

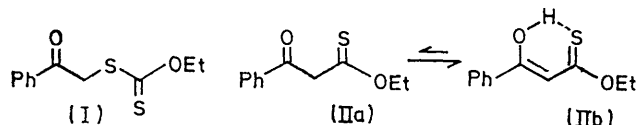
Preparation and Properties of β -Oxo-thionesters

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O-Ethyl *S*-phenacyl dithiocarbonate (I) and its *S*-acetyl analogue (III) are converted respectively into *O*-ethyl (benzoyl)thioacetate (II) and acetothioacetate (IV) by sulphide contraction. Keto-enol equilibria and alkylation of the anions of these β -oxo-thionesters have been investigated briefly.

ALTHOUGH β -thio-esters,¹ β -oxo-thioesters,² and also β -oxo-dithioesters³ are quite well known, there appear to be no reports of β -oxo-thionesters. Presumably this reflects the fact that the latter cannot be made by conventional acid-catalysed equilibration between an appropriate oxygen analogue and hydrogen sulphide.

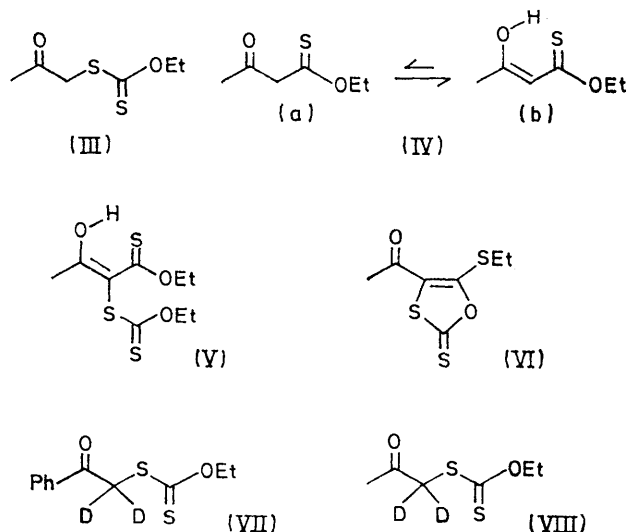
In the course of experiments concerning the alkylation of sulphur-activated carbanions, we found that treatment of *O*-ethyl *S*-phenacyl dithiocarbonate (I) with sodium hydride in tetrahydrofuran (THF) followed by quenching with sodium dihydrogen phosphate buffer gave, as major product, the α -oxo-thionester (II). We now describe the preparation and some properties of this type of compound.



A number of by-products were obtained in the earlier preparations of compound (II); the amounts of these could be reduced by performing the reaction in ether, the product being further purified by extraction into alkali. The assignment of structure (II) was based on analytical and spectroscopic data (see below and Experimental section) and confirmed by conversion of (II) into ethyl benzoylacetate on treatment with aqueous silver nitrate in aqueous acetone (accompanied by precipitation of silver sulphide). Thionesters readily undergo silver-ion-catalysed hydrolysis to carboxylate esters.⁴

In an analogous way *S*-acetyl *O*-ethyl dithiocarbonate (III) was converted into *O*-ethyl acetothio-

acetate (IV). Two by-products were relatively assigned structures (V) and (VI) (see Experimental section). A product analogous to (V) was also isolated from the reaction of the phenacyl ester (I).



Further study of the conditions for the conversion of the oxo-dithiocarbonates into the β -oxo-thionesters showed that at -15°C in ether compounds (I) and (III) reacted with sodium hydride with evolution of hydrogen to give, apparently, the respective sodium salts, since quenching with deuterium oxide buffer at that temperature gave the dideuterated dithiocarbonates (VII) and (VIII), respectively. Above 0°C , rearrangement of the sodium salts occurred. The reaction is thus an example of 'sulphide contraction *via* alkylative coupling'

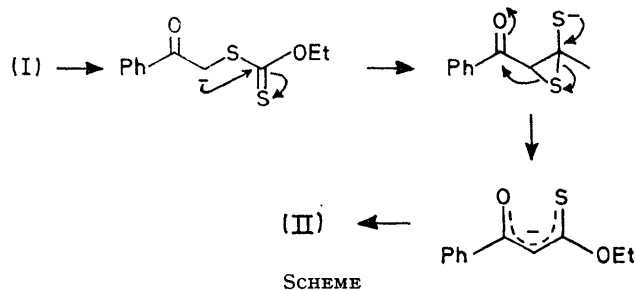
¹ R. Mayer and P. Barthel, *Chem. Ber.*, 1960, **93**, 428; S. Bleisch and R. Mayer, *ibid.*, 1967, **100**, 93.

