Sulphur Extrusion. Part 4.† A Halogen-catalysed Conversion of Thiocarbonyl Compounds into their Corresponding Oxygen Analogues using Alkoxides and Hydroxide

By **Harjit Singh,* Paramjit Singh,** and **Nageshwar Malhotra,** Department of Chemistry, Guru Nanak Dev University, Amritsar 143005, India

The conversion of thiocarbonyl compounds (thioureas, thioamides, and thiones) into their oxygen analogues has been performed using either (*i*) potassium t-butoxide with iodine, bromine, or chlorine, (*ii*) sodium ethoxide with bromine or chlorine, or (*iii*) sodium hydroxide with bromine or chlorine under phase transfer catalysis.

ADEQUATE synthetic methodology for the chemical transformation of carbonyl into thiocarbonyl functions is available.[1,2] In order to increase the synthetic versatility of this reaction, investigation of the reagents for carrying out the reverse conversion, i.e. thiocarbonyl into carbonyl, is of considerable importance. The different reagents used for this conversion meet with varying degrees of success, having different limitations and giving different side-reactions, and include iodate or bromate in alkaline solutions,[3] sodium peroxide,[4] $KMnO_4$–$K_2S_2O_4$–KOI,[5] methyl iodide–potassium t-butoxide,[6] thiophosgene,[7] dimethyl sulphoxide (DMSO)–acids,[8,9] DMSO–iodine,[10] trimethyloxonium tetrafluoroborate,[11] bis-(*p*-methoxyphenyl) telluroxide,[12] dibromotetrachloroethane and diaryl telluroxide,[13] singlet oxygen,[14] dimethyl selenoxide,[15] and benzeneseleninic acid.[16] However, dibenzoyl peroxide,[17] and lead tetra-acetate and H_2O_2–I_2 [18] give mostly disulphides during such conversions.

During our investigation of the reaction of 4,4,6-trimethyl-1-phenyl-3,4-dihydropyrimidine-2(1*H*)-thione (2; Y = S) with iodocarbene generated from iodoform and potassium t-butoxide, the formation of a substantial amount of (2; Y = O) and iodine was noticed.[19] Since such conversions have been reported with iodine and DMSO,[10] the transformation of (2; Y = S) into (2; Y = O) might have taken place with iodine and potassium t-butoxide. Hence we have investigated the title reactions.[20]

RESULTS AND DISCUSSION

The chemical conversions of dihydropyrimidine systems are important for the procurement of modified nucleosides.[21] 6-Methyluracil-2(3*H*)-thione (1; Y = S), on refluxing in t-butyl alcohol containing potassium t-butoxide and a catalytic amount of iodine, gave 6-methyluracil in 95% yield with isolation of elemental sulphur. Likewise, 4,4,6-trimethyl-1-phenyl-3,4-dihydropyrimidine-2(1*H*)-thione (2; Y = S) gave the corresponding ketone (2; Y = O) in 90% yield. Under similar conditions, however, 4,4,6-trimethyl-3,4-dihydropyrimidine-2(1*H*)-thione remained unchanged.

Similarly, 3,4-dihydroisoquinoline-1(2*H*)-thione (4; Y = S),[22] quinazoline-4(3*H*)-thione (5; Y = S), pyridine-2(1*H*)-thione (6; Y = S), pyrrolidine-2-thione (7; Y = S), and thiobenzamide (8; Y = S) gave the corresponding oxygen analogues in 85, 35, 70, 20, and 90% yields respectively. In the case of diphenylthiourea (9; Y = S) and triphenylphosphine sulphide, the reaction did not proceed. These conversions did not occur with potassium t-butoxide in the absence of iodine or with other alkoxides, *viz.* sodium ethoxide, sodium methoxide, or aqueous sodium hydroxide, even in the presence of iodine.

When a catalytic amount of bromine was used, the reactions were completed in much less time and even diphenylthiourea and triphenylphosphine sulphide could be converted into their oxygen analogues. Moreover, sodium ethoxide, which could not perform these conversions in the presence of iodine, converted thiobenzamide into benzamide in the presence of bromine.

† Part 3, H. Singh, A. S. Ahuja, and C. S. Gandhi, *J. Chem. Res.*, 1979, (*S*) 264; (*M*) 2935.

Subsequently, chlorine was used as a catalyst and the exothermic reactions, which otherwise resulted in the formation of tarry mixtures, had to be performed at a lower temperature and took much less time to reach completion (Table).

In none of these reactions was there noticed the formation of a disulphide, normally a major drawback of such a reaction. It has further been found that bromine catalysed these conversions with DMSO much more effectively than iodine,[10] but when chlorine was used, the reaction was so vigorous that the reaction mixture caught fire.

