A new efficient synthesis of α-methyl-β-ketoesters through an Eschenmoser sulfide reaction

Christian Bellec and Olivier Gaurat

Abstract: Various α-methyl-β-ketoesters were readily synthesized through Eschenmoser condensation of thioamides with a commercially available bromoester. β-Enaminoesters were easily prepared through this sulfide contraction reaction and were hydrolysed to afford the corresponding β-ketoesters in moderate to good yields.

Key words : α-alkylated-β-ketoesters, Eschenmoser, β-enaminoesters.

Résumé : Divers β-cétoesters-α-méthylés sont facilement préparés par condensation d'Eschenmoser de thioamides avec un bromoester commercial. Les β-énaminoesters, facilement préparés par cette réaction d'extrusion de soufre, sont hydrolysés pour conduire aux β-cétoesters correspondants avec des rendements bons à modérés.

Mots clés : β-cétoesters α-alkylés, Eschenmoser, β-énaminoesters.

Introduction

β-Ketoesters are widely recognized as very useful auxiliaries for several organic syntheses. Many synthetic approaches to α-unsubstituted compounds have been reported in the literature over the years (1–3). Conversely, investigations into reactions giving α-alkylated β-ketoesters directly have been more limited. Most often, these latter compounds have been obtained by alkylation of unsubstituted moieties, with the obvious disadvantages associated with this methodology (4, 5).

For some time, we have been interested in the synthesis of β-enaminoesters using the Eschenmoser coupling reaction (6, 7). Such enaminoesters are particularly suitable intermediates for the synthesis of various alkaloids (8, 9). More recently, we became interested in a new application of the efficient Eschenmoser alkylation sulfur contraction reaction for a short and convenient access to α-monoalkylated β-ketoesters that could take its place among other methodologies.

In the literature, various synthetic routes have been exploited for access to α-alkylated β-ketoesters. The direct alkylation method with aliphatic substrates, initially reported by Robinson (1), has been seldom used and leads generally to poor yields (10). Indeed, it is often difficult to avoid a double condensation or an *O*-alkylation process, although some recent modifications of the work-up procedure gave rise to better results (11, 12).

Received 10 December 2003. Published on the NRC Research Press Web site at http://canjchem.nrc.ca on 2 November 2004.

C. Bellec[1,2] and O. Gaurat. Laboratoire de Chimie des Hétérocycles (UMR 7611), Université Pierre et Marie Curie, 4 Place Jussieu, 75252 Paris CEDEX 05, France.

[1]Present address: Laboratoire de Chimie organique, Université Pierre et Marie Curie, Case courrier 64, 4 Place Jussieu, 75252 Paris CEDEX 05, France.

[2]Corresponding author (e-mail: bellec@ccr.jussieu.fr).

The preparation of β-ketoesters from malonic acid ester precursors has generally been rarely used for monoalkylated compounds (2, 4, 13). Other synthetic approaches, using a modified Reformatsky reaction (14–16), treatment of an acylpyrazole with an organozinc reagent (17), or α-diazo-β-hydroxyester rearrangment (18), have been described but do not have, on the whole, general applicability. Oxidation of β-hydroxyesters has most often been carried out with nonalkylated substrates (19, 20).

We wish to report herein a new methodology that provides direct access to α-substituted β-ketoesters from enaminoesters. These substrates are readily prepared through an Eschenmoser sulfide reaction involving condensation of thioamides with bromoesters and are then hydrolyzed, in a final step, to afford the desired ketoesters with moderate to good yields.

Results and discussion

Synthesis of thioamides

The synthesis of thioamides **2a–2f** was carried out by condensation of acyl chlorides **1a**–**1f** with pyrrolidine in the presence of pyridine. Amide moieties obtained in a first step were not isolated but were directly transformed into thioamides using P_4S_{10} (Scheme 1).

