787. *Studies of Heterocyclic Compounds. Part II.*[1] *The Reaction of Thioamides with γ-Bromo-αβ-unsaturated Carbonyl Compounds*

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Thioamides react with γ-bromo-αβ-unsaturated carbonyl compounds to give 4,5-dihydrothiazoles.

Bromination of cyclopent-2-enone with *N*-bromosuccinimide gives in high yield a monobromo-ketone which was considered to be 5-bromocyclopent-2-enone,[2] but was later stated by other workers[3] to be the 4-bromo-isomer on the basis of proton magnetic resonance data. We required 5-bromocyclopent-2-enone for reaction with thioamides in a projected synthesis of 6*H*-cyclopenta[*d*]thiazolium salts (I), and allowed the product from the bromination of cyclopent-2-enone to react with thioacetamide in boiling benzene. An insoluble oily hydrobromide was obtained which was converted into the more easily purified perchlorate. Both salts, on being neutralised, gave a stable steam-volatile base showing strong infrared carbonyl absorption at 1754 cm.$^{-1}$ (CCl_4). This absorption establishes the presence of a cyclopentanone rather than a cyclopent-2-enone ring in the base * and consequently in the bromide and perchlorate. According to the Hantzsch thiazole synthesis, 5-bromocyclopent-2-enone with thioacetamide would give either the salt (II) or its cyclisation product (I; $R^1 = Me$, $R^2 = H$, $X = Br$), neither of which contains the cyclopentanone ring. We concluded, therefore, that bromination of cyclopent-2-enone with *N*-bromosuccinimide gives 4-bromocyclopent-2-enone, and that the foregoing salts and base are derived from this bromo-ketone.

Salts of the type (II) are intermediates in the Hantzsch synthesis, and in many cases have been isolated and subsequently cyclised.[4] The reaction of 4-bromocyclopent-2-enone with thioacetamide could give such a salt (III) which, however, would be incapable of cyclisation to a thiazole. Structure (III) itself is at variance with the infrared data, and mechanistic considerations involving an intramolecular Michael-type addition reaction of the salt (III) pointed to structure (IV) for the bromide ($X = Br$) and perchlorate ($X = ClO_4$). The base then has structure (V). These structures were confirmed by the

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* Cyclopentanone and cyclopent-2-enone show carbonyl absorption (CCl_4) at 1746 and 1714 cm.$^{-1}$, respectively.

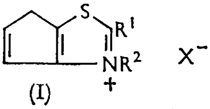
[1] Part I, B. B. Molloy, D. H. Reid, and F. S. Skelton, *J.*, 1965, 65.

[2] K. Hafner and K. Goliasch, *Chem. Ber.*, 1961, **94**, 2909.

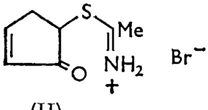
[3] C. H. De Puy, M. Isaks, and K. L. Eilers, *Chem. and Ind.*, 1961, 429; C. H. De Puy, M. Isaks, K. L. Eilers, and G. F. Morris, *J. Org. Chem.*, 1964, **29**, 3503.

[4] M. Steude, *Annalen*, 1891, **261**, 22; F. E. Hooper and T. B. Johnson, *J. Amer. Chem. Soc.*, 1934, **56**, 470; E. H. Huntress and K. Pfister, *ibid.*, 1943, **65**, 1667; A. R. Todd, F. Bergel, and Karimullah, *Ber.*, 1936, **69**, 217; D. H. Reid and W. G. Salmond, unpublished results.

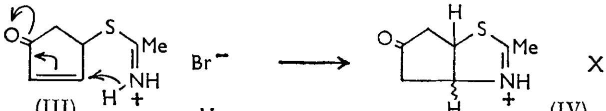
proton magnetic resonance spectra of the perchlorate (IV; X = ClO_4) and the base (V). The former in trifluoroacetic acid shows a singlet (2·9 H) at δ 2·79 (protons of the methyl group), a broad singlet (0·85 H) at δ 10·25 ((proton attached to nitrogen), a quartet (1 H) at δ 4·95, 5·09, 5·20, and 5·35 (proton at C-6a), a quartet (1 H) with broad components centred at δ 5·71 (proton at C-3a), and a doublet (3·6 H) with broad components at δ 3·20 and 3·30 (two pairs of methylene protons at C-4 and C-6).



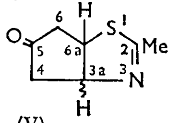
(I)



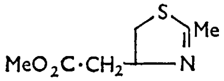
(II)



(III) (IV)



(V)



(VI)

Methyl γ-bromocrotonate contains the reactive γ-bromo-αβ-unsaturated carbonyl grouping involved in the foregoing reaction and, when allowed to react with thioacetamide, also gave a thiazoline the infrared and proton magnetic resonance spectra of which confirm the assigned structure (VI). The oily bromide and perchlorate of compound (VI) did not crystallise, but the proton magnetic resonance spectrum of the base (VI) in trifluoroacetic acid was consistent with *N*-protonation.

EXPERIMENTAL

Melting points were determined on a Kofler hot-stage apparatus. Perchloric acid refers to 70—72% w/w perchloric acid of AnalaR grade. Acetonitrile was purified by boiling it over phosphoric anhydride, then distilled, and it was redistilled before use.