² M. W. Cronyn, M. P. Chang, and R. A. Wall, *J. Amer. Chem. Soc.*, 1955, **77**, 3031.

³ A. Thuillier and J. Vialle, *Bull. Soc. chim. France*, 1962, 2182; R. Mayer and H. Hartmann, *Chem. Ber.*, 1964, 1886.

⁴ S. A. Karjala and S. M. McElvain, *J. Amer. Chem. Soc.*, 1933, **55**, 2966.

recently described and developed by Eschenmoser,⁵ and may be rationalised as shown in the Scheme. We have not investigated whether the inclusion of a thiophile, *e.g.* triphenylphosphine, as in Eschenmoser's procedure, can lead to an improvement in yield of β -oxo-thionester.



The β -oxo-thionesters are stable, yellow, sweetish smelling liquids which are extracted completely into aqueous *M*-sodium hydroxide but not into aqueous sodium carbonate. They are therefore quite acidic with pK_a values comparable with those of β -oxo-esters.

The spectroscopic properties of compounds (II) and (IV) (see Experimental section) are consistent with the compounds being highly enolised. Chelated enol structures (IIb) and (IVb) are assigned rather than the corresponding thioenols forms because of the characteristic low field positions of the n.m.r. signals attributed to the chelated protons: τ -4.03 and -3.57 for (IIb) and (IVb), respectively. Thioenol protons tend to absorb at much higher field (τ 2-5).^{6,7} Immediately after distillation, the n.m.r. spectra of compounds (II) and (IV) indicated a much higher proportion of keto tautomer than in old samples. This behaviour contrasts with that of simple β -oxo-esters, where the enol form is more volatile. A few hours after distillation, no signals due to the keto form were detected in the ¹H n.m.r. spectrum of compound (II) (in CCl₄). Equilibration of compound (IV) was much slower; after many hours in the presence of a trace of trifluoroacetic acid, the ¹H n.m.r. spectrum (in CCl₄) showed that 5% of keto form was present.

Summarised in Table 1 are the enol contents for some β -oxo-esters and certain thio-analogues. It is apparent that replacement of EtO by EtS has no effect on the tautomeric equilibrium, whereas substitution of ester carbonyl O by S leads to a marked displacement of the equilibrium in favour of the enol form. Since hydrogen bonding to sulphur should be less efficient than to oxygen, the observation is presumably a consequence of either the greater stability of the keto-form of a β -oxo-ester relative to that of a β -oxo-thionester (delocalisation energy of ester group > that of thionester group) or of the greater delocalisation energy of the chelated enol of the β -oxo-thionester. Some support for the latter presumption is provided by the first ionisation potentials as found by

⁵ A. Eschenmoser, *Quart. Rev.*, 1970, **24**, 366; M. Roth, P. Dubs, E. Gotschi, and A. Eschenmoser, *Helv. Chim. Acta*, 1971, **54**, 710; W. Hefte, R. W. Balsiger, and K. Thoma, *ibid.*, 1974, **57**, 1242.

⁶ Z. Reyes and R. M. Silverstein, *J. Amer. Chem. Soc.*, 1958, **80**, 6367; F. Duus, *Tetrahedron*, 1972, **28**, 5923; 1974, **30**, 3753.

photoelectron spectroscopy.⁸ That for compound (IV) is 9.0 eV, whereas the corresponding value for ethyl acetoacetate is 8.38 eV.

TABLE 1

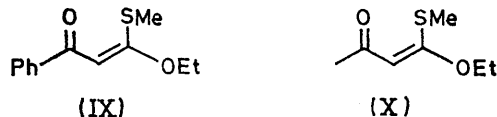
Enol contents of some β -oxo-esters and thio-analogues.

Compound	% Enol at equilibrium ^a
	28 ^b
	28 ^c
	94 ^d
	95 ^e
	50 ^{f,g}
	ca. 100 ^d
	ca. 98 ^e

^a Solvent CCl₄ at ca. 25 °C unless otherwise stated. ^b M. T. Rogers and J. L. Burdett, *Canad. J. Chem.*, 1965, **43**, 1516. ^c F. Duus, P. Jakobsen, and S.-O. Lawesson, *Tetrahedron*, 1968, **24**, 5323. ^d Ref. 7. ^e This work. ^f H. Wamhoff, G. Höffer, H. Lander, and F. Korte, *Annalen*, 1969, **722**, 12. ^g Solvent C₆H₁₂.