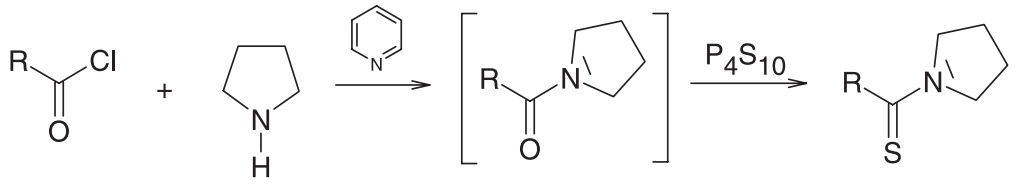
Synthesis of α-substituted β-ketoesters

Various α-substituted β-ketoesters were produced by hydrolysis of the corresponding enaminoesters, which were most often not isolated. The synthesis of these enaminoesters was first carried out by adapting the modified Eschenmoser coupling reaction previously described for thiolactams (6). Thus, a mixture of triethylamine and triphenylphosphine in dry acetonitrile was slowly added to a solution of thioamide **2** and commercially available 2-bromopropionic acid ethylester (**3**) in refluxing CH_3CN (Scheme 2).

The condensation was monitored by gas chromatography. Despite a good rate of thioamide transformation (except in

 doi: 10.1139/V04-088

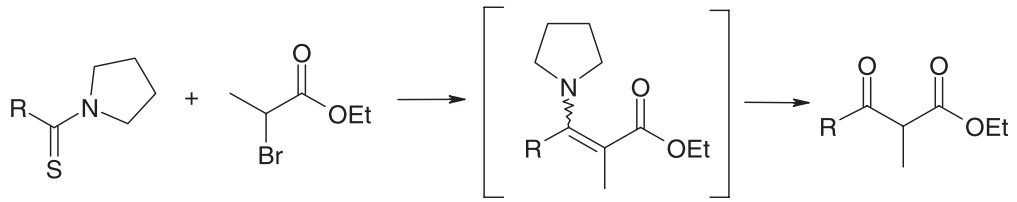
Scheme 1. Preparation of thioamides **2a**–**2f**.



1a – 1f **2a – 2f**

Compound	R
a	*n*-Pr
b	*i*-Bu
c	*t*-Bu
d	*n*-Pent
e	Ph
f	$(CH_2)_2COOMe$

Scheme 2. Preparation of β-enaminoesters **5a**–**5f**.



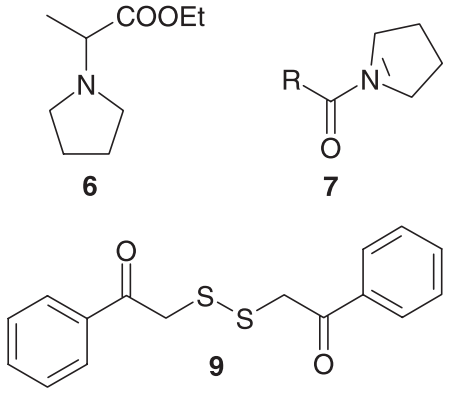
2a – 2f **3** **4a – 4f** **5a – 5f**

the case of **2c**, for which no reaction was observed), several by-products were observed in the crude reaction mixture. Besides the α-substituted β-ketoester **5** and the desulfuration product $Ph_3P=S$, the aminoester **6** (Scheme 3), amide **7**, and sulfide **8** ($EtOOC–CH(CH_3)–S–CH(CH_3)–COOEt$) were also detected.

Although the condensation was carried out under a nitrogen atmosphere and despite the use of an anhydrous solvent, some of the thioamide **2** was generally transformed in the reaction mixture to the corresponding amide **7**. Similarly, the presence of lactam as a by-product in the Eschenmoser sulfide contraction of thiolactams with halogenoesters has been reported by some authors (21, 22). The formation of the aminoester **6** could be explained by a nucleophilic substitution of pyrrolidine on the bromoester **3**. Indeed, pyrrolidine was formed in situ by hydrolysis of the enaminoester. Michael and co-workers reported, in a similar manner, the presence of the disulfide **9** in an Eschenmoser reaction with bromoacetophenone (23).

