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CYCLOADDITION OF DIETHYLAMINOPROPYNE ACROSS AMIDE CARBONYL GROUPS

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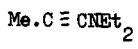
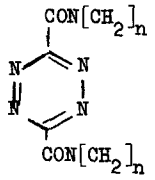
The preparation of pyridazines by Diels-Alder addition of ynamines to 1,2,4,5-tetrazines, followed by extrusion of nitrogen, has been described by several authors[1,2]. When 1-diethylaminopropyne (1) and the 1,2,4,5-tetrazine-3,6-dicarboxamides (2, n=4 and 5) were dissolved together in chloroform at room temperature the expected pyridazines (3, n=4 and 5) were obtained together with orange-red 1:1 adducts that had not lost nitrogen. The products, which were formed in roughly equal amounts, were readily separated by chromatography (alumina-ethyl acetate).

The n.m.r. spectra of the red compounds, unlike those of the pyridazines (3), showed non-equivalence of the N-ethyl groups; one CH_2 gave a quartet and the other a multiplet, the multiplicity being due to non-equivalence of the geminal protons and coupling to the methyl group, i.e. an ABX_3 pattern. Two triplets were observed for the terminal CH_3 groups. On raising the temperature of a pyridine solution to ca. 115° the non-equivalence disappeared and a normal quartet and triplet were observed. These results are indicative of a diethylamide group, and the structure (4) is consistent with the colour and analytical and spectroscopic data. Details are given in the Table.



(1)



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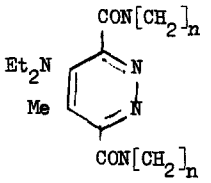

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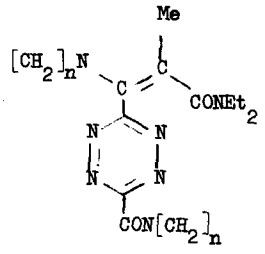

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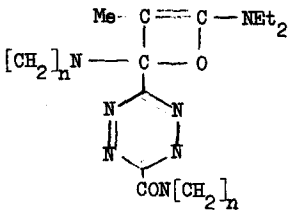

(5)

The new tetrazines (4) must be produced by cycloaddition of the ynamine across an amide carbonyl group and subsequent fission of the intermediate (5). Similar additions of ynamines across carbonyl groups of aldehydes and ketones[3], ketenes[4], and isocyanates[5] and across carbon dioxide[6] have been reported. No reaction was observed between (1) and N-benzoylpiperidine, and from (1) and 1,2,4,5-tetrazine-3,6-dicarboxy-n propylamide only the pyridazine was formed. The tetrazines (2, n=4) (m.p. 215-216°) and the dipropylamide (too unstable to be purified) were made by the standard method[7] from ethyl diazoacetate and pyrrolidine or n-propylamine with oxidation of the intermediate dihydrotetrazines, m.p. 218-219° and 307-308°, with nitrous acid in acetic acid and with nitrous fumes in dichloromethane respectively. The tetrazines (4) did not react further with (1) at room temperature, either because of steric restraints imposed by the extended conjugated system or because the tetrazine nucleus is no longer as electron-deficient as that in (2).

Table - ^{1}H n.m.r. Data

Compound	m.p.	Chemical shifts (p.p.m.) in $CDCl_3$ with Me_4Si as internal standard				
		Piperidine or pyrrolidine α-protons	NCH_2CH_3	CH_3	remaining piperidine or pyrrolidine protons	NCH_2CH_3
(3, n=4)	126-127.5°	4.0-3.2(m,8H)	3.2(q,4H)	2.3(s,3H)	1.95(m,8H)	1.1(t,6H)
(3, n=5)	106-107	3.8(m,4H), 3.3(m,4H)	3.15(q,4H)	2.25(s,3H)	1.65(m,12H)	1.1(t,6H)
(4, n=4)	126-128	4.2-3.4(m,8H)	3.4-2.7 ($q+ABX_3$,4H)	2.0(s,3H)	1.95(m,8H)	1.05(2t,6H)
(4, n=5)	90-91	4.0-3.6(m,8H)	3.5-2.6 ($q+ABX_3$,4H)	1.95(s,3H)	1.7-1.6(m,12H)	1.05(2t,6H)

Spectra were recorded with ca. 10% solutions on a Varian A60 or a Perkin Elmer R12 spectrometer.

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