

Simple and Regioselective Synthesis of *N*-Substituted Pyrimidine-2(1*H*)-ones and -thiones

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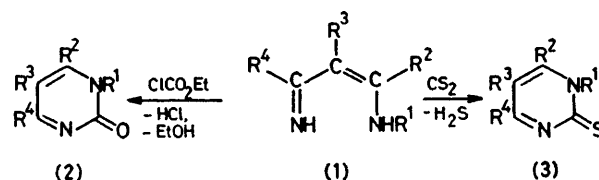
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Summary The di-imines (1), obtained by the reaction of Schiff bases with saturated nitriles, react with ethyl chloroformate and carbon disulphide giving rise to an efficient method for synthesising pyrimidine-2(1*H*)-ones and -thiones, respectively.

DI-IMINES (1) are readily prepared by reaction of Schiff bases with saturated nitriles in the presence of aluminium trichloride as catalyst.¹ We have used compounds (1) as intermediates in the synthesis of various heterocycles. Pyrimidines, pyridines, and dihydropyrimidines are obtained by reaction of (1) with saturated nitriles,² acetylenedicarboxylates,³ and Schiff bases⁴ or carbonyl compounds,⁵ respectively.

We now describe a simple and regioselective synthesis⁶ of pyrimidine-2(1*H*)-ones and -thiones by reaction of (1) with ethyl chloroformate and carbon disulphide.[†]

Pyrimidin-2(1*H*)-ones (2) are obtained as a single product in one step by reaction of (1) with ethyl chloroformate in a



molar ratio of 1 : 4.[‡] Their formation can easily be explained through a simple condensation process.

Pyrimidine-2(1*H*)-thiones (3) are obtained by heating a

TABLE. Pyrimidine-2(1*H*)-ones (2) and -thiones (3) obtained from the di-imines (1).

R ¹	R ²	R ³	R ⁴	(2)		(3)	
				% Yield	M.p./°C	% Yield	M.p./°C
Ph	<i>p</i> -ClC ₆ H ₄	Me	Ph	89	228—230	80	270—272
Ph	Ph	Me	<i>p</i> -ClC ₆ H ₄	88	190—192	87	243—245
<i>c</i> -C ₆ H ₁₁ ^a	Ph	Me	<i>p</i> -MeC ₆ H ₄	85	198—200	95	196—198
<i>c</i> -C ₆ H ₁₁	Ph	Me	Ph	80	194—196	84	221—223
Ph	Ph	Me	Ph	92	213—215	87	298—299
Ph	Ph	Me	<i>c</i> -C ₆ H ₁₁	88	242—244	92	241—243
Ph	Ph	H	Ph	92	246—247		
<i>p</i> -MeC ₆ H ₄	Ph	H	Ph	89	243—245		
Ph	<i>p</i> -ClC ₆ H ₄	Me	<i>p</i> -MeC ₆ H ₄			91	292—294
<i>o</i> -MeC ₆ H ₄	Ph	Me	<i>p</i> -MeC ₆ H ₄			92	210—212

^a Cyclohexyl.

[†] The structures of compounds (2) and (3) were corroborated by alternative syntheses.

[‡] In a typical procedure, ethyl chloroformate (0.04 mol) was added to (1) (0.01 mol) in pyridine (50 ml) at 0 °C. The stirred mixture was warmed to room temperature, and after 2 h treated with 1 *N* KOH (50 ml). The products (2) were extracted with ether.

solution of (1) in carbon disulphide at 70 °C for 5 h. H₂S is evolved, and the products (3) are obtained by recrystallization from hexane-tetrahydrofuran (6:1) following removal of the excess of carbon disulphide *in vacuo* (see Table for yields).§

(Received, 19th March 1979; Com. 283.)

§ Similar results were observed for reactions in benzene or tetrahydrofuran.

¹ H. Hoberg and J. Barluenga, *Synthesis*, 1970, 142.

² H. Hoberg and J. Barluenga, *Synthesis*, 1970, 363.

³ J. Barluenga, S. Fustero, and V. Gotor, *Synthesis*, 1975, 191.

⁴ V. Gómez-Aranda, J. Barluenga, V. Gotor, and S. Fustero, *Synthesis*, 1974, 720.

⁵ J. Barluenga, M. Tomás, S. Fustero, and V. Gotor, *Synthesis*, 1979, 346.

⁶ For a review of the more classical methods, see 'The Chemistry of Heterocyclic Compounds' ('The Pyrimidines,' suppl. 1), ed. A. Weissberger, Wiley-Interscience, New York, 1970, pp. 1—398.