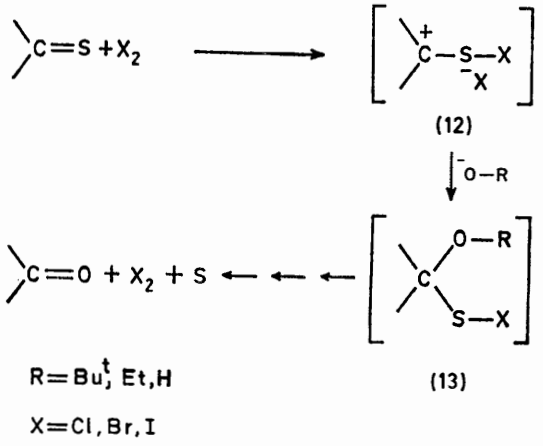
Yields of products (Y = O)[a] and reaction times using potossium t-butoxide and halogen

		Iodine		Bromine		Chlorine	
Y = S	Eluant	Yield (%)[b]	Time (h)	Yield (%)[b]	Time (h)	Yield (%)[b]	Time (h)
(1)[c]		95	30	85	20	83	18
(2)[d]	EtOAc–C_6H_6 (1 : 4)	90	36	90	20	80	10
				50[e]	40[e]	65[e]	63[e]
(3)	EtOAc–C_6H_6 (1 : 4)			43[e]	60[e]	50[e]	60[e]
(4)[f]	MeOH–C_6H_6 (1 : 4)	85	30	80	25	80	16
				50[e]	90[e]	48[e]	80[e]
(5)	EtOAC–C_6H_6 (1 : 4)	35	48	70	20	65	16
(6)	MeOH : $CHCl_3$ (1 : 4)	70	45	65	25	61	20
(7)	$CHCl_3$: C_6H_6 (1 : 6)	20	22	50	10	43	7
(8)	$CHCl_3$: C_6H_6 (1 : 4)	90	40	85	18	90	10
				68[g]	20[g]	60[g]	15[g]
(9)	C_6H_6			55	10	45	6
(10)[h]	G.l.c.			35[e]	48[e]	38[e]	36[e]
(11)	Crystallised from C_6H_6			10	85	10	85
				64[e]	50[e]	82[e]	43[e]

[a] Products were identified by comparison (R_F, mixed m.p., i.r. spectra), with authentic samples. Except for (1; Y = 0), (2; Y = 0), and (4; Y = 0), all products were available commercially. [b] Yields were not optimised. [c] D. J. Brown, *J. Appl. Chem.*, 1952, **2**, 239. [d] Ref. 19. [e] Data for the reaction run with sodium ethoxide. [f] M.p. 188—189 °C [lit., 58 °C (R. V. Davies, B. Iddon, H. Suschitzky, and M. W. Gittos, *J. Chem. Soc., Perkin Trans. 1*, 1978, 180)], $\nu_{max.}$ 1680 (CONH) and 3 250 cm^{-1} (NH), δ ([$^2H_6$]DMSO) 2.52 (2 H, t, CH_2, overlapped with DMSO signal), 3.4 (2 H, t, CH_2), 6.45—8.27 (4 H, m, ArH), and 11.25 br (1 H, NH, exchanged with D_2O), *m/e* 147 (M^+), 146 (M − H), 145 (M − 2 H), 144 (145 − H), and 119 (M − CH_2=CH_2) (Found: C, 73.25; H, 5.05; N, 9.75. Calc. for C_9H_9NO: C, 73.47; H, 5.44; N, 9.52%). [g] Figures for reactions run under phase transfer catalysis. [h] Yields of phenol and thiophenol were determined by g.l.c.

Phase transfer catalysis facilitates a variety of organic reactions.[23] The conversion of (2; Y = S), (3; Y = S), (4; Y = S), thiophenol (10), and triphenylphosphine sulphide (11), into their oxygen analogues was studied under phase transfer conditions using 50% aqueous sodium hydroxide and triethylbenzylammonium chloride (TEBACl) as phase transfer catalyst in the presence of a catalytic amount of bromine or chlorine (Table). For these compounds the reaction did not succeed when iodine was used. In the case of thiocamphor and benzyl dithiobenzoate, a multitude of products was formed but the product mixtures exhibited carbonyl absorption bands in their i.r. spectra. The formation of a mixture of products has been reported in a similar reaction of thiocamphor with benzeneseleninic acid.[16]

From these observations, it may be concluded that with a more electronegative catalyst, the reaction could be performed with a milder base and under milder conditions. Thus the reaction might be initiated by attack of the halogen at sulphur, creating an electrophilic site at the thiocarbonyl carbon atom (12) at which the alkoxide or hydroxide ion would attack to form (13) (Scheme). However, the mode of the subsequent transformation of (13) into the carbonyl compound, sulphur, and X_2 is not readily apparent from the available data and needs further study.[10] Nevertheless, as the reaction proceeded equally well in the presence of hydroquinone, the possibility of a radical mechanism was ruled out.



SCHEME

EXPERIMENTAL

M.p.s were determined in capillaries and are uncorrected. ^1H N.m.r. spectra were recorded on a Tesla BS 487C 80 MHz instrument using tetramethylsilane as internal standard. Elemental analyses were performed at the Chemistry Department, Calcutta University. I.r. spectra were recorded with a Spectromom 2000 spectrophotometer. Mass spectra were run on Hitachi–Perkin–Elmer RMU-60D or Varian MAT CM-7 instruments. For t.l.c., plates coated with silica gel G were run in chloroform, ethyl acetate, or benzene or their mixtures, and spots were developed in an iodine chamber.