As several by-products were present in the crude reaction mixture, it was difficult to purify the β-ketoester **5** by chromatography on a silica gel column. With various eluents, the yield of the α-substituted β-ketoester was poor to moderate, and some fractions always contained $Ph_3P=S$ and Ph_3P. Therefore, it was necessary to modify the reaction conditions to minimize the formation of by-products in the condensation–extrusion process and to facilitate the elimination of these by-products in the experimental work-up. With Ph_3P as the thiophilic agent, the major difficulty was in eliminating the desulfuration product $Ph_3P=S$. In the case of thiolactam condensation, this problem was resolved by acidic extraction of the cyclic enaminoester with HCl (2 mol/L) (6), but with thioamides, the hydrolysis of the formed enaminoester, leading to the ketoester, was too rapid to permit a satisfactory extraction. So our idea was to mod-

Scheme 3.



6 **7** **9**

Table 1. Reaction conditions for transformation of **2a** to **3a**.

Thiophilic reagent	Reaction time (h)	Sulfide **8** (%)
Ph_3P	6	25
$P(OEt)_3$	3	11.5
$P(NR_2)_3$	1	Traces

Table 2. Comparative results for various thiophilic reagents.

Thioamide	Thiophilic reagent	Sulfide **8** (%)	Thioamide **2** transformed (%)	β-Ketoester **5** isolated yield[a] (%)	Yield from lit.[b] (%)
2a	Ph_3P	25	100	28	58[c], 64[d]
	$P(OEt)_3$	11	94	47	
	$P(NR_2)_3$	<1	100	60	
2b	$P(OEt)_3$	10	95	60	80[e]
	$P(NR_2)_3$	<1	80	70	
2d	$P(OEt)_3$	35	88	30	75[e]
	$P(NR_2)_3$	<1	86	72.5	
2e	Ph_3P	27	85	40	52[f], 71[g]
	$P(OEt)_3$	9	93	60	
	$P(NR_2)_3$	<1	100	67	

Note: For **2c**, no reaction was observed, irrespective of which desulfuration reagent was employed.
[a]After purification by chromatography.
[b]Obtained using other synthetic methods.
[c]From ref. 26.
[d]From ref. 27.
[e]From ref. 15.
[f]From ref. 4.
[g]From ref. 17.

ify the thiophilic reagent. The use of triethylphosphite ($P(OEt)_3$) in CH_3CN and the same work-up as with Ph_3P did not result in a significant modification of the sulfide yield. On the other hand, when the condensation was carried out without solvent (5 mL of CH_3CN being added in the desulfuration step to obtain a concentrated but homogeneous medium), the sulfide yield relative to the enaminoester–ketoester yield was substantially reduced. Unfortunately, the solubility of $(EtO)_3P{=}S$ in water is very low, and the work-up only led to its partial elimination. Hence, another thiophilic agent, $P(NR_2)_3$, was employed. Indeed, tris(alkylamino)phosphines have been reported to be good reagents for the transformation of disulfides to sulfides and for the reduction of thiiranes to olefins (24, 25). The same work-up as with $P(OEt)_3$ was carried out without solvent, but under a nitrogen atmosphere. In the same reaction time, a better transformation rate of the thioamide **2** was observed (Table 1), but, notably, only traces (<1% by gas chromatographic analysis) of the sulfide **8** were detected.

Nevertheless, purification of the β-ketoester on a silica gel column always resulted in some fractions that were contaminated with the desulfuration product $S{=}P(NE_2)_3$, no matter which elution solvent was employed. However, the presence of **8** in very small amounts permitted an appreciable improvement in the extraction yield of the α-substituted β-ketoester **5** in the chromatographic step. Table 2 shows comparative results for the various thiophilic agents employed. For comparison, we have also listed the yields reported in the literature for many different methods and experimental conditions.

