

Acylation with 1,1,1-Trifluoroacetone of the Azaallyl Carbanion from Ethyl Bis(methylthio)methyleneaminoacetate

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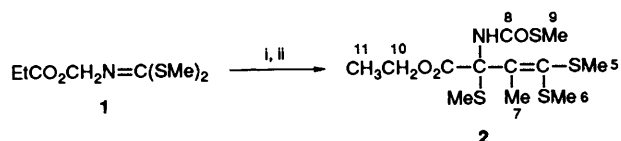
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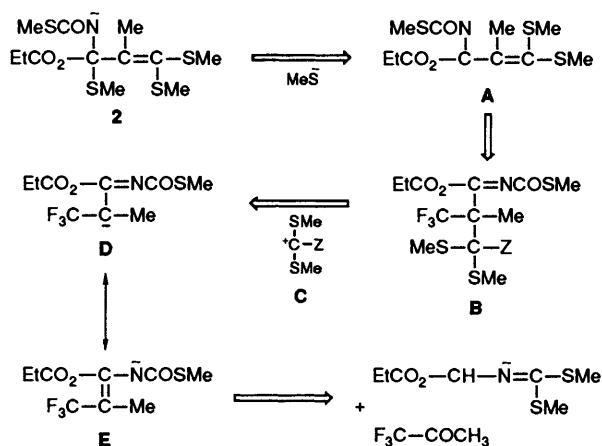
Ethyl bis(methylthio)methyleneaminoacetate **1** reacts with 1,1,1-trifluoroacetone in potassium *tert*-butoxide to afford ethyl 3-methyl-2,4,4-tris(methylthio)-2-(methylthiocarbonylamino)but-3-enoate **2**, an unexpected product, whose structure has been determined by X-ray analysis.

In connection with our interest in the preparation of 1,3-azoles,¹ we treated ethyl bis(methylthio)methyleneaminoacetate **1** with 1,1,1-trifluoroacetone in potassium *tert*-butoxide–THF at low temperature and obtained the thiocarbamate **2** (Scheme 1) rather than the expected 1,3-oxazole derivative.²



Scheme 1 Reagents and Conditions: i, KO^tBu –THF, -78°C , 0.5 h; ii, CF_3COCH_3 –THF, 0°C for 2 h, 20°C for 1.5 h

Formation of **2** is explicable only in terms of 1,1,1-trifluoroacetone acting as an acylation agent towards the azaallylic carbanion³ from **1** (Scheme 2).



Scheme 2

An X-ray structural analysis of **2** has been carried out and this has allowed a complete interpretation of the UV, IR, ^1H - and ^{13}C NMR spectral results.

Formation of the thiocarbamate **2**, can be understood by retrosynthetic analysis (Scheme 2). Development of the synthetic equivalence of the synthon **C**, as well as its origin and its possible reaction with the salt of the enamine **E**, indicates the strong electron withdrawing character of the gem-bis(methylthio)methylene group.³

The UV absorption maxima are assignable to the π – π^* (214.6) and n – π^* (262.5 nm) transitions, which suffer a strong

bathochromic shift due to the methylthio groups.⁴ The IR absorption maxima are assignable to the monothiocarbamate NH (3375 cm^{-1}), the ester (1712) and the monothiocarbamate (1680 cm^{-1}) (ref. 5, p. 160). The singlet signals in the ^1H NMR spectrum are assignable to the methyl groups: δ 2.00, (7-Me), 2.18, (10-Me), 2.26 and 2.33 (5-Me and 6-Me; can be interchanged) and 2.49 (9-Me) (ref. 5, p. 122); δ 7.14 (br s, monothiocarbamate NH) (ref. 5, p. 137). In the ^{13}C NMR spectrum δ_{C} 13.05 is a quadruplet of triplets ($\text{CH}_3\text{CH}_2\text{CO}_2$). Direct ^{13}C – ^1H coupling for the remaining five methyl groups, allowed the following assignments: δ_{C} 20.98 (7-Me),⁸ 12.36 (SMe; characteristic for 2-thiomethoxycarbonylamino-3-arylacrylates), 17.15 and 16.87 (both quadruplets with the same order of magnitude for J), 13.97 (quadruplet, 10-Me, J value 10 Hz higher than that for preceding quadruplets); in the same way, the signals at δ 62.64 (tq) and at 69.97 (m) were assigned to 11-Me and 2-Me; δ 133.92 (m, 4-Me), 142.23 (qd, 3-Me), 168.70 (q, 1-Me) and 164.48 (q, 8-Me).¹