General Procedure.—(a) *Reaction of thiones with alkoxides in the presence of iodine, bromine, or chlorine.* A catalytic amount of iodine (*ca.* 40 mg), bromine (2—3 drops), or

chlorine (flushed for few seconds through the cooled reaction mixture) was added to a solution of the thione (0.001 mol) in t-butyl alcohol (60 ml) containing potassium t-butoxide (5 g). A brisk reaction (exothermic in the case of bromine and chlorine) took place and the iodine or bromine was dissolved. The reaction mixture was refluxed on a water-bath and the progress of the reaction was monitored by t.l.c. In the reaction with chlorine the cooled reaction mixture was gradually warmed to room temperature at which it was then kept with occasional shaking. After the reaction was complete the solvent was distilled off and the residue was taken up in the minimum amount of water. The mixture was centrifuged and the sulphur was separated off. The aqueous portion, after neutralisation with acetic acid, was extracted with ethyl acetate (2 × 50 ml).* The extract was washed with sodium thiosulphate solution and water, dried (Na_2SO_4), and the solvent distilled off. The products were isolated by column chromatography of the residue over silica gel (Table).

(b) *Reaction of thiones with hydroxide under phase transfer catalysis in the presence of bromine or chlorine.* A cooled solution of sodium hydroxide (50%, 25 ml) was added to a solution of the thione (Table) (0.001 mol) in dichloromethane (60 ml) containing a catalytic amount of TEBACl (0.2 g) and bromine or chlorine. The mixture was stirred at room temperature and the progress of the reaction was monitored (t.l.c.). After the reaction was complete, the mixture was diluted with water. The organic phase was separated and washed several times with dilute HCl (5%) and then water, and then dried (Na_2SO_4). The solvent was distilled off and the products were isolated by column chromatography of the residue over silica gel (Table).

[1/004 *Received*, 5*th January*, 1981]

* 6-Methyluracil was isolated as a precipitate formed after acidification of the aqueous solution.

REFERENCES

[1] C. S. Rao, M. P. Dave, P. N. Mody, and A. D. Pandya, *Indian J. Chem.*, 1976, **14**, 999.
[2] J. W. Scheeren, P. H. J. Ooms, and R. J. F. Nivard, *Synthesis*, 1973, 149.
[3] H. H. Capps and W. M. Dehn, *J. Am. Chem. Soc.*, 1932, **54**, 4301.
[4] M. J. Kalm, *J. Org. Chem.*, 1961, **26**, 2925.
[5] R. T. C. Loh and W. M. Dehn, *J. Am. Chem. Soc.*, 1926, **48**, 2956.
[6] R. K. Gompper, and W. Elser, *Liebigs Ann. Chem.*, 1969, **725**, 64 (*Chem. Abstr.*, 1969, **71**, 90728m).
[7] S. Abugar, S. Sharma, and R. N. Iyer, *Indian J. Chem., Sect. B*, 1980, **19**, 211.
[8] M. Mikolajczyk and J. Luczak, *Synthesis*, 1974, 491.
[9] M. Mikolajczyk and J. Luczak, *Chem. Ind. (London)*, 1974, 701.
[10] M. Mikolajczyk and J. Luczak, *Synthesis*, 1975, 114.
[11] R. Mukherji, *Indian J. Chem., Sect. B*, 1977, **15**, 502.
[12] D. H. R. Barton, S. V. Ley, and C. A. Meerholz, *J. Chem. Soc., Chem. Commun.*, 1979, 755.
[13] S. V. Ley, C. A. Meerholz, and D. H. R. Barton, *Tetrahedron Lett.*, 1980, 1785.
[14] J. E. Gano and S. Atik, *Tetrahedron Lett.*, 1979, 4635.
[15] M. Mikolajczyk and J. Luczak, *J. Org. Chem.*, 1978, **43**, 2132.
[16] N. J. Cssans, S. V. Ley, and D. H. R. Barton, *J. Chem. Soc., Perkin Trans. 1*, 1980, 1650.
[17] L. Vaino and A. Schinuer, *Chem. Ber.*, 1914, **47**, 699.
[18] W. Walter and J. Goss in ' The Chemistry of Amides,' ed. J. Zabicky, Interscience, New York, 1970, p. 383.
[19] H. Singh and P. Singh, *Tetrahedron*, 1981, **37**, 1215.
[20] Preliminary communication, H. Singh, P. Singh, and N. Malhotra, *Synth. Commun.*, 1980, **10**, 591.
[21] H. Singh and P. Singh, *J. Chem. Soc., Perkin Trans. 1*, 1980, 1013 and references therein.
[22] M. W. Gittos, M. R. Robinson, J. P. Verge, R. V. Davies, B. Iddon, and H. Suschitzky, *J. Chem. Soc., Perkin Trans. 1*, 1976, 33.
[23] W. P. Weber and G. W. Gokel, ' Phase Transfer Catalysis in Organic Synthesis,' Springer–Verlag, New York, 1977.