Thus, with tris(dimethylamino)phosphine or tris(diethylamino)phosphine as the thiophilic reagent, α-alkylated β-ketoesters were synthesized via an Eschenmoser reaction in moderate to good yields. We have performed several other syntheses using different bromoesters, but no other series has been investigated in a systematic manner. However, even from these limited experiments, this method remains efficient and leads, after extraction, to similar yields to those in Table 2.

Conclusion

We have shown that several α-substituted β-ketoesters can be easily obtained by an efficient direct condensation of bromoesters with thiolactams through the Eschenmoser sulfur extrusion reaction. This strategy represents a quick and convenient route that can take its place among the available methodologies that provide access to these compounds.

Experimental

General procedure for thioamide synthesis

In a mixture of 150 mL of pyridine and about 0.2 mol of pyrrolidine, a slight excess (<1.1 equiv.) of acyl chloride **1** was added dropwise at room temperature. The stirred solution was refluxed for 30 min. After cooling, P_4S_{10} was added and the mixture was heated for 2 h and then poured into 500 mL of 1 mol/L HCl. The mixture was stirred for 1 h and was then extracted three times with 150 mL of dichloromethane (CH_2Cl_2). The combined organic layers were washed successively with 2 × 150 mL of 1 mol/L HCl, 2 × 150 mL of water, and 2 × 100 mL of a saturated solution of sodium hydrogen carbonate ($NaHCO_3$), then dried over magnesium sulfate ($MgSO_4$) and evaporated. The residue was purified by chromatography on a silica gel column.

1-Pyrrolidin-1-yl butan-1-thione (2a)

Condensation of 15.62 g (0.22 mol) of pyrrolidine and 25 g (0.235 mol, 1.07 equiv.) of butanoyl chloride **1a** gave, after chromatography using ethyl acetate (EtOAc)/cyclohexane (1/1), 28.76 g of **2a**. Yield 83%. Oil. ^{1}H NMR: 3.90 and 3.66 (t, J = 7 Hz, 4H), 2.70 (t, J = 7.5 Hz, 2H), 2.10–2.00 (m, 4H), 1.80 (m, 2H), and 1.05 (t, J = 7.5 Hz, 3H). ^{13}C NMR: 200.6, 50.9, 46.1, 26.6, 24.6, 22.5, and 14.1. IR

($CHBr_3$): 1480 cm^{-1}. Anal. calcd. (%) for $C_8H_{15}NS$: C 61.12, H 9.62, N 8.91; found: C 61.25, H 9.57, N 8.84.

3-Methyl-1-pyrrolidin-1-yl butan-1-thione (2b)

Using the same procedure, condensation of 6.39 g (0.09 mol) of pyrrolidine and 12.05 g (0.1 mol, 1.1 equiv.) of isobutyryl chloride **1b** gave, after chromatography using EtOAc/cyclohexane (1/1), 11.9 g of **2b**. Yield 77%. Yellow oil. ^{1}H NMR: 3.85 and 3.55 (2t, J = 7 Hz, 4H), 2.54 (d, J = 7.5 Hz, 2H), 2.30 (m, 1H), 2.02 and 1.85 (2t, J = 7 Hz, 4H), and 0.94 (d, J = 7.5 Hz, 6H). ^{13}C NMR: 199.7, 53.6, 51.1, 50.7, 28.9, 26.1, 24.0, and 22.1. IR ($CHBr_3$): 1480 cm^{-1}. Anal. calcd. (%) for $C_9H_{17}NS$: C 63.13, H 10.00, N 8.18; found: C 63.03, H 10.11, N 8.23.

2,2-Dimethylpyrrolidin-1-yl propan-1-thione (2c)

Using the same work-up, condensation of 14.2 g (0.2 mol) of pyrrolidine and 25 g (0.21 mol, 1.05 equiv.) of pivaloyl chloride **1c** gave, after chromatography using EtOAc/cyclohexane (1/1), 32.3 g of **2c**. Yield 94%. Oil. 1H NMR: 3.90 and 3.75 (2t, J = 7 Hz, 4H), 2.10 and 1.80 (2t, J = 7Hz, 4H), and 1.36 (s, 9H). ^{13}C NMR: 208.5, 57.6, 52.7, 43.5, 30.2, 27.3, and 22.9. IR ($CHBr_3$): 1430 cm^{-1}. Anal. calcd. (%) for $C_9H_{17}NS$: C 63.13, H 10.00, N 8.18; found: C 63.27, H 10.02, N 8.12.