The mass fragmentation is in good agreement with structure **2**. The intensity for the molecular ion is very small (agrees with literature⁹ results) and the base peak results from the loss of a thiomethoxy fragment and successive loss of methanethiol ($M^+ - 260$) and ethylene¹⁰ ($M^+ - 232$). Loss from the molecular peak of ethoxy, methanethiol and carbon monoxide give successively the $M^+ - 310$, 262 and 234. The relative abundance observed for $M^+ + 1$ and $M^+ + 2$ of the $M^+ - 308$ and 260 ions, confirms the presence of three sulfur atoms in the first and two in the last ion.

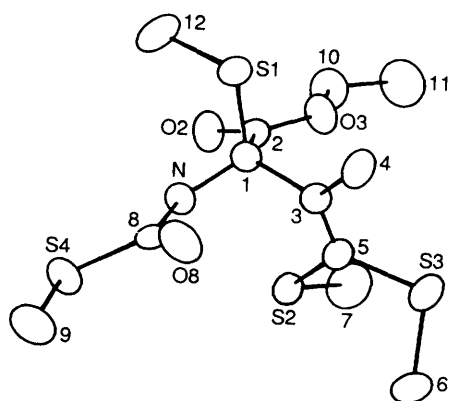
A molecular and crystallographic study of compound **2** was carried out in order to confirm its structure and, from the position of the sulfur atoms on the chain, gain insight into the mechanism of the reaction between the azaallylic carbanion and the trifluoroacetone.

Experimental

M.p.s were measured with a Büchi 520 apparatus and are uncorrected. UV–VIS spectra (in nm) were recorded on a Perkin-Elmer Lambda 3 spectrophotometer with data station 3600; and IR spectra (in KBr, frequencies in cm^{-1}) on a Perkin-Elmer 253 spectrophotometer. ^1H NMR spectra were obtained on a (79.542 MHz for ^1H and 20.00 MHz for ^{13}C) Varian FT80, with CDCl_3 as solvent and tetramethylsilane as the internal reference. Chemical shifts are given as δ values. Mass spectrum (70 eV) was recorded on a Varian Mat 711 instrument by direct introduction. Analysis was performed on a Perkin-Elmer 240 elemental analyser.

Table 1 Fractional atomic coordinates (Å), for compound **2**, C₁₂H₂₁-NO₃S₄, with esds in parenthesis

Atom	x	y	z
S(1)	0.2176(1)	0.2610(1)	0.0543(1)
S(2)	0.2412(1)	-0.0416(1)	0.4625(1)
S(3)	0.4391(1)	0.1900(1)	0.5057(1)
S(4)	0.0044(1)	0.2430(1)	0.5562(1)
O(2)	0.1252(2)	-0.1593(3)	0.0576(3)
O(3)	0.2799(2)	-0.0913(3)	0.0132(3)
O(8)	0.1728(2)	0.4337(3)	0.5070(3)
N(1)	0.1319(2)	0.1449(3)	0.3237(3)
C(1)	0.2143(2)	0.1404(3)	0.2104(4)
C(2)	0.2005(2)	-0.0556(4)	0.0872(4)
C(3)	0.3072(2)	0.2143(3)	0.3147(3)
C(4)	0.3760(2)	0.3713(4)	0.2893(5)
C(5)	0.3254(2)	0.1324(3)	0.4179(4)
C(6)	0.4209(3)	0.1966(7)	0.7333(5)
C(7)	0.3018(3)	-0.2153(4)	0.3963(6)
C(8)	0.1175(2)	0.2907(3)	0.4595(3)
C(9)	0.0043(3)	0.4545(5)	0.7260(5)
C(10)	0.2708(3)	-0.2728(5)	-0.1165(5)
C(11)	0.3661(4)	-0.3004(7)	-0.1593(8)
C(12)	0.1077(3)	0.1525(7)	-0.0589(6)