The ¹³C n.m.r. spectra of compounds (II) and (IV) are summarised in Table 2. Both spectra could be fully assigned by assuming the presence of keto-enol mixtures and making appropriate comparisons.⁹

The sodium salts of the β -oxo-thionesters (II) and (IV) were methylated with methyl iodide in THF. The anions are tridentate nucleophiles which might in principle be alkylated on carbon, oxygen, or sulphur; as expected however the respective products (IX) and (X) obtained in moderate yield were keten hemithioacetals derived from *S*-methylation.



EXPERIMENTAL

Instruments used were as follows: i.r. spectra Perkin-Elmer 257 (liquid film unless stated); ¹H n.m.r. Perkin-Elmer 2841.

⁷ M. Saquet and A. Thuillier, *Bull. Soc. chim. France*, 1967, 2841.

⁸ G. Mines, Physical Chemistry Laboratory, Oxford, personal communication.

⁹ J. B. Stothers, 'Carbon-13 N.M.R. Spectroscopy,' Academic Press, London, 1972.

Elmer R10, R14, or R32 (liquid samples in CCl_4 , solid samples in CDCl_3 , Me_4Si as internal standard); ^{13}C n.m.r. Bruker HFX 90 (22.63 MHz) with broad band proton decoupling.

Unless otherwise stated, light petroleum had b.p. 30–40°.

O-Ethyl *S*-Phenacyl Dithiocarbonate (I).—Phenacyl chloride (15 g, 0.1 mol) in acetone (100 ml) was added slowly with stirring to potassium *O*-ethyl dithiocarbonate (16 g, 0.1 mol) in acetone (350 ml). After 1 h, the solvent was removed under reduced pressure and the residue was

0.2 mmHg to give *O*-ethyl (benzoyl)thioacetate (3.5 g, 34%) as a bright yellow viscous liquid (Found C, 63.5; H, 6.0; S, 15.4. $\text{C}_{11}\text{H}_{12}\text{O}_2\text{S}$ requires C, 63.25; H, 5.75; S, 15.65%), ν_{max} 1 690, 1 610, 1 575, 1 455, 1 400, 1 260, 1 180, 765, and 690 cm^{-1} , τ -4.03 (1 H, s, chelated enolic OH), 2.1–2.7 (5 H, m, Ph), 3.73 (1 H, s, vinylic enolic H), 5.49 (2 H, q, J 7 Hz, $\text{O}\cdot\text{CH}_2\cdot\text{CH}_3$), and 8.60 (3 H, t, J 7 Hz, $\text{O}\cdot\text{CH}_2\cdot\text{CH}_3$). Signals at τ -4.03 and 3.73 slowly disappeared in the presence of $\text{D}_2\text{O}\text{-CF}_3\cdot\text{CO}_2\text{D}$ the latter signal being considerably less readily removed. Immediately after distillation

TABLE 2

 ^{13}C N.m.r. data for β -oxo-thionesters ^a

Compound	(IIa)				(IVa)				
	C-1	C-2	C-3	C-4	C-5	C-6	C-7	C-8	C-9
(IIa)	13.3	68.2	212.9	56.6	190.0	132.7	126.7	127.5	129.0
(IIb)	13.7	64.9	207.7	100.2	171.9	134.3	126.0	128.2	131.1
(IVa)	13.4	68.2	212.7	61.4	197.4	29.0			
(IVb)	13.7	64.6	207.9	102.6	176.4	22.8			

^a Chemical shifts in p.p.m. downfield from tetramethylsilane for solutions in CCl_4 .

partitioned between water (100 ml) and ether (100 ml). The ethereal layer was decanted, washed with water and brine, dried (MgSO_4), and evaporated to give the dithiocarbonate (22.6 g, 94%) as a light yellow oil (lit.,¹⁰ m.p. 32°), ν_{max} 2 900, 1 680, 1 595, 1 580, 1 450, 1 290, 1 230, 1 110, 1 050, 980, 750, 690, and 650 cm^{-1} , τ 2.0–2.5 (5 H, m, Ph), 5.37 (2 H, s, α to CO), 5.40 (2 H, q, J 7 Hz, $\text{O}\cdot\text{CH}_2\cdot\text{CH}_3$), and 8.60 (3 H, t, J 7 Hz, $\text{O}\cdot\text{CH}_2\cdot\text{CH}_3$), M^+ 240.