1-Pyrrolidin-1-yl hexan-1-thione (2d)

Condensation of 12.6 g (0.177 mol) of pyrrolidine and 25 g (0.186 mol, 1.05 equiv.) of hexanoyl chloride **1d** gave, after chromatography with EtOAc/cyclohexane (1/1), 30.2 g of **2d**. Yield 92%. Oil. ^{1}H NMR: 3.80 and 3.50 (2t, J = 7 Hz, 4H), 2.62 (t, J = 7 Hz, 2H), 2.05 and 1.88 (2q, J = 7 Hz, 4H) 1.70 (m, 2H), 1.32–1.25 (m, 4H), and 0.84 (t, J = 7 Hz, 3H). ^{13}C NMR: 201.2, 54.3, 51.0, 44.6, 32.0, 29.1, 26.8, 24.8, 22.9, and 14.4. IR ($CHBr_3$): 1430 cm^{-1}. Anal. calcd. (%) for $C_{10}H_{19}NS$: C 64.83, H 10.34, N 7.56; found: C 64.90, H 10.28, N 7.51.

1-Thiobenzoyl pyrrolidine (2e)

Condensation of 5.32 g (0.075 mol) of pyrrolidine and 11.24 g (0.08 mol, 1 equiv.) of benzoyl chloride **1e** gave, after chromatography with EtOAc/cyclohexane (1/1), 14 g of a yellow solid **2e**. Yield 97.5%; mp 73 °C. ^{1}H NMR: 7.30–7.20 (m, 5H), 3.90 and 3.39 (2t, J = 7 Hz, 4H), and 2.00–1.90 (m, 4H). ^{13}C NMR: 197.4, 144.3, 129.0, 128.6, 126.0, 54.2, 53.8, 26.8, and 25.0. IR ($CHBr_3$): 1505, 1490, and 1475 cm^{-1}. Anal. calcd. (%) for $C_{11}H_{13}NS$: C 69.09, H 6.85, N 7.33; found: C 68.98, H 6.80, N 7.40.

4-Pyrrolidin-1-yl-4-thioxobutanoic acid methylester (2f)

For the synthesis of the intermediate amide, the following specific procedure was used: 6.39 g (0.09 mol) of pyrrolidine was condensed with 15.05 g (0.1 mol, 1.1 equiv.) of 3-carbomethoxy propanoyl chloride. After reaction, pyridine was evaporated under reduced pressure. Dichloromethane (200 mL) was added. The mixture was washed twice with 100 mL of water. The organic layer was dried (Na_2SO_4) and concentrated to give the crude amide (yield 79%), which was used directly without further purification in the next step. The thionation was achieved with a solution of 13 g (0.07 mol) of amide in 400 mL of dried tetrahydrofuran (THF). Following the addition of 15.5 g of P_4S_{10}, the mixture was heated for 4 h. Using the same work-up as described in the general procedure, 10.9 g of **2f** were obtained after chromatography with EtOAc/cyclohexane (1/2). Yield 60%. Oil. ^{1}H NMR: 3.80 and 3.60 (2t, J = 7 Hz, 4H), 3.63 (s, 3H), 2.90 and 2.80 (2t, J = 6 Hz, 4H), and 2.10–1.90 (m, 4H). ^{13}C NMR: 197.4, 172.6, 53.4, 51.2, 50.1, 36.3, 32.3, 25.8, and 23.7. IR ($CHBr_3$): 1725 and 1480 cm^{-1}. Anal. calcd (%) for $C_9H_{15}NO_2S$: C 53.73, H 7.46, N 6.96; found: C 53.82, H 7.38, N 6.93.

