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SYMMETRICAL PYRROMETHANES FROM PYRROLE NITRATIONS

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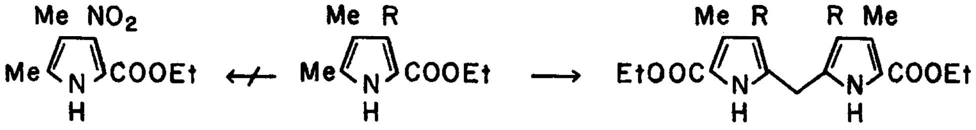
The nitration of pyrroles by a variety of reagents is well documented[2] and proceeds by attack on free positions as well as through the elimination of selected substituents. We now report the first example of the coupling of pyrroles during attempted nitrations.

Numerous examples[3] of non-conventional electrophilic aromatic substitutions have been observed in which substitution occurs at an alkyl side chain. In several instances[4] these substitutions have also resulted in the formation of diphenylmethanes. When applied to α-methylpyrroles, such coupling reactions have in certain instances[5,6] yielded symmetrical pyrromethanes directly, presumably through α-methyl substituted intermediates.[7] However, heretofore, such couplings of pyrroles have not been observed under nitration conditions.

In an attempt to nitrate ethyl 4,5-dimethylpyrrole-2-carboxylate (I, R = H), the pyrrole was added to ice-cold nitric acid-acetic anhydride (acetyl nitrate). However, diethyl 3,3'-dimethyl -2,2'-pyrromethane-5,5'-dicarboxylate (II, R = H) was isolated in a 28% yield instead.



I

II

The structure of the pyrromethane,[6] mp 188.5-9°, was confirmed by a satisfactory combustion analysis and the spectral data: ir (KBr) 3400 (NH) and 1720 cm^{-1} (C=O); pmr (DMSO-d_6) δ 1.25 (t, J = 7 Hz, 6H, ester CH$_3$'s), 1.94 (s, 6H, C-3 and C-3' CH$_3$'s), 3.81 (s, 2H, bridge CH$_2$), 4.21 (q, J = 7 Hz, ester CH$_2$'s), 6.50 (d, J = 3 Hz, 2H, C-4 and C-4' CH's), and 11.4 ppm (broad, 2H, NH's). Furthermore, the corresponding iodopyrrole, ethyl 4,5-dimethyl-3-iodopyrrole-2-carboxylate[8] (I, R = I), in fuming nitric acid also yielded a pyrromethane (II, R = I) (mp 212-4°) rather than undergo substitution of iodine by the nitro group.

The generality of this new coupling procedure was further demonstrated by the treatment of a fully substituted pyrrole with nitric acid. A 90 mg sample of ethyl 3,4,5-trimethylpyrrole-2-carboxylate was added in portions to 2 ml of ice-cold conc. nitric acid. The solution was stirred for 10 minutes at 0° and then poured into water. The solid was collected and crystallized from aqueous ethanol to give 56 mg (65%) of diethyl 3,3',4,4'-tetramethyl-2,2'-pyrromethane-5,5'-dicarboxylate (II, R = CH_3), mp 196-8° (lit.[5] mp 196-7°). The yield of product, which was twice that obtained by the bromination procedure,[5] suggests that this reaction may be the preferred method for the preparation of selected symmetrical pyrromethanes.

Although no intermediates were detected, an α-nitromethyl function is strongly implicated. Such an α-substituted intermediate would be consistent with other examples of pyrromethane formation. At least one example of preferential nitration at an alkyl side group attached to a heterocycle is known. In that case Bordwell[9] treated 2,3-dimethylthianaphthalene with acetyl nitrate in acetic anhydride and obtained among other products the 2-nitromethyl derivative. Work in this area is continuing.

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References and Notes

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