyano-1,3-cycloheptadiene (VI) is certainly formed via the same mechanism as (IV).

4a-(N-Methyl-N-phenylamino)-7-dimethoxyfumaroyl-4a(H)-3,4-dicarbomethoxy [c] cyclopentenopyridine (VII) results from the addition of two DMAD molecules on (Ic).

EXPERIMENTAL

Elementary analyses were performed by the microanalytical service of St-Jérôme, Marseille. Infra-red spectra were run on a Perkin-Elmer 457 spectrophotometer. Nmr spectra were recorded on a Bruker CW 80 at 80 Mhz. All syntheses were carried out using stoichiometric amounts of reagents stirred in anhydrous methanol. The formed products were separated from the reaction mixture by liquid chromatography on silica gel Merck-60 (benzene/ethyl acetate, 85-15).

Dimethyl 2-cyanocyclopentyl-N-aminofumarate (compound II)

Yield : 70% ; ir (KBr) : 3180 (chelated N-H) ; 2200 (C≡N) ; 1740 (C=O ester) ; 1670 (C=O, chelated ester) ; 1635, 1610 (C=C) ; ¹H-nmr (CDCl₃) : 9.9 (s, 1H, NH) ; 5.6 (s, 1H, CH=C) ; 3.9 (s, 3H, OCH₃-ester) ; 3.7 (s, 3H, OCH₃-ester) ; 2.8-1.8 (m, 6H, -CH₂-).

2,3-Dicarbomethoxy [b] cyclopenta-1,4-diazepine (compound III)

Yield 50% ; ir (KBr) : 3200, 3100 (N-H) ; 1740 (C=O, ester) ; 1690 (C=O, chelated ester) ; 1635 (C=C) ; ¹H-nmr (CDCl₃) : 8.0 (s, 1H, NH) ; 6.6 (d, 1H, =CH-NH, J = 1.8 Hz) ; 3.8 (s, 3H, OCH₃-ester) ; 3.2 (s, 3H, OCH₃-ester) ; 2.8-1.9 (m, 6H, -CH₂-) ; ¹³C-nmr (CDCl₃)⁵⁻⁶ : 164.22, 163.98 (C=O-esters) ; 141.13, 128.22 (2C) ; 118.13 (unprotonated ethylenic C) ; 96.14 (=CH-N) ; 53.11, 51.88 (CH₃-ester) ; 39.74, 35.86, 20.62 (-CH₂-).

4-Anilino-2,3-dicarbomethoxy-1-cyano-1,3-cycloheptadiene (compound IV)

Yield 35% ; ir (KBr) : 3200 (N-H) ; 2800 (C-H) ; 2220 (conjugated C≡N) ; 1740 (C=O-ester) ; 1670 (C=O-chelated ester) ; ¹H-nmr (CDCl₃) : 11.4 (s, 1H, NH) ; 7.3 (m, 5H, C₆H₅) ; 3.8 (s, 3H, OCH₃-ester) ; 3.7 (s, 3H, OCH₃-ester) ; 2.7-2.0 (m, 6H, -CH₂-) ; ¹³C-nmr (CDCl₃) : 168.28, 165.03 (C=O-esters) ; 146.97, 138.21 (unprotonated ethylenic C) ; 129.77, 127.12, 125.30 (aromatic C) ; 118.68 (CN) ; 113.48, 93.67 (unprotonated ethylenic C) ; 52.52, 51.15 (CH₃-esters) ; 34.04, 30.93, 27.56 (-CH₂-).

4a-N-Dimethoxyfumaroylanilino-4a(H)-3,4-dicarbomethoxy [c]cyclopentenopyridine (compound V)

Yield 20% ; ir (KBr) : 3310, 3025, 2840 (C-H) ; 1750, 1745, 1728, 1725 (C=O-esters) ; 1645, 1605 (C=C), (C=N) ; ¹H-nmr (CDCl₃) : 7.1 (m, 5H, -C₆H₅) ; 7.0 (s, 1H, CH=N) ; 6.8 (s, 1H, CH=C) ; 5.6 (t, 1H, cyclic CH=C) ; 3.8 (s, 3H, OCH₃-ester) ; 3.8 (s, 3H, OCH₃-ester) ; 3.6 (s, 3H, OCH₃-ester) ; 3.6 (s, 3H, OCH₃-ester) ; 2.8-2.4 (m, 4H, -CH₂-) ; ¹³C-nmr (CDCl₃) : 165.31, 165.17, 164.40, 163.94 (C=O esters) ; 145.96, 142.27, 141.49, 120.09 (unprotonated ethylenic C) ; 133.10 (CH=N) ; 124.79, 124.29, 122.06 (ethylenic C) ; 122 (protonated fumaroyl C) ; 52.70, 52.06, 51.74 (CH₃-esters) ; 49.73 (head bridged C) ; 41.34, 28.06 (-CH₂-).

4-(N-Methyl-N-phenylamino)-2,3-dicarbomethoxy-1-cyano-1,3-cycloheptadiene (compound VI)

Yield 20% ; ir (KBr) : 2960 (C-H) ; 2213 (conjugated C≡N) ; 1735, 1710 (C=O-esters) ; 1605 (C=C) ; ¹H-nmr (CDCl₃) : 7.2 (m, 5H, -C₆H₅) ; 3.7 (s, 3H, OCH₃-ester) ; 3.6 (s, 3H, OCH₃-ester) ; 3.2

(s, 3H, N-CH₃) ; 2.6, 1.8 (m, 6H, -CH₂-).

4a-(N-Methyl-N-phenylamino)-7-dimethoxyfumaroyl-4a(H)-3,4-dicarbomethoxy [c] cyclopentenopyridine (compound VII)

Yield 45% ; ir (KBr) : 2965 (C-H) ; 1735, 1730, 1725, 1720 (C=O, esters) ; 1650 (C=C) ; ¹H-nmr (CDCl₃) : 7.2-6.7 (m, 5H, -C₆H₅) ; 6.6 (s, 1H, C=C-H) ; 6.3 (s, 1H, C=C-H) ; 3.8 (s, 3H, OCH₃-ester) ; 3.7 (s, 3H, OCH₃-ester) ; 3.6 (s, 3H, OCH₃-ester) ; 3.5 (s, 3H, OCH₃-ester) ; 3.0 (s, 3H, N-CH₃) ; 3.1-2.6 (m, 4H, -CH₂-) ; ¹³C-nmr (CDCl₃) : 165.81, 165.50 (2C), 165.13 (C=O ester) ; 147.56 ; 143.00 ; 139.10 ; 138.76 (unprotonated ethylenic C) ; 129.08 (aromatic C, para) ; 128.49, 119.50 (aromatic C, ortho/meta) ; 128.76 (CH-N) ; 121.78 (protonated fumaroyl C) ; 119.91 (unprotonated ethylenic C) ; 52.79, 52.56, 52.38, 52.19 (CH₃-esters) ; 50.69 (head bridged C) ; 38.69, 36.55 (cyclic -CH₂-, CH₃-N) ; 32.58 (cyclic CH₂).

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