General procedure for an Eschenmoser coupling reaction with Ph_3P as the thiophilic agent

Typically, a mixture of thioamide **2** (6.3 mmol) and bromoester **3** (0.019 mol, 3 equiv.) in 50 mL of acetonitrile (CH_3CN) was heated for 30 min. A solution of 1.26 mmol (2 equiv.) of Ph_3P and 1.26 mmol (2 equiv.) of triethylamine (Et_3N) in CH_3CN (30 mL) was added dropwise. After addition, the mixture was refluxed for 4 h. The solvent was removed in vacuo and the resulting residue was dissolved in CH_2Cl_2 (150 mL). The organic layer was washed with a solution of 1 mol/L HCl (150 mL). The aqueous layers were extracted with CH_2Cl_2 (3 × 75 mL). The combined organic phases were successively washed with saturated $NaHCO_3$ solution (50 mL) and water (50 mL) and were then dried ($MgSO_4$). After evaporation of the solvent, crude β-ketoester **5** was obtained. In some cases, portions of phosphorated by-products were precipitated out in ethanol at –18 °C. Thus, purification of the ketoesters by chromatography on a silica gel column was facilitated.

General procedure for an Eschenmoser coupling reaction with triethylphosphite as the thiophilic agent

A mixture of 5.4 mmol of thioamide **2** and 8.11 mmol of bromoester **3** (1.5 equiv.) was heated at 80 °C for 30–45 min. Then a mixture of triethylamine (8.11 mmol, 1.5 equiv.) and 8.11 mmol (1.5 equiv.) of $P(OEt)_3$ was added. A precipitate of ammonium bromide was formed, and 5 mL of CH_3CN was added. The residue was refluxed until no further change in the ratio of the different compounds was observed by gas chromatography (2–5 h). After addition of CH_3CN (15 mL) and 1 mol/L HCl (1 mL) at room temperature, the resulting mixture was stirred and hydrolysis of the enaminoester was monitored by TLC. The solvent was removed and CH_2Cl_2 (50 mL) was added. The organic layer was washed with a saturated $NaHCO_3$ solution. The aqueous layer was extracted with CH_2Cl_2 (2 × 50 mL). The combined organic layers were dried ($MgSO_4$) and condensed to give crude β-ketoester **5**, which was chromatographed on a silica gel column using various mixtures of EtOAc/cyclohexane as eluant.

General procedure for an Eschenmoser coupling reaction with tris(dimethylamino)phosphine as the thiophilic agent

A mixture of 5 mmol of thioamide **2** and 7.5 mmol (1.5 equiv.) of bromoester **3** was heated at 80 °C for 30–45 min under a nitrogen atmosphere. A mixture of 6 mmol (1.2 equiv.) of Et_3N and 7.5 mmol (1.5 equiv.) of tris(dimethylamino)phosphine was then added, followed by the addition of dry CH_3CN (5 mL). The resulting mixture

was refluxed until no further change in the ratio of the different compounds was observed by gas chromatography. After addition of CH_3CN (10 mL) and 1 mol/L HCl (1 mL) the mixture was stirred for an additional 30 min and the same type of work-up as previously described in the second procedure was achieved. Thus, crude β-ketoester **5** was obtained and then chromatographed as above.

2-Methyl-3-oxo-hexanoic acid ethylester (5a)

Oil. ^{1}H NMR: 12.5 (broad s, weak), 4.12 (q, 2H), 3.40 (q, 1H), 2.5–2.4 (2dxt, ^3J = 7 Hz, ^2J = 26 Hz, 2H), 1.98 (t, 3H), 1.55 (m, 2H), 1.25 (d, 3H), and 0.84 (t, 3H). ^{13}C NMR: 205.6, 170.4, 61.0, 52.6, 43.0, 16.8, 13.8, 13.3, and 12.5. IR ($CHBr_3$): 1750 and 1720 cm^{-1}. Anal. calcd. (%) for $C_9H_{16}O_3$: C 62.76, H 9.36; found: C 62.71, H 9.41.

