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AROMATIC RING SYNTHESIS BY N-AMINOPYRROLE DIELS-ALDER REACTION. CHARACTERIZATION OF THE HETEROATOM FRAGMENT

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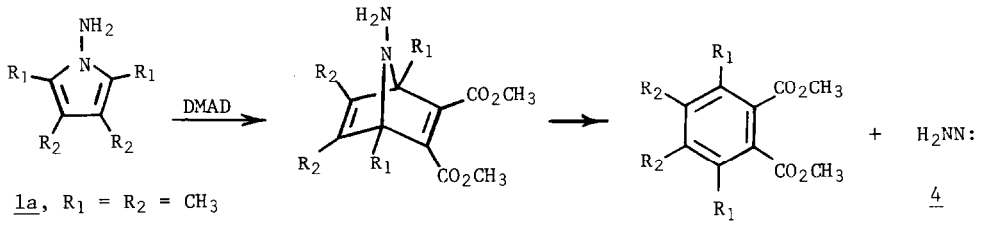
Aminonitrenes are produced on reaction of N-aminopyrroles with dimethyl acetylenedicarboxylate; a new reaction of dialkyl aminonitrenes is described.

Recently, we reported the utilization of N-aminopyrroles in a Diels-Alder based substituted benzene ring synthesis; e.g., 1 → 2 → 3.[1] In this note, we describe chemistry observed for the heteroatom fragment extruded in this process.



1a, $R_1 = R_2 = CH_3$
b, $R_1 = CH_3$; $R_2 = H$

2

3

4

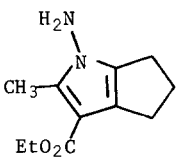
On heating 1a or 1b with 3 equiv of dimethyl acetylenedicarboxylate (DMAD) in refluxing chloroform solution, benzene derivatives 3a or 3b are formed in good yield[1] together with dimethylmaleate (^{1}H NMR and GC analysis). The production of dimethylmaleate in reactions of N-aminopyrroles with DMAD seems to be general. Furthermore, the species responsible for DMAD reduction also undergoes competitive reaction with simple olefins. This was demonstrated with N-aminopyrrole 5, which on reaction with excess DMAD gave the benzene derivative[1] and dimethylmaleate in a ratio of 4:1, repsectively. When this experiment was repeated in the presence of

norbornylene (2 equiv) or cyclohexene (solvent), dimethylmaleate was absent from the reaction mixture.

These data suggest that diimide is produced in the reaction of N-aminopyrroles with DMAD. A reasonable mechanism for diimide formation would involve decomposition of the N-aminopyrrole-DMAD adduct to give aminonitrene 4,[2] which rearranges to diimide. In the presence of highly reactive olefins[3] diimide reduction of DMAD should be retarded. Our data, however, do not allow us to differentiate between diimide and aminonitrene 4 as the actual reducing species.[3b]

Aminonitrenes (diazenes) have been proposed as intermediates in a variety of hydrazine-based reactions, the most notable of which include the oxidation of 1,1-disubstituted hydrazines and the thermal decomposition of 1,1-disubstituted 2-sulfonylhydrazine salts. Using such methods, 1,1-dibenzylaminonitrene has been generated; subsequent elimination of N_2 gives bibenzyl.[4a] In accord with the N-aminopyrrole → aminonitrene supposition, treatment of N,N-dibenzylaminopyrrole 6 with excess DMAD in refluxing m-dichlorobenzene solution gives benzene derivative 3b and bibenzyl in isolated yields of 51 and 20%, respectively.

We have discovered what seems to be a previously unreported reaction of dialkylaminonitrenes. Treatment of 7a with DMAD (3 equiv, $CHCl_3$, 25°C, 2 hr) results in formation of 3a (80%) and 1-methyl-3,4-dimethoxycarbonyl-2-pyrazoline 8 (43% isolated yield). In similar fashion, 7b gives 3a (87%) and pyrazoline 10 (30%).[5] Pyrazoline 8 was characterized by dehydrogenation (NiO_2)[6] to the known 1-methyl-3,4-dimethoxycarbonylpyrazole (9).[7]



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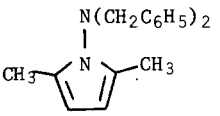

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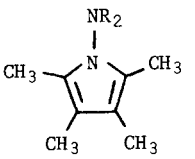
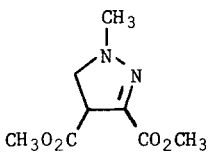


7a, R = CH_3
b, R = $CH_2CH_2OCH_2CH_2$
c, R = $CH_2CD_2OCD_2CH_2$



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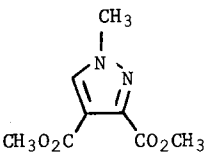

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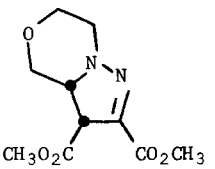

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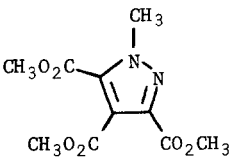

