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STEREOSELECTIVE SYNTHESIS OF S-(trans-PROP-1-ENYL)-CYSTEINE SULPHOXIDE

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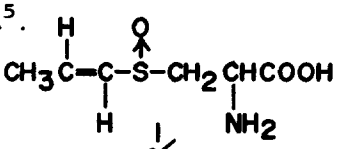
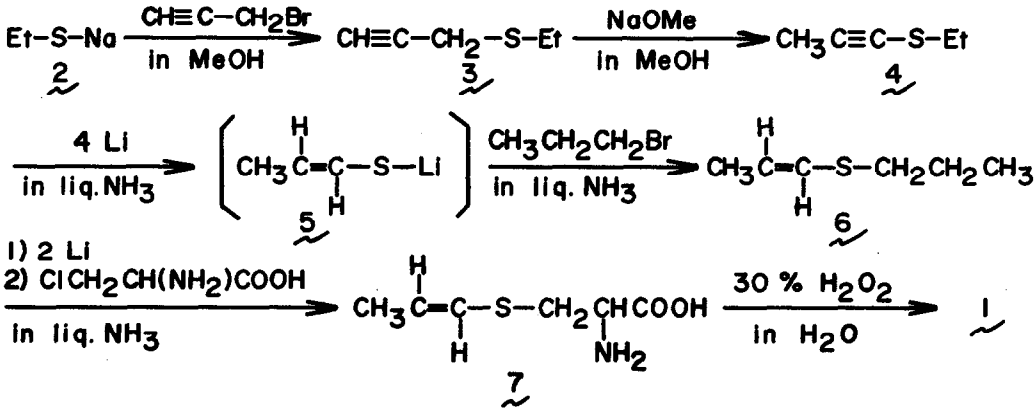
S-(Prop-1-enyl)-L-cysteine and its derivatives have been isolated from Allium plants such as onion and chive[1]. Particularly, a sulphoxide (1) of this amino acid has been shown to be the metabolic precursor of the onion lachrymator; thiopropanal S-oxide[2]. Carson et al. have established that the double bond of the amino acid has the trans configuration[3], and also synthesized the cis isomer stereoselectively[4]. However, the synthesis of the naturally occurring trans isomer has not yet been accomplished[5].



In this paper, we report the stereoselective synthesis of the trans isomer (1).

Sodium ethanethiolate (2) reacted with propargyl bromide to give ethyl prop-2-ynyl sulphide (3), which was isomerized to ethyl prop-1-ynyl sulphide (4), b.p. 34.5°/ 15 mmHg; IR ν_{max}^{film} cm^{-1}: 2200 (-C≡C-); MS: m/e 100 ($M^{+\cdot}$); PMR (CCl_4) δ : 1.32 (3H, t), 1.92 (3H, s), 2.59 (2H,q) in 75 % yield. A C-S cleavage and a trans hydrogenation of the product (4) by a treatment of four equivalents of Li in liquid NH_3 gave an intermediate thiolate (5) and the successive reaction of 5 with propyl bromide led to propyl trans-prop-1-enyl sulphide (6), IR ν_{max}^{film} cm^{-1}: 935 (prop-1-enyl), 960 (trans double bond); MS: m/e 116 ($M^{+\cdot}$); PMR (CCl_4) δ : 0.98 (3H, t), 1.59 (2H, m), 1.75 (3H, d), 2.54 (2H, t), 5.50 (1H, m), 5.83 (1H,d, J=15.8 Hz) in 43 % yield. In this step, the trans sulphide was stereoselectively yielded in 100 %. There was no trace of the cis isomer. As other products, ethyl propyl sulphide and propyl prop-1-ynyl sulphide were found[6]. The pure trans sulphide (6) was easily isolated by

distillation and the preparative GLC. Furthermore, reductive cleavage of a C-S bond of 6 by Li in liquid NH_3 followed by the addition of β-chloro-L-alanine[7] gave S-(trans-prop-1-enyl)-cysteine (7), IR ν_{max}^{film} cm^{-1}: 960 (trans double bond); MS m/e (relative intensity): 161 (M^+, 31.8), 116 (16.1), 88 (70.3), 87 (100), 74 (71.2), 59 (48.9), 45 (72.1), 41 (40.5), 39 (45.2); PMR (D_2O-NaOD) δ : 1.62 (3H, d), 2.90 (2H, dd), 3.36 (1H, dd), 5.66 (1H, m), 5.92 (1H,d, J=15.8 Hz) in 65 % yield. Finally, the oxidation of 7 by H_2O_2 in ice water afforded S-(trans-prop-1-enyl)-cysteine sulphoxide (1), IR ν_{max}^{KBr} cm^{-1}: 1010 (sulphoxide), 960 (trans double bond) in an almost quantitative yield.



REFERENCES AND FOOTNOTES

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5. Reduction of the triple bond of S-(prop-1-ynyl)-L-cysteine with Na in liq. NH_3 didn't afford S-(trans-prop-1-enyl)-L-cysteine but L-alanine : J.F.Carson and L.E.Boggs, J.Org.Chem., 30, 895 (1965).
6. α,β-Unsaturated sulphides -C=C-SR and -C≡C-SR exculsively undergo cleavage of the bond between S and R (alkyl) in reactions with alkali metals: L.Brandsma and P.J.W.Schuijl, Rec.Trav.Chim., 88, 513 (1969); L.Brandsma, ibid., 89, 593 (1970). However, reductive cleavage of ethyl prop-1-ynyl sulphide (4) by Li or Na gave ethyl propyl sulphide (32 % yield) as a by-product. This fact indicates that the bond between S and C (prop-1-ynyl moiety) is readily cleaved.
7. β-Chloro-L-alanine was prepared by the method of Fischer and Raske: E.Fischer and K.Raske, Ber., 40, 3717 (1907).