2,5-Dimethyl-3-oxo-hexanoic acid ethylester (5b)

Oil. ^{1}H NMR: 12.7 (broad s, weak), 4.10 (q, J = 7 Hz, 2H), 3.42 (q, J = 7 Hz, 1H), 2.40–2.30 (2dxd, ^3J = 6.5 Hz, ^2J = 22 Hz, 2H), 2.25 (d, J = 7 Hz, 3H), 2.10 (m, 1H), 1.19 (t, J = 7 Hz, 3H), and 0.85 (t, J = 7 Hz, 3H). ^{13}C NMR: 204.9, 170.1, 60.8, 51.7, 49.9, 23.8, 22.1, 22.0, 13.7, and 12.2. IR ($CHBr_3$): 1750 and 1720 cm^{-1}. Anal. calcd. (%) for $C_{10}H_{18}O_3$: C 64.48, H 9.74; found: C 64.55, H 9.71.

2-Methyl-3-oxo-octanoic acid ethylester (5d)

Oil. ^{1}H NMR: 12.8 (broad s, weak), 4.11 (q, J = 7 Hz, 2H), 3.43 (q, J = 7 Hz, 1H), 2.50–2.40 (2dxt, ^3J = 7 Hz, ^2J = 26 Hz, 2H), 1.52 (m, 2H), 1.27 (d, J = 7 Hz, 3H), 1.25–1.22 (m, 4H), 1.20 (t, J = 7 Hz, 3H), and 0.82 (t, J = 7 Hz, 3H). ^{13}C NMR: 207.5, 169.6, 61.1, 52.0, 41.2, 31.2, 23.2, 22.4, 14.5, 13.8, and 12.7. IR ($CHBr_3$): 1750 and 1720 cm^{-1}. Anal. calcd. (%) for $C_{11}H_{20}O_3$: C 65.97, H 10.96; found: C 66.07, H 10.11.

2-Methyl-3-oxo-3-phenyl propanoic acid ethylester (5e)

Oil. ^{1}H NMR: 12.5 (broad s, weak), 7.90–7.35 (m, 5H), 4.30 (q, J = 7.1 Hz, 1H), 4.05 (q, J = 7 Hz, 2H), 1.42 (d, J = 7.1 Hz, 3H), and 1.15 (t, J = 7 Hz, 3H). ^{13}C NMR: 196.0, 170.8, 134.2, 131.8, 127.1, 126.9, 61.3, 48.3, 13.9, and 13.7. IR ($CHBr_3$): 1740, 1680, and 1595 cm^{-1}. Anal. calcd. (%) for $C_{12}H_{14}O_3$: C 69.88, H 6.84; found: C 69.79, H 6.78.

2-Methyl-3-oxo-hexandioic acid-1-ethyl-6-methylester (5f)

Oil. ^{1}H NMR: 4.12 (q, J = 7 Hz, 2H), 3.60 (s, 3H), 3.50 (q, J = 7 Hz, 1H), 2.85–2.75 (t, J = 6.5 Hz, 2H), 2.56 (t, J = 6.5 Hz, 2H),), 1.30 (d, J = 7 Hz, 3H), and 1.21 (t, J = 7 Hz, 3H). ^{13}C NMR: 203.9, 172.6, 170.1, 61.1, 52.6, 51.5, 35.7, 27.5, 13.8, and 12.4. IR ($CHBr_3$): 1730 cm^{-1} (broad). Anal. calcd. (%) for $C_{10}H_{16}O_5$: C 55.54, H 7.46; found: C 55.62, H 7.53.

