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REACTION OF 2-BENZAMIDO-2-BENZYLTHIOPROPANOIC ACID WITH N-CHLOROSUCCINIMIDE

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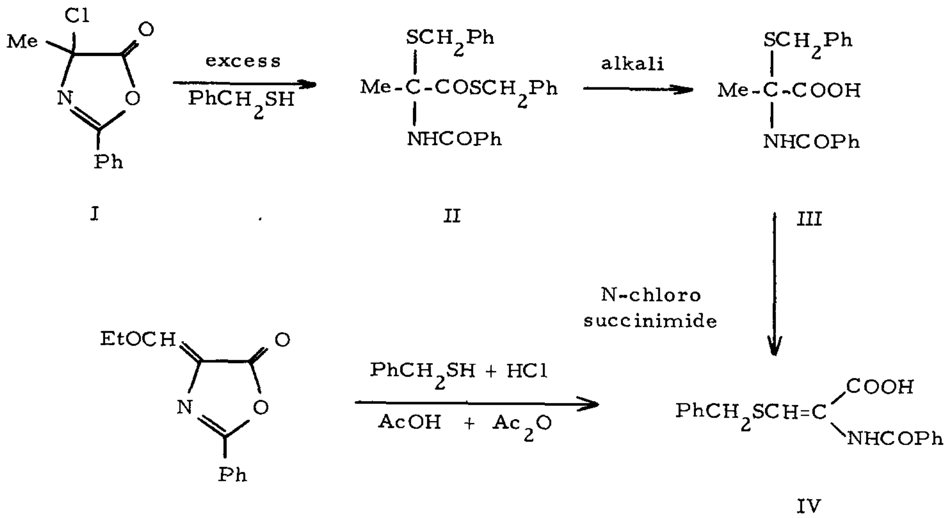
4-Methyl-2-phenyl-2-oxazolin-2-one is readily chlorinated by sulphuryl chloride to give the chloro-oxazolinone (I), from which the chlorine may be displaced by suitable nucleophiles[2]. With α-toluenethiol, the ring is also attacked and S-benzyl 2-benzamido-2-benzylthiopropanethioate (II)[3] is formed in high yield. The thiolester is smoothly hydrolysed by dilute aqueous caustic soda containing catalytic amounts of α-toluenethiol to give the 2-benzamido-2-benzylthiopropanoic acid (III)[3], m.p. 132-134°, in 67% yield. The structure was confirmed by infrared and p.m.r. spectroscopy and by an alternative synthesis of the methyl ester by benzylation of methyl 2-benzamido-2-mercaptopropanoate, the preparation of which is described in the accompanying communication[2].

In surveying the available methods for removing a benzyl protecting group from sulphur, we reacted the acid (III) with N-chlorosuccinimide in the expectation that an α-chlorosulphide would be formed and would be sensitive to hydrolysis under very mild conditions[4]. When the reactants were dissolved in warm benzene and left for two hours, a colourless acid, m.p. 201-202°, was deposited in 71% yield. Microanalysis and mass spectrometry showed that the compound, $C_{17}H_{15}NO_3S$, was derived by oxidation of the acid (III). The infrared spectrum confirmed the presence of carboxylic acid (2650-2500 and 1705 cm^{-1}) and benzamido groups (3255 and 1655 cm^{-1}). In the p.m.r. spectrum, no signal attributable to methyl protons was observed, and the methylene group of the benzylthio moiety gave rise to two singlets at 4.09 and 4.21 p.p.m. with areas in the ratio 2:1. The region 7.2-8.2 p.p.m. contained signals of total area equivalent to twelve protons, reduced to eleven by D_2O exchange. On this evidence we formulated the product as a mixture of cis-trans isomers of 2-benzamido-3-benzylthioacrylic acid (IV). An authentic sample of this compound, prepared as shown by the method of Cornforth[5], was a single isomer and had properties identical (thin layer chromatography, p.m.r.) with those of the major isomer obtained from the rearrangement. Because of the small differences observed in the p.m.r. spectra of the isomers (IV), and some controversy in the recent literature[6] we have deferred the assignment of a particular structure to this isomer for closer study. The identification was consolidated by comparison of the methyl esters formed with diazomethane by the authentic acid and the major rearrangement product.

The mechanism of the reaction is unknown. The carboxyl group appears to be implicated since the methyl ester of acid (III) reacts with N-chlorosuccinimide only to give a tarry mixture in which none of the ester of (IV) could be detected by thin layer chromatography. Nor is the acid (IV) produced by a separate reaction between toluene sulphenyl chloride and 2-benzamidoacrylic acid. We have undertaken a study of the reaction of less complex molecules with N-chlorosuccinimide in an attempt to identify the site of initial attack.

REFERENCES

1. This work was supported by a grant (No. C68/16899) from the Australian Research Grants Committee to Dr. F. W. Eastwood and I.D.R.
2. P. M. Pojer and I. D. Rae, accompanying communication
3. The formula was established by appropriate microanalytical data.
4. D. L. Tuleen, J. Org. Chem., **32**, 4006 (1967).
5. J. W. Cornforth, in "The Chemistry of Penicillin", p.819 (ed. H.T. Clarke et al.) Princeton University Press, 1949.



REFERENCES (continued)

6. R. Filler, Adv. Heterocyclic Chem., 4, 96 (1965); A.G. Brown and T.C. Smale, Chem. Commun., 1489 (1969); A. P. Morgenstern, C. Schutij and W. Th. Nauta, Chem. Commun., 321 (1969); K. Brocklehurst, H.S. Price and K. Williamson, Chem. Commun., 884 (1968).