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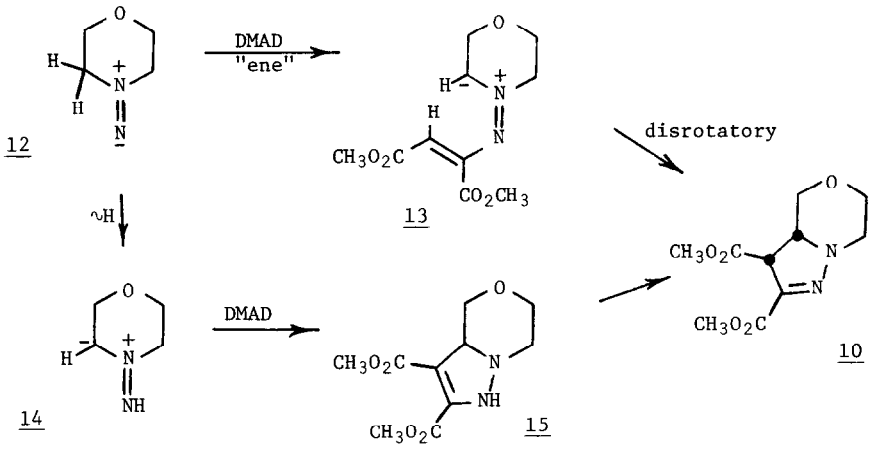
With regard to the mechanism of pyrazoline formation, we now consider two interesting possibilities[8] illustrated in Scheme 1 with morpholinonitrene (12). An "ene" reaction of 12 with DMAD would generate ylide 13 which would be expected to undergo thermal, disrotatory electrocyclization to 10.[9] Alternatively, rearrangement of 12 to azomethinimine 14 and cycloaddition of 14 to DMAD would give 15; tautomerization of 15 might then give pyrazoline 10.

Scheme 1



Azomethinimines have been proposed as intermediates in the diazene → hydrazone rearrangement.[4b] Studies by others indicate that tautomerization of diazenes to hypothetical azomethinimines requires a protic reaction medium; tetrazines rather than hydrazones are obtained under aprotic conditions.[4b] Hydrazones have not been detected in reactions of 7 with DMAD (even under protic solvent conditions), and we find that treatment of 1,1,4,4-tetramethyltetrazine[10] with DMAD gives dimethyl 2-dimethylaminomaleate (30%, mp 82-83°C)[11] rather than 8. Furthermore, if 14 is involved in the formation of 10, then tautomerization of 15 to cis-dihydro 10 is noteworthy.[5] On the other hand, recent spectroscopic studies of a 1,1-dialkylaminonitrene indicate that there is considerable double bond character in the nitrogen-nitrogen bond.[12] These observations lend support to the "ene" proposition; however, further experiments are required before a more definitive mechanism can be advanced.

Pyrazoline formation resulting from DMAD addition to N-aminopyrroles is potentially much more efficient than suggested by experiments already discussed.[13] Unfortunately, 3,4-dimethoxycarbonyl-2-pyrazolines 8 and 10 react with DMAD to give pyrazoles; e.g., 8 → 11. This novel formation of 11 and related pyrazoles is discussed in the following note.

Acknowledgment

This work was supported by the National Institutes of Health Grant GM 26568 and CA 25787.

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2. Some years ago L. A. Carpino found that certain N-amino-7-azanorbornadiene derivatives thermally lose the nitrogen bridge to give an aromatic ring (private communication to D. M. Lemal in reference 4b). In more recent and independent work by Carpino, the ejected species was found to have reducing properties (private communication from L. A. Carpino).
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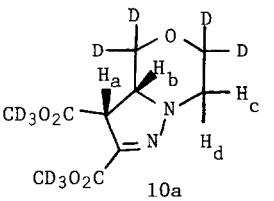
5. Stereochemistry of 10 was determined by ^{1}H NMR analysis ($CDCl_3$) of the decadeutero derivative 10a prepared from hexadeutero-DMAD and 7c; H_a and H_b appear as doublets at δ 4.20 and 3.98 ppm (J_{ab} = 12 Hz), while H_c and H_d appear as doublets at δ 3.85 and 3.42 (J_{cd} = 14 Hz). In methanol with suspended sodium carbonate, 10a undergoes clean epimerization to the trans-dihydro isomer; H_c and H_d appear as a pair of doublets (J_{cd} = 14 Hz), while H_a and H_b appear as overlapping signals at δ 4.2-4.4 ppm. Thus, 7b must be converted to 10 by a kinetically determined process. For NMR data on analogous systems, see reference 9a and references cited therein.



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7. K. T. Potts and V. P. Singh, Chem. Commun., 66 (1969).
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9. For analogous electrocyclizations, see (a) T. Sasaki, K. Kanematsu, and A. Kakehi, J. Org. Chem., 37, 3106 (1972); (b) J. Elguero, Bull. Soc. Chim. France, 1925 (1971).
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13. Attempts to generate aminonitrene 12 in the presence of DMAD by thermal decomposition of the 2-sulfonylhydrazine sodium salt or by hydrazine oxidation did not give pyrazoline 10; addition of the reagent to DMAD to give the hydrazone of dimethyl oxalacetate was observed under these reaction conditions.

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