New Method for Converting Thioamides into Nitriles: Use of Diethyl Azodicarboxylate and Triphenylphosphine

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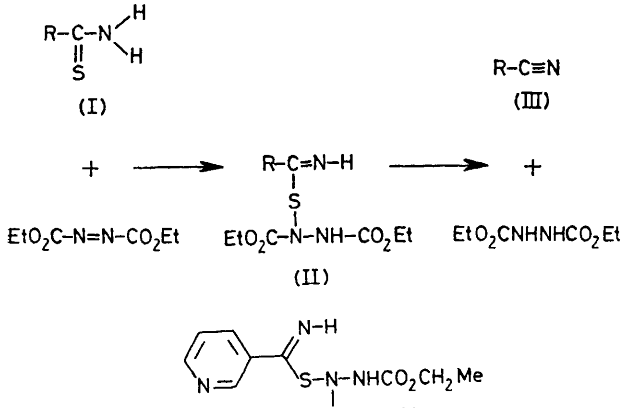
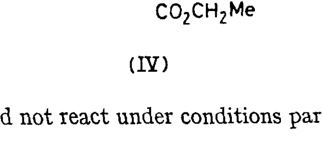
Summary Primary thioamides are transformed by diethyl azodicarboxylate and triphenylphosphine into nitriles.

Diethyl azodicarboxylate together with triphenylphosphine converts thioureas into carbodi-imides,[1] secondary thioamides into ketenimines,[2] and formamides into isonitriles.[3] The reagent combination is now found to be effective at room temperature in transforming primary thioamides into nitriles. This new method complements other procedures which require treatment of thioamides with either dichlorocarbene,[4] or triphenylphosphine, carbon tetrachloride, and triethylamine in concert.[5] Moreover it is apparently specific for thioamides,† unlike the aforementioned methods which are also applicable to amides.





(IV)

A typical procedure involves the addition of diethyl azodicarboxylate (1 equiv.) to a solution of the thioamide (1 equiv.) in tetrahydrofuran (or ether) at room temperature. After the mixture has been stirred for a suitable period

Table

Thioamide (I) R	% Yield of nitrile[a]	% Yield of isolated nitrile (III)[b]
Me	64[c]	> 50% as a solution in ether or THF
	86	
Ph	81	59
3-C_5H_5N	77	62
4-C_5H_5N	82	66

[a] The yields of products in crude reaction mixtures were estimated by g.l.c. on 3% OV 275 on Chromosorb W (acid washed) 100—120 mesh. [b] The products were identified by physical and spectroscopic measurement, and by comparison with authentic samples. [c] The reaction was performed in ether; other reactions were carried out in tetrahydrofuran (THF).

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† Benzamide did not react under conditions parallel to those used for thiobenzamide.

(1—3 h), a solution of triphenylphosphine in the same solvent is slowly added at such a rate that the reaction temperature does not exceed 35—40 °C. Work up after a further period (1—2 h) affords the nitrile (see Table).

These reactions involve the formation of the 1 : 1 adducts (II) between diethyl azodicarboxylate and the thioamides (I), comparable to those adducts which have been shown to be produced between diethyl azodicarboxylate and thioureas[1] or secondary thioamides.[2] The adducts (II) are then desulphurised by triphenylphosphine to generate the nitriles (III) together with triphenylphosphine sulphide and diethylhydrazodicarboxylate. The intermediate (IV) formed with thionicotinamide was isolated as a finely divided white solid [m.p. 68·5—71 °C (decomp.)] from a reaction solution prior to the addition of triphenylphosphine. It gave i.r. and n.m.r. spectra consistent with structure (IV), and afforded correct microanalytical data.

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