**Fig. 1**

Synthesis of Ethyl 3-Methyl-2,4,4-tri(methylthio)-2-(methylthiocarbonylamino)but-3-enoate 2.—Compound **1** was synthesized from ethyl glycinate hydrochloride, carbon disulphide and methyl iodide following a published procedure.¹

Condensation between α -metallated **1 and trifluoroacetone.** A solution of **1** (1 g, 5 mmol) in dry THF (4 ml) was dropwise added to a stirred solution of KOBu^t (0.85 g, 7.5 mmol) in dry THF (50 ml; kept at -78 °C under N₂). After 0.5 h at -78 °C, a solution of the trifluoroacetone (7.5 mmol) in dry THF (4 ml) was slowly added. The reaction mixture was kept at -78 °C during 0.5 h, and then at 0 °C for 2.5 h and at 20 °C for 1.5 h; it was then hydrolysed and extracted with diethyl ether (3 × 230 ml). The combined organic layers were dried (MgSO₄) and evaporated to dryness, and the residue was treated with pentane to precipitate **2**; the latter was recrystallized from hexane-ethyl acetate, m.p. 114–116 °C (Found: C, 40.4; H, 6.0; N, 3.7; S, 36.4. C₁₂H₂₁NO₃S₄ requires C, 40.6; H, 5.9; N, 3.9; S, 36.1%); λ_{max} (EtOH)/nm 214.6 (ϵ 3883 dm³ mol⁻¹ cm⁻¹) and 262.5 (7479); ν_{max} (KBr)/cm⁻¹ 3375, 1712, 1680 and 710; δ_{H} (CDCl₃) 1.28 (t, 3 H, *J* 7.9, CH₃CH₂), 2.00 (s, 3 H, CH₃C=), 2.18 (s, 3 H, C-SCH₃), 2.26 (s, 3 H), 2.33 [s, 3 H, =C(SCH₃)₂], 2.49 (s, 3 H, NHCOSCH₃), 4.22 (q, 2 H, *J* 7.9, CH₂CH₃) and 7.14 (br s, 1 H, NH); δ_{C} (DCCl₃) 12.36 (q, ¹*J* 141.94, NHCOSCH₃), 13.05 (q t, ²*J* 127.15, ²*J* 2.45, CH₃CH₂), 13.97 (q, ¹*J* 149.99, C-SCH₃), 16.87 [q, ²*J* 140.20, =C(SCH₃)₂], 17.15 [q, ²*J* 140.40, =C(SCH₃)₂], 20.98 (q, ²*J* 129.20, =C-CH₃), 62.64 (t, q, ²*J* 148.27, ²*J* 4.30, CH₂CH₃), 69.97 (m, quaternary C), 132.92 [m, =C(SMe)₂], 142.23 (q d, ²*J* 2.0, ³*J* 7.12, =C-CH₃), 164.48 (q,

²*J* 4.83, ³*J* 4.83, NHCOSCH₃) and 168.70 (q, ³*J* 3.35, CO₂Et); *m/z* (70 eV) 355 (1), 310 (13), 309 (13), 308 (100), 392 (4), 280 (3), 265 (3), 262 (4), 261 (4), 260 (36), 234 (3), 232 (8), 206 (10), 184 (30), 130 (8) and 75 (32).