Infrared spectra were recorded with a Grubb–Parsons type G.S.2A instrument. Proton magnetic resonance spectra were measured at *ca.* 34° with a Perkin-Elmer R10 spectrometer operating at 60 Mc./sec., at a sweep rate of 1·6 c./sec./sec. and sweep width of 600 c./sec. Chemical shifts (δ) are given in p.p.m. downfield from tetramethylsilane as internal reference. Solutions in deuterochloroform were 0·4-M, those in trifluoroacetic acid 0·5-M.

Reaction of 4-*Bromocyclopent*-2-*enone with Thioacetamide*.—A solution of 4-bromocyclopent-2-enone (16·04 g., 0·1 mole) in dry benzene (40 ml.) was added dropwise during 20 min. to a stirred solution of thioacetamide (7·48 g., 0·1 mole) in dry benzene (40 ml.) at the boiling point. The resulting mixture was boiled for 30 min. A dark brown oil separated from the hot solution and crystallised on being cooled. The supernatant liquid was decanted and the residual bromide (IV; X = Br) was washed with benzene, dried *in vacuo*, and dissolved in the minimum volume of ethanol. Addition of an excess of perchloric acid followed by ether gave colourless crystals (10·10 g., 40%). Dissolution in ethanol followed by the addition of ether gave 4,5,6,6a-*tetrahydro*-2-*methyl*-5-*oxo*-3aH-*cyclopenta*[d]*thiazolium perchlorate* (IV; X = ClO_4) as colourless needles, m. p. 183·5—187·5° (Found: C, 32·8; H, 4·2; N, 5·2. $C_7H_{10}ClNO_5S$ requires C, 32·9; H, 3·9; N, 5·5%), $\nu_{max.}$ (Nujol) 1716 (C=O) and 1608 cm.$^{-1}$ (C=N). This salt gives an intensely purple solution ($\lambda_{max.}$ 594 mμ) on being boiled with *p*-dimethylaminobenzaldehyde in acetic anhydride.

Boiling equimolecular amounts of the perchlorate (IV; X = ClO_4) and 2,4-dinitrophenylhydrazine in ethanol gave the 2,4-*dinitrophenylhydrazone*, orange-yellow prisms (from acetic acid), m. p. 208·5—212·5° (Found: C, 35·8; H, 3·3; N, 16·0. $C_{13}H_{14}ClN_5O_8S$ requires C, 35·8; H, 3·2; N, 16·1%).

An aqueous solution of the perchlorate (IV; X = ClO_4) (2·57 g.) was neutralised with a slight excess of sodium hydrogen carbonate. The solution was extracted with ether, and the ether extracts were washed once with water, dried (Na_2SO_4), and evaporated. Distillation of the residual oil gave 4,5,6,6a-*tetrahydro*-2-*methyl*-5-*oxo*-3aH-*cyclopenta*[d]*thiazole* (V) (0·69 g., 44%) as a colourless liquid, b. p. 115—118°/2·5 mm. (Found: C, 54·1; H, 6·2; N, 8·8; S, 20·4. C_7H_9NOS requires C, 54·2; H, 5·8; N, 9·0; S, 20·7%), $\nu_{max.}$ (CCl_4) 1754 (C=O) and 1630 cm.$^{-1}$ (C=N). The n.m.r. spectrum ($CDCl_3$) showed a singlet (3·3 H) at δ 2·24 (protons of the methyl group), a quartet (1 H) at δ 4·17, 4·31, 4·43, and 4·57 (proton at C-6a), a quartet (1 H) with broad components centred at δ 5·14 (proton at C-3a), and a complex group of signals (3·9 H) at δ 2·6—3·1 (methylene protons at C-4 and C-6). The base (V) is fairly soluble in cold water.

Reaction of Methyl γ-Bromocrotonate with Thioacetamide.—A solution of methyl γ-bromocrotonate (1·79 g., 10 mmoles) and thioacetamide (0·75 g., 10 mmoles) in acetonitrile (20 ml.) was boiled for 1 hr. Solvent was removed at reduced pressure, and a solution of the residue in water (50 ml.) was neutralised with an excess of sodium hydrogen carbonate before being extracted with ether (3 × 100 ml.). The ether extracts were washed once with water, dried (Na_2SO_4), and evaporated. Distillation of the residual liquid gave *methyl 4,5-dihydro-2-methylthiazol-4-ylacetate* (VI) as a colourless oil (820 mg., 58%), b. p. (heating block) 70—80°/1 mm. (Found: C, 48·4; H, 6·5. $C_7H_{11}NO_2S$ requires C, 48·5; H, 6·4%), $\nu_{max.}$ (liquid film) 1739 (ester C=O) and 1637 cm.$^{-1}$ (C=N). The n.m.r. spectrum ($CDCl_3$) showed a singlet at δ 2·22 (protons of the ring-methyl group), a singlet at δ 3·73 (protons of the methoxycarbonyl group), a triplet with broad components at δ 4·71, 4·83, and 4·95 (C-4a proton), and a complex group of signals at δ 2·3—3·6 (protons of the ring and side-chain methylene groups). The n.m.r. spectrum of the base (VI) in trifluoroacetic acid showed a singlet (2·9 H) at δ 2·74 (ring-methyl protons), a singlet at δ 3·91 (protons of the methoxycarbonyl group), a broad singlet at δ 10·73 (proton attached to nitrogen), a doublet (1·9 H) at δ 3·14 (J = 6·7 c./sec.) (protons of the side-chain methylene group), a quintet (1 H) at δ 5·26 (proton at C-4), and a complex group of signals at δ 3—4·4 (C-5 methylene protons).

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