2-(1-Ethoxycarbonyl-ethylsulfanyl)-propanoic acid ethylester (8)

Oil. ^{1}H NMR: 4.15–4.05 (2q, J = 7 Hz, 4H), 3.60–3.45 (2q, J = 7.2 Hz, 2H), 1.55–1.45 (2d, J = 7.2 Hz, 6H), and 1.43–1.32 (2t, J = 7 Hz, 6H). ^{13}C NMR: 172.6, 172.5, 61.0, 60.9, 41.2, 41.1, 17.6, 16.8, 13.9, and 13.8. IR ($CHBr_3$): 1735 cm^{-1}. Anal. calcd. (%) for $C_{10}H_{18}O_4S$: C 51.26, H 7.74; found: C 51.19, H 7.71.

References

1. R. Robinson. J. Chem. Soc. **109**, 1038 (1916).
2. D.S. Breslow, E. Baumgarten, and C.R. Hauser. J. Am. Chem. Soc. **66**, 1286 (1944).
3. C.R. Hauser and B.E. Hudson. *In* Organic chemistry. Vol. 1. *Edited by* R. Adams. John Wiley and Sons, New York. 1942. p. 266.
4. R.E. Ireland and J.A. Marshall. J. Am. Chem. Soc. **81**, 2907 (1959).
5. E.C. Taylor, G.H. Hawks, and A. Mc Killop. J. Am. Chem. Soc. **90**, 2421 (1968).
6. P. Marchand, C. Bellec, M.-C. Fargeau-Bellasoued, and G. Lhommet. Synthesis, **11**, 1118 (1994).
7. A. Bardou, J.-P. Celerier, and G. Lhommet. Tetrahedron Lett. **38**, 8507 (1997).
8. J. Blot, A. Bardou, C. Bellec, M.-C. Fargeau-Bellasoued, J.-P. Celerier, and G. Lhommet. Tetrahedron Lett. **38**, 8511 (1997).
9. O. David, J. Blot, C. Bellec, M.-C. Fargeau-Bellassoued, J.-P. Celerier, G. Lhommet, and J.-C. Gramain. J. Org. Chem. **64**, 3122 (1999).
10. A. Doutheau and J. Gore. Tetrahedron, **32**, 2705 (1976).
11. P.L. Stotter and K.A. Hill. Tetrahedron Lett. **40**, 4067 (1972).
12. A. Choudary and A.L. Baumstark. Synthesis, **9**, 688 (1989).
13. W. Wierenga and H.L. Skulnick. J. Org. Chem. **44**, 310 (1979).
14. E.E. Blaise. C. R. Acad. Sci. Paris, **132**, 478 (1901).
15. H.B. Kagan and Y.-H. Suen. Bull. Soc. Chim. Fr. **6**, 1819 (1966).
16. S.M. Hannick and Y. Kishi. J. Org. Chem. **48**, 3833 (1983).
17. C. Kashima, L. Kita, K. Takahashi, and A. Hosomi. J. Heterocycl. Chem. **32**, 723 (1995).
18. K. Nagao, M. Chiba, and S.-W. Kim. Synthesis, **3**, 197 (1983).
19. A.B. Smith and P.A. Levenberg. Synthesis, **7**, 567 (1981).
20. S. Katayama, K. Fukuda, T. Watanabe, and M. Yamauchi. Synthesis, **3**, 178 (1988).
21. K. Shiosaki, G. Fels, and H. Rapoport. J. Org. Chem. **46**, 3230 (1981).
22. K. Shiosaki and H. Rapoport. J. Org. Chem. **50**, 1229 (1985).
23. R. Ghirlando, A.S. Howard, R.B. Katz, and J.P. Michael. Tetrahedron, **40**, 2879 (1984).
24. D.N. Harpp and J.G. Gleason. J. Org. Chem. **35**, 3259 (1970).
25. N.P. Neureiter and F.G. Bordwell. J. Am. Chem. Soc. **81**, 578 (1958).
26. K. Tsuzuki, M. Akeyoshi, and S. Omura. Bull. Chem. Soc. Jpn. **58**, 395 (1985).
27. H.J. Bestman, G. Graf, H. Hartung, and S. Kolewa. Chem. Ber. **103**, 2794 (1970).