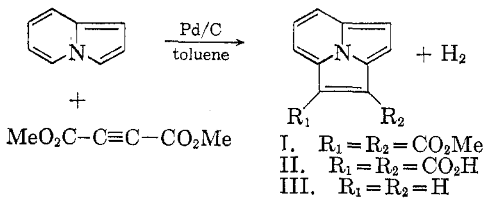
Reaction of Dimethyl Acetylenedicarboxylate with Pyrrocoline

Sir:

The Diels-Alder condensation is an important synthetic procedure for the formation of six-membered rings. A consideration of possible mechanisms[1a,b,c] for the Diels-Alder reaction would suggest that the formation of five- and seven-membered rings should be possible. We have now found that the reaction of pyrrocoline with dimethyl acetylenedicarboxylate under dehydrogenation conditions provides an interesting example of the formation of a five-membered ring and offers an exceptionally direct method for the synthesis of cycl[3,2,2]azine derivatives.[2]

In their studies on the reaction of various heterocyclic amines with dimethyl acetylenedicarboxylate, Diels and his co-workers discovered a series of interesting products which were formulated in a rather unusual fashion.[3] However, apparently because of its unavailability, pyrrocoline was not investigated. Recently, Godfrey observed that the reaction of 1,2,6,7-dibenzopyrrocoline with dimethyl acetylenedicarboxylate in the presence of a dehydrogenation catalyst gave a product corresponding to a 1:1 adduct with loss of hydrogen.[4] That addition had occurred across the 3 and 5 positions of the pyrrocoline ring to give a cycl[3,2,2]azine derivative was suggested by a comparison of the ultraviolet absorption spectrum of the adduct with known cycl[3,2,2]azine derivatives.[2] This hypothesis has now been verified for the case of pyrrocoline itself where the adduct (I) has been degraded to the parent heterocycle (III).



I. $R_1 = R_2 = CO_2Me$
II. $R_1 = R_2 = CO_2H$
III. $R_1 = R_2 = H$

Treatment of pyrrocoline[5] with dimethyl acetylenedicarboxylate in boiling toluene using a 5% palladium-on-charcoal catalyst afforded a dark crystalline solid which, after chromatography over alumina with benzene as solvent, gave I as yellow prisms, m.p. 91–92° (Found: C, 65.45; H, 4.31; N, 5.57), in 50–66% yield. Hydrolysis of this diester in methanolic potassium hydroxide followed by acidification yielded the corresponding acid II as yellow crystals, m.p. > 320° (Found: C, 62.77; H, 3.21; N, 6.17) in essentially quantitative yield. Decarboxylation of II proceeded in 70–80% yield using copper chromite in quinoline to cycl[3,2,2]-azine (III), whose identity was proved by mixture melting point and infrared spectral comparison with an authentic sample.[2]

In addition to I, a second substance was obtained from the chromatogram as colorless crystals, m.p. 180–180.5° (Found: C, 64.48; H, 5.07; N, 5.50), in 10–15% yield. Although the structure of this product has not yet been established, its composition would suggest that it is the result of a simple substitution reaction of the type well known for pyrrole.[6]

The possible extension of this method using dienophiles other than dimethyl acetylenedicarboxylate as well as nuclei other than pyrrocoline is under investigation.

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[1] (a) C. K. Ingold, *Structure and Mechanism in Organic Chemistry*, Cornell University Press, Ithaca, N. Y., 1953, p. 711; (b) C. Walling and J. Peisach, *J. Am. Chem. Soc.*, **80**, 5819 (1958); (c) R. B. Woodward and T. J. Katz, *Tetrahedron*, **5**, 70 (1959).

[2] (a) R. J. Windgassen, Jr., W. H. Saunders, Jr., and V. Boekelheide, *J. Am. Chem. Soc.*, **81**, 1459 (1959); (b) V. Boekelheide and R. J. Windgassen, Jr., *J. Am. Chem. Soc.*, **80**, 2020 (1958).

[3] See O. Diels and H. Schrum, *Ann.*, **530**, 68 (1937) for leading references.

[4] J. C. Godfrey, *J. Org. Chem.*, **24**, 581 (1959). We are indebted to Dr. Godfrey for disclosing his observations to us at an early stage and for subsequent suggestions and stimulating informal discussions.

[5] V. Boekelheide and R. J. Windgassen, Jr., *J. Am. Chem. Soc.*, **81**, 1456 (1959).

[6] O. Diels, K. Alder, H. Winckler, and E. Petersen, *Ann.*, **498**, 1 (1932) and earlier papers.

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