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THE ADDITION OF 2,4,6-TRINITROPHENOL TO N,N-DICYCLOHEXYL CARBODIIMIDE

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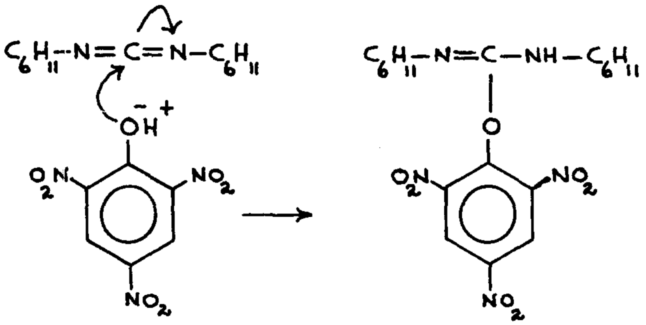
During attempts to synthesise the 2,4,6-trinitrophenyl esters of N-tritylglycine and carbobenzyloxy-L-phenylalanine via the carbodiimide procedure[1], a bright-yellow crystalline substance was obtained in both cases which on analysis and mass-spectrometry proved to be the 2,4,6-trinitrophenyl pseudourea ether of dicyclohexylcarbodiimide. No evidence of formation of the desired aminoacid esters was obtained. This finding prompted us to study the interaction of 2,4,6-trinitrophenol with dicyclohexylcarbodiimide, and the results of such study are herein reported.

N,N-dicyclohexyl-O-2,4,6-trinitrophenyl pseudourea ether (1) :- To a solution of 2,4,6-trinitrophenol (0.290 g., 0.126 mmoles) in ethyl acetate (2.5 ml.) was added a solution of dicyclohexylcarbodiimide (0.248 g., 1.2 mmoles) in 0.5 ml. of ethyl acetate. A small amount of white crystalline material separated immediately. The reaction mixture was allowed to stand for 2.5 hours at room temperature. The insoluble crystalline material was removed by filtration (Fraction A), and the clear yellow filtrate evaporated to dryness to give a pale yellow oil which crystallised on trituration with ether (Fraction B).

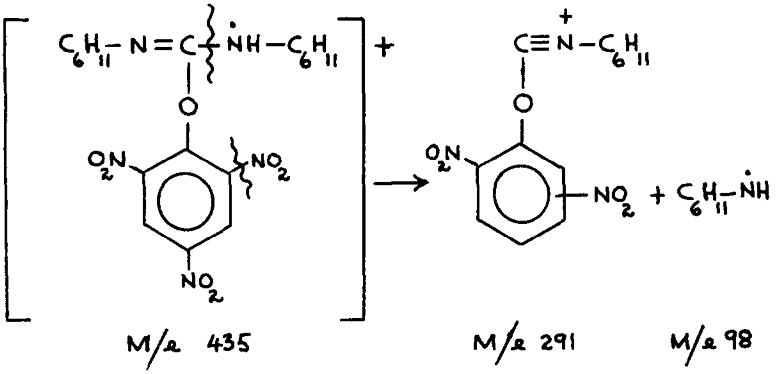
Fraction A :- Crystallisation from ethanol gave white blades identified as dicyclohexylurea (0.044 g., 0.17 mmoles) m.p., 223-224°, m.w. 224 (mass spectrometry), ν_{max} (KBr) 3330, 2920, 1630 and 1580 cm^{-1}.

Fraction B :- Recrystallisation from isopropanol and washing with ether gave bright-yellow needles of (1) (yield 46%, after recrystallisation) m.p., 207-210°, shrinkage at 203°, m.w., 435 (mass-spectrometry), λ_{max} (EtOH) 215 mμ(ε, 22,200), ν_{max} (KBr) 3315, 3080, 2925, 2850, 1650, 1612, 1555 and 1355 cm^{-1}. (Found :- C, 52.67; H, 6.10; N, 15.98. $C_{19}H_{25}O_7N_5$ requires :- C, 52.41; H, 5.74; N, 16.09%.)



(1)

Fragmentation of (1) by means of mass spectrometry[2] gave besides the parent peak (M/e 435) a strong peak of M/e 291 and further peaks including one at M/e of 98, supporting the following breaking pattern :-



Experiments with protected amino acids :- Reaction between carbobenzyloxy-L-phenylalanine (0.328 g., 1.1 mmoles), 2,4,6-trinitrophenol (0.290 g., 0.126 mmoles) and dicyclohexylcarbodiimide (0.248 g., 1.2 mmoles) in ethyl acetate (4.5 ml.) at room temperature for 2.5 hours produced a 55% yield of N,N-dicyclohexyl-O-2,4,6-trinitrophenyl pseudourea ether (1). Similar results were obtained using N-trityl glycine.

Khorana[3] has described the preparation of N,N-di-p-tolyl-O-alkyl pseudourea ethers via the alkoxide catalysed addition of alcohols to di-p-tolylcarbodiimide. He has also shown that addition does not take place with dicyclohexylcarbodiimide. With respect to other phenols, it has been shown that p-nitrophenol does not add to dicyclohexylcarbodiimide under the conditions of our experiments[1,4].

N,N-dicyclohexyl-O-2,4,6-trinitrophenyl pseudourea ether (1) is stable under acidic conditions, but rapidly decomposed by alkali, triethylamine and diethylamine into intensely coloured products. These reactions are at present under investigation and will be reported at a later date.

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