S-Acetonyl *O*-Ethyl Dithiocarbonate (III).—Redistilled chloroacetone (18.5 g, 0.2 mol) in acetone (100 ml) was added with stirring to potassium *O*-ethyl dithiocarbonate (32 g, 0.2 mol) in acetone (240 ml) over 10 min. The solvent was removed and the residue was added to water (200 ml) and extracted with ether (2×100 ml). The ethereal layer was washed with water and brine, dried (MgSO_4), and evaporated. The residue was distilled at 84–86° and 0.2 mmHg to give the dithiocarbonate (32.4 g, 91%) as a light yellow oil (Found: C, 40.5; H, 5.65; S, 35.6. $\text{C}_6\text{H}_{10}\text{O}_2\text{S}_2$ requires C, 40.5; H, 5.65; S, 35.95%), ν_{max} 1 720, 1 355, 1 220, 1 110, 1 050, and 1000 cm^{-1} , τ 5.33 (2 H, q, J 7 Hz, $\text{O}\cdot\text{CH}_2\cdot\text{CH}_3$), 6.07 (2 H, s, $\text{S}\cdot\text{CH}_2$), 7.74 (3 H, s, MeCO), and 8.54 (3 H, t, J 7 Hz, $\text{O}\cdot\text{CH}_2\cdot\text{CH}_3$), λ_{max} 276 nm (ϵ 1.05×10^4), M^+ 178.

O-Ethyl (Benzoyl)thioacetate (II).—Sodium hydride (60% oil suspension; 2.5 g) was washed with light petroleum (3×50 ml) and suspended in stirred ether (100 ml) under nitrogen at 10 °C. *O*-Ethyl *S*-phenacyl dithiocarbonate (12.0 g, 0.05 mol) in ether (50 ml) was added dropwise over 30 min, and after a further 30 min the mixture was poured onto aqueous potassium dihydrogen phosphate (17 g in 200 ml). The ethereal layer was decanted, and the aqueous layer was extracted with ether (2×100 ml). The extracts were washed with brine, concentrated (to 100 ml), and extracted with aqueous *m*-potassium hydroxide (2×50 ml). The latter extracts were immediately poured onto potassium dihydrogen phosphate (17 g in 200 ml), and extracted with ether (3×75 ml). The ethereal solution was dried (MgSO_4) and evaporated and the residue was distilled at 126° and

45% of the keto form was observed; by subtraction it has the following spectrum: τ 1.9–2.7 (5 H, m, Ph), 5.49 (2 H, q, J 7 Hz, $\text{O}\cdot\text{CH}_2\cdot\text{CH}_3$), 5.67 (2 H, s, CH_2 α to C=O and C=S), and 8.66 (3 H, t, J 7 Hz, $\text{O}\cdot\text{CH}_2\cdot\text{CH}_3$), λ_{max} (MeOH) 345 nm (ϵ 2.06×10^4), λ_{max} (MeOH-KOH, *i.e.* enolate) 366 nm (ϵ 2.84×10^4), M^+ 208.