Good crystals for X-ray diffraction were obtained for compound **2**, by evaporation of an ethanol solution. A crystal of dimensions 0.2 × 0.3 × 0.3 mm was used for data collection on a PW1100 diffractometer, employing graphite-monochromated Cu-K α radiation.

C₁₂H₂₁NO₃S₄, *M_w* = 355.56, colourless prismatic crystals, triclinic, space group *P*⁻¹, with *a* = 14.88(1), *b* = 8.37(1), *c* = 7.95(1) Å, α = 111.61(1), β = 83.98(2), γ = 105.8(1), *V* = 885.7(2) Å³, *Z* = 2, μ = 49.18 cm⁻¹, *D_c* = 1.348(2) g cm⁻³, Cu-K α = 1.5418, *F*(000) = 376, at room temperature.

Intensity measurements, structure determination and refinement. The intensities for 2965 independent reflections up to $\theta \leq 65^\circ$ were recorded using an $\omega/2\theta$ scan mode technique. The standard reflections measured every 90 min showed no crystal decomposition. 2657 Reflections were considered as observed with the criterium $I \geq 2\sigma(I)$ and used in subsequent calculations. The data were corrected for Lorentz and polarization factors and also an absorption correction was applied. The structure was solved by direct methods, MULTAN¹² and Fourier synthesis. Refinement was done by full-matrix least squares analysis with anisotropic temperature factors. All H-atoms were found in a difference synthesis and included in subsequent refinements as isotropic contributions. A convenient weighting scheme¹³ was used to prevent bias on $\langle w\Delta^2F \rangle$ vs. $\langle F_o \rangle$ and vs. $\langle \sin\theta/\lambda \rangle$. Final full matrix anisotropic weighted refinement (isotropic for H atoms) gave the discrepancy index *R* = 4.6 and *R_w* = 5.6. Scattering factors for neutral atoms were taken from the literature.¹⁴ Most calculations were performed using the XRay 70 System.¹⁵

Discussion

Final atomic co-ordinates for compound **1** are given in Table 1 and a projection of the structure with the labelling of the atoms, is shown in Fig. 1. Listings of bond lengths and bond angles together with the thermal parameters have been deposited with the Cambridge Crystallographic Data Centre.*

The molecule consists of the ethylbut-3-enoate open chain with two methylthio substituents at each end of the double bond and an asymmetric carbon atom containing a methylthio and a methylthiocarbonylamino group. The bond distances and angles for the three different types of the methylthio groups present in the molecule are: S(1)–C(12) = 1.790(5) Å and C(1)–S(1)–C(12) = 102.4°; S(4)–C(9) = 1.788(4) and C(8)–S(4)–C(9) = 100.9(3)°; S(2)–C(7), S(3)–C(6) = 1.803(5) and 1.784(5) Å and C(5)–S(2)–C(7), C(5)–S(3)–C(6) = 102.3(4) and 104.9(4)° respectively, within the range found for the C–S bond.¹⁶

The steric compression about the asymmetric centre is, however, remarkable. Bond distances on the asymmetric centre are greater than expected values:¹⁷ thus, C(1)–S(1) = 1.856(4), C(1)–C(2) = 1.539(4), C(1)–C(3) = 1.542(4) and N(1)–C(1) = 1.444(4) Å¹⁸ (from expected 1.81, 1.52, 1.53, 1.42 Å respectively).

The thioamide group [N(1)–C(8) = 1.350(3) and C(8)–O(8) = 1.203(3) Å] shows some polarization.¹⁸ The α,β -unsaturated ester [C(2)–O(2) = 1.199(4), C(2)–O(3) = 1.322(4), C(3)–C(5) = 1.333(5)] as expected, shows bond distances having no conjugate polar effect of the carbonyl group on the double bond.

* See 'Instructions for Authors (1992),' *J. Chem. Soc., Perkin Trans. 1*, 1992, Issue 1.

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