1,3-Dipolar Cyclo-additions of Mesoionic Compounds: Cyclizations utilizing Precursors to the Mesoionic Systems

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1,3-DIPOLAR cyclo-additions with mesoionic ring systems have been described in the literature.[1] The mesoionic compounds studied were usually prepared by cyclo-dehydration of appropriately substituted carboxylic acids with agents such as acetic anhydride. Competing reactions and poor yields in these cyclizations often made the preparation of the mesoionic compounds difficult.[2] It would be a particular advantage, therefore, to effect these 1,3-dipolar cyclo-additions utilizing the precursors of the *mesoionic* ring systems, the appropriate dipolarophiles, and acetic anhydride. Indications of the likely success of this approach were found in the report that *N*-acyl-*N*-alkyl- or *N*-aryl-α-amino-acids, dimethyl acetylenedicarboxylate, and acetic anhydride gave the same pyrroles as were obtained from the corresponding anhydro-5-hydroxyoxazolium hydroxides and the acetylenic ester.[3]

We now describe the ready formation of cyclo-addition products utilizing the precursors of several mesoionic ring systems. This more direct method offers a very convenient route to substituted pyrroles and pyrazoles and should be capable of adaptation to the preparation of other ring systems.

Reaction of *N*-benzoylsarcosine[4] (I; X = O) (the precursor of the unknown anhydro-5-hydroxy-3-methyl-2-phenyloxazolium hydroxide) and dimethyl acetylenedicarboxylate in the presence of acetic anhydride gave, after an initial exothermic reaction and warming for 1 hr. at 125—130°, a 68% yield of dimethyl 1-methyl-2-phenyl pyrrole-3,4-dicarboxylate (II) [m.p. 118—119° (lit.[5] m.p. 117—118°)]. This same product was also obtained in 78% yield from *N*-thiobenzoylsarcosine[6] (I; X = S) (the precursor of anhydro-5-hydroxy-3-methyl-2-phenylthiazolium hydroxide) and dimethyl acetylenedicarboxylate under analogous conditions. In the former reaction, carbon dioxide was identified as the effluent gas and in the latter reaction, carbonyl sulphide was evolved. This indicates that the mesoionic compound was probably involved as an intermediate and that cyclo-addition to the dimethyl acetylenedicarboxylate occurred faster than the competing acetylation of the 4-position of the mesoionic system. Similarly, reaction of (I; X = O or S) with ethyl propiolate† gave ethyl 1-methyl-2-phenylpyrrole-3-carboxylate (III; R = H) in *ca.* 30% yield‡ [colourless plates, m.p. 49—50°, ν_{max} (Nujol) 1710 (C=O) cm.$^{-1}$, λ_{max} (MeOH) 203, 220, and 273 mμ (log ε 4·26, 4·07, and 3·79); n.m.r. ($CDCl_3$) τ 9·02, 8·90, 8·78 (t, 3, *J* 7·0 Hz, CH_3 of Et), 6·55 (s, 3, N–CH_3), 6·05, 5·93, 5·82, 5·70, (q, 2, *J* 7·0 Hz, ·CH_2· of Et), 3·39, 3·34 (AB, d, 1, *J* 2·25 Hz, 4-H), 3·30, 3·25 (AB, d, 1, *J* 2·25 Hz, 5-H), 2·59 (s, 5, phenyl); *m/e* 229 (33% M^+)].

When ethyl phenylpropiolate[7] was used as the dipolarophile, ethyl 2,4-diphenylpyrrole-3-carboxylate (III; E=Ph) was obtained in *ca.* 30% yield [colourless needles, m.p. 84—85°, ν_{max} (Nujol) 1700 (C=O) cm.$^{-1}$, λ_{max} (MeOH) 203, 222, and 280 mμ (log ε 5·57, 5·34, and 3·98); n.m.r. ($CDCl_3$) τ 9·27, 9·15, 9·03 (t, 3, *J* 7·0 Hz, CH_3 of Et), 6·57 (s, 3, N–CH_3), 6·22, 6·11, 5·99, 5·86 (q, 2, *J* 7·0 Hz, ·CH_2· of Et), 3·34 (s, 1, 5-H), 2·60 (s, 10, phenyl); *m/e* 305 (100% M^+)].

Reaction of *N*-nitrososarcosine (IV) (the precursor of 3-methylsydnone) with dimethyl acetylenedicarboxylate and acetic anhydride at 120—130° for 1 hr. gave a 60% yield of dimethyl 1-methylpyrazole-3,4-dicarboxylate (V) [colourless needles, m.p. 68–69°, ν_{max} (Nujol) 1745 (C=O) cm.$^{-1}$; λ_{max} (MeOH) 198 and 224 mμ (log ε 4·35 and 4·06); n.m.r. ($CDCl_3$) τ 6·13 (s, 3, N-CH_3), 6·03 (s, 3, 4-CO_2CH_3), 6·00 (s, 3, 3-CO_2OCH_3), 2·09 (s, 1, 5-H); *m/e* 198 (90% M^+)].

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† Two isomeric products are possible from the reaction of these dipolarophiles. One product only was always obtained and structural assignments were made mainly on the basis of their compatability with the observed n.m.r. spectral data.

‡ All products obtained gave satisfactory analytical data and their mass-spectral fragmentation patterns were consistent with the assigned structures.

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