O-Ethyl Acetothioacetate.—Sodium hydride (60% oil suspension; 2.4 g) was washed with light petroleum (3×50 ml) and suspended in stirred dry ether (100 ml) under nitrogen at 10 °C. *S*-Acetonyl *O*-ethyl dithiocarbonate (8.9 g, 0.05 mol) in ether (20 ml) was added dropwise over 20 min, and after a further 10 min the mixture was poured onto potassium dihydrogen phosphate (16 g in 100 ml). The ethereal layer was decanted, and the aqueous layer was extracted with ether (2×50 ml). The combined ethereal phase was washed with brine, dried (MgSO_4), and evaporated. The residue was dissolved in light petroleum and chromatographed on silica gel (400 g) [elution with light petroleum-ether (9:1)]. The appropriate fractions were pooled, evaporated, and distilled at 93–94° and 21 mmHg to give *O*-ethyl acetothioacetate (1.75 g, 24%) as a light yellow mobile liquid (Found C, 49.4; H, 6.75; S, 21.65. $\text{C}_6\text{H}_{10}\text{O}_2\text{S}$ requires C, 49.3; H, 6.9; S, 21.95%), ν_{max} 1 610, 1 250, and $1 220\text{ cm}^{-1}$, τ -3.57 (1 H, s, chelated enolic OH), 4.47 (1 H, s, vinylic enolic H), 5.52 ($\frac{1}{2}$ H, q, J 7 Hz, $\text{O}\cdot\text{CH}_2\cdot\text{CH}_3$ of keto-form), 5.60 (2 H, q, J 7 Hz, $\text{O}\cdot\text{CH}_2\cdot\text{CH}_3$ of enol form), 6.27 ($\frac{1}{2}$ H, s, CH_2 α to C=O in keto-form), 7.86 ($\frac{3}{2}$ H, s, CH_3 α to CO of keto-form), 8.01 (3 H, s, allylic CH_3 of enol form), 8.59 ($\frac{3}{2}$ H, t, J 7 Hz $\text{O}\cdot\text{CH}_2\cdot\text{CH}_3$ of keto-form), 8.63 (3 H, t, J 7 Hz, $\text{O}\cdot\text{CH}_2\cdot\text{CH}_3$ of enol form) (this spectrum is consistent with a 4:1 enol-keto ratio, on addition of $\text{CF}_3\cdot\text{CO}_2\text{D}$ the ratio slowly moves to 19:1 and with D_2O the singlets at -3.57 and 4.47 disappear very slowly); λ_{max} (MeOH) 240 (ϵ 1.04×10^4) and 314 nm (9.4×10^3), λ_{max} (MeOH-KOH, *i.e.* enolate) 337 nm (ϵ 3.7×10^4), M^+ 146.

In an earlier preparation from *S*-acetonyl *O*-ethyl

¹⁰ B. Groth, *Arkiv Kemi.*, 1924, 9, 63.

dithiocarbonate (3.6 g) with sodium hydride in THF a product (300 mg), b.p. (partial decomp.) 120° at 0.1 mmHg, was obtained which had τ -5.05 (1 H, s, chelated enolic OH), 5.5 (4 H, quintet, J 7 Hz, CH_2 of two EtO), 7.65 (3 H, s, allylic CH_3), and 8.61 (6 H, t, J 7 Hz, CH_3 of EtO), M^+ 266. The compound was tentatively assigned structure (V).

The residue from the distillation in another preparation (7.1 g of dithiocarbonate) was extracted several times with light petroleum, the extract was evaporated, the residue triturated with ether, and the resulting solid crystallised from light petroleum (b.p. 60–80°) to give pale yellow needles (250 mg), m.p. 67–69°, ν_{max} (CCl_4) 1 690 and 1 660 cm^{-1} , τ 7.0 (2 H, q, J 7 Hz, $\text{CH}_2\cdot\text{CH}_3$), 7.6 (3 H, s, MeCO), and 8.56 (3 H, t, J 7 Hz, $\text{CH}_2\cdot\text{CH}_3$) M^+ , 220 (Found: C, 38.35; H, 3.8; S, 43.25. $\text{C}_7\text{H}_8\text{O}_2\text{S}_3$ requires C, 38.2; H, 3.65; S, 43.6%), tentatively identified as 4-acetyl-5-ethylthio-1,3-oxathiole-2-thione (VI).

S-(α -Dideuteriophenacyl) *O*-Ethyl Dithiocarbonate.—Sodium hydride (60% oil suspension, 0.4 g) was washed with light petroleum (2 \times 50 ml) and suspended in stirred dry ether (30 ml) under nitrogen at -15 °C. Ethanol (0.05 ml) and *O*-ethyl *S*-phenacyl dithiocarbonate (1.2 g, 0.005 mol) in ether (5 ml) were added dropwise. When effervescence ceased (10 min), potassium dihydrogen phosphate (1.36 g) in deuterium oxide (5 ml) was added rapidly. The ethereal layer was decanted, washed with brine, dried (MgSO_4), and evaporated to give the dideuterio-derivative (VII) (1.07 g, 85%), b.p. 130° at 0.04 mmHg, τ 2–2.5 (5 H, m, aromatic), 5.39 (2 H, q, J 7 Hz, $\text{O}\cdot\text{CH}_2\cdot\text{CH}_3$), and 8.57 (3 H, t, J 7 Hz, $\text{O}\cdot\text{CH}_2\cdot\text{CH}_3$), M^+ 242.

