Induced Conjugate Addition of Simple 2-Lithio-1,3-dithians to Cyclic α,β-Unsaturated Ketones

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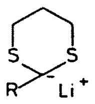
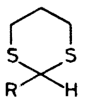
Summary In sharp contrast to prior observations that 2-lithio-1,3-dithians undergo only carbonyl (1,2-) additions to enones, the successful conjugate (1,4-) addition of the parent 2-lithio-1,3-dithian and its simple derivatives has been achieved by the addition of 1·0—2·0 equiv. of hexamethylphosphoramide to the reaction mixture.



(I)



(II)

R = H, Me, Me$_3$Si, *etc.*

DITHIAN anions (I), which are widely utilized as reagents for nucleophilic acylations,[1,2] react readily with α,β-unsaturated cyclic ketones but yield only the products of carbonyl (1,2-) addition.[1–4] We have observed that the presence of 1 or 2 mol of hexamethylphosphoramide (HMPT) per mol of the 2-lithio-1,3-dithian induces a major change in the course of the reaction, producing instead the conjugate (1,4-) addition compounds.

Metallation of the parent dithian (II, R = H) was carried out conventionally by the addition of n-butyl-lithium in hexane to *ca.* 0·4 M of dithian in tetrahydrofuran

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(THF) at −78 °C, followed by maintaining the solution at −20 °C for 1 h.[2a] The colourless solution was cooled to −78 °C and a concentrated solution of cyclohex-2-enone in THF–hexane (1 : 1) added. After 1—5 min at −78 °C, the mixture was quenched by the addition of saturated aqueous ammonium chloride. Analysis by g.l.c. revealed only the product of 1,2-addition (IV, $n = 1$).

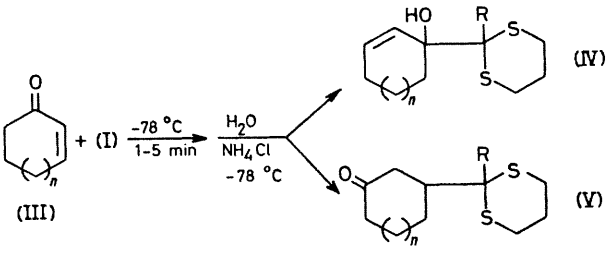

TABLE. Addition of 2-lithio-1,3-dithians to cyclic enones[a]

(I) R =	(III) n =	Additive[b] (mmol/mmol of dithian)	1,4-Addition[c] (V) %	1,2-Addition[c] (IV) %
H	0	None	0	>99
H	0	HMPT (2·0)	98	2
H	1	None	0	>99
H	1	HMPT (2·0)	95	5
		HMPT (1·0)	88	12
Me	1	None	0	>99
Me	1	HMPT (2·0)	97	3
Me_3Si	1	None	0	>99
Me_3Si	1	HMPT (2·0)	>95	<5
H	2	None	<1	>99
H	2	HMPT (2·0)	74	26

[a] Addition of 2·5 mmol of enone to 2·5 mmol of (I) in *ca.* 6 ml of tetrahydrofuran–hexane (*ca.* 4 : 1) at −78 °C, followed by quenching after 1—5 min with saturated aq. NH_4Cl. [b] Additive mixed, at −78 °C, with (I) prior to addition of enone. [c] By g.l.c. analysis (after aqueous workup) with Carbowax or OV-17 columns. Yields were 50—80%. No attempt was made to optimize yields.

Addition of 2·0 mol of HMPT per mol of the lithio reagent (I) to the solution at −78 °C resulted in an immediate yellow–orange coloration. Addition of the solution of the cyclohex-2-enone to this mixture resulted in a rapid discharge of the colour. Quenching of the mixture with aqueous ammonium chloride, as before, yielded a different addition product, (V), the result of conjugate addition of the reagent to the cyclohex-2-enone. Other examples are summarized in the Table.

The reaction represents a true direct conjugate addition rather than an initial kinetically controlled 1,2-addition followed by rearrangement as has been observed with 2-lithio-2-aryl-1,3-dithians.[5] Addition of HMPT to solutions of the lithium salt of (IV) produced no rearrangement to the conjugate addition product, even after 24 h at room temperature.

This development has potential in synthesis, and the role of HMPT is interesting mechanistically.

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[1] For a recent review see: O. W. Lever, Jr., *Tetrahedron*, 1976, **32**, 1943.

[2] For specific discussions of 2-lithio-1,3-dithian and 2-substituted derivatives with leading references, see: D. Seebach and E. J. Corey, *J. Org. Chem.*, 1975, **40**, 231; D. Seebach, *Synthesis*, 1969, 17.

[3] D. Seebach, M. Kolb, and B.-Th. Grobel, *Chem. Ber.*, 1973, **106**, 2277; See footnote 4b in D. Seebach and R. Burstinghaus, *Angew. Chem.*, 1975, 37; F. A. Carey and A. S. Court, *J. Org. Chem.*, 1972, **37**, 1926; E. J. Corey and D. Crouse, *ibid.*, 1968, **33**, 298.

[4] More highly stabilized sulphur-containing acyl carbanion equivalents have been observed to undergo conjugate additions to enones. For examples see: D. Seebach and R. Burstinghaus, *Angew. Chem.*, 1975, 37; A.-R. B. Manes and R. A. J. Smith, *J.C.S. Chem. Comm.*, 1975, 216; K. Ogura, M. Yamashita, and G. Tsuchihashi, *Tetrahedron Letters*, 1978, 1303; R. J. Cregge, J. L. Herrmann, J. E. Richman, R. F. Romanet, and R. H. Schlessinger, *ibid.*, 1973, 2595; J. E. Richman, J. L. Herrmann, and R. H. Schlessinger, *ibid.*, 1973, 3276.

[5] P. C. Ostrowski and V. V. Kane, *Tetrahedron Letters*, 1977, 3549.