S-(1,1-Dideuterioacetyl) *O*-Ethyl Dithiocarbonate.—In a similar experiment, *S*-acetyl *O*-ethyl dithiocarbonate (0.9 g) gave the dideuterio-derivative (VIII) (0.60 g, 65%), τ 5.33 (2 H, q, J 7 Hz, $\text{O}\cdot\text{CH}_2\cdot\text{CH}_3$), 7.74 (3 H, s, MeCO), and 8.55 (3 H, t, J 7 Hz, $\text{O}\cdot\text{CH}_2\cdot\text{CH}_3$), M^+ 180.

Reaction of O-Ethyl (Benzoyl)thioacetate with Silver Nitrate.—*O*-Ethyl (benzoyl)thioacetate (0.04 g, 0.0016 mol) was dissolved in acetone (20 ml) and aqueous silver nitrate (2*N*, 2 ml) was added with shaking. The solution became deep orange and a black precipitate gradually appeared. After 3 h the liquid was filtered and evaporated. The residue was extracted with light petroleum and the extract dried (MgSO_4) and evaporated to give a light yellow liquid

(95 mg, 25%), identified as ethyl benzoylacetate by chromatographic and spectroscopic comparisons with an authentic sample.

3-Ethoxy-3-methylthio-1-phenylprop-2-en-1-one (IX).—Sodium hydride (60% oil suspension; 0.25 g) was washed with light petroleum (2 \times 50 ml) and suspended in stirred THF (20 ml) under nitrogen at 20 °C. *O*-Ethyl (benzoyl)thioacetate (1.2 g, 0.006 mol) in THF (5 ml) was added dropwise, and hydrogen was evolved leaving a bright yellow solution. After 30 min methyl iodide (1 g, 0.007 mol) was added, and the solution was stirred for a further 2 h. The solution was then poured onto water (100 ml) and extracted with ether (2 \times 40 ml). The combined extracts were washed with brine, dried (MgSO_4), and evaporated. The solid residue was recrystallised twice from ethanol to give the methylthio-derivative (0.54 g, 42%) as needles, m.p. 129–132° (Found C, 64.95; H, 6.45; S, 14.15. $\text{C}_{12}\text{H}_{14}\text{O}_2\text{S}$ requires C, 64.85; H, 6.35; S, 14.4%), ν_{max} (CCl_4) 1 630, 1 510, 1 470, 1 260, 1 190, and 900 cm^{-1} , τ 2.1–2.6 (5 H, m, Ph), 3.52 (1 H, s, vinyl H), 5.79 (2 H, q, J 7 Hz, $\text{O}\cdot\text{CH}_2\cdot\text{CH}_3$), 7.70 (3 H, s, SMe), and 8.55 (3 H, t, J 7 Hz, $\text{O}\cdot\text{CH}_2\cdot\text{CH}_3$), λ_{max} 323 nm (ϵ 2.33×10^4), M^+ 222.

4-Ethoxy-4-methylthiobut-3-en-2-one (X).—Sodium hydride (60% oil suspension; 0.4 g) was washed with light petroleum (2 \times 50 g) and suspended in stirred THF (25 ml) under nitrogen at 0 °C. *O*-Ethyl acetothioacetate (0.73 g, 0.005 mol) in THF (5 ml) was added dropwise, and evolution of hydrogen was observed. After 5 min methyl iodide (1 ml, 0.02 mol) was added and the solution was left at 0 °C for 30 min. The solution was poured onto water (100 ml) and extracted with ether (50 ml). The ethereal layer was washed with water, dried (MgSO_4), and evaporated. The solid residue was recrystallised twice from petroleum giving the methylthio-derivative (0.15 g, 20%) as plates, m.p. 48–49°, ν_{max} (Nujol) 1 660, 1 500, 1 240, and 1 150 cm^{-1} , τ 4.42 (1 H, s, vinyl H), 5.96 (2 H, q, J 7 Hz, $\text{O}\cdot\text{CH}_2\cdot\text{CH}_3$), 7.81 (3 H, s, SMe), 7.97 (3 H, s, MeCO), and 8.58 (3 H, t, J 7 Hz, $\text{O}\cdot\text{CH}_2\cdot\text{CH}_3$), λ_{max} (MeOH) 295 nm (ϵ 1.55×10^4), M^+ 160.

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