A Convenient Method for Preparation of 2-(Methylthio)alkanoic Acids and Their Related Compounds Using the Carbanions of Substituted Malonic Esters

Katsuyuki OGURA,* Hiroshi ITOH, Toshio MORITA, Kunio SANADA, and Hirotada IIDA
Department of Synthetic Chemistry, Faculty of Engineering, Chiba University, Yayoicho 1-33, Chiba 260
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Starting from alkyl- or aryl-substituted malonic esters prepared by various methods, 2-(methylthio)alkanoic acids are synthesized by successive treatment with sodium ethoxide and with S-methyl methanethiosulfonate, followed by alkaline hydrolysis which causes concurrent decarboxylation. Production of 2-(phenylthio)alkanoic acids is also achieved in a similar manner.

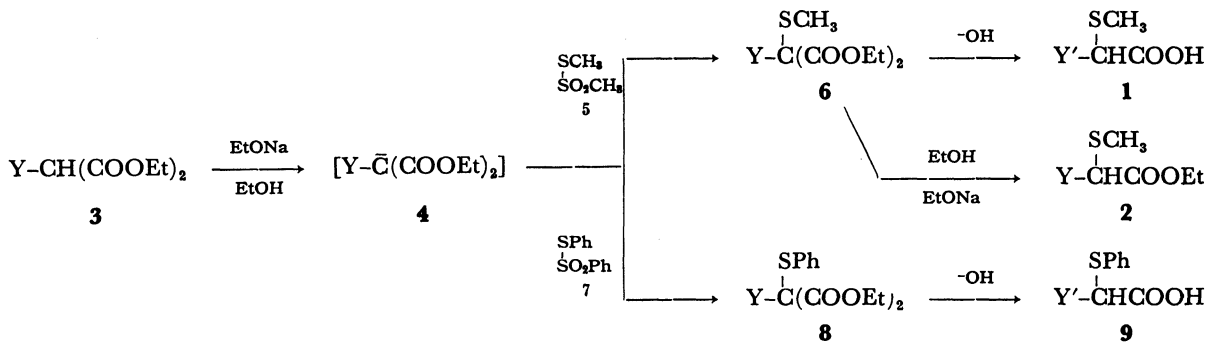
A 2-(methylthio)alkanoic acid (**1**) and its ester (**2**) are well known to be useful intermediates for making a variety of organic compounds such as a 2-alkenoic acid, an aldehyde, a ketone, and an epoxide.[1-6] For preparation of **1** and **2**, there have been explored many kinds of methods including substitution of 2-haloalkanoic ester with methanethiolate anion,[7] methylation of 2-mercaptoalkanoic ester,[7,8] alkylation of (methylthio)-acetic acid,[4] direct sulfenylation of alkanoic acid or its ester,[3,4,9] Michael addition of a carbanion to methyl α-(methylthio)acrylate,[10] and reaction of (ethoxycarbonyl)(methylthio)methyl cation with 1-alkene or arene.[11] Now we wish to describe a convenient route leading to **1**, which comprises the reaction of *S*-methyl methanethiosulfonate (**5**) with the carbanion (**4**) of an alkyl- or aryl-substituted malonic ester (**3**) and subsequent hydrolysis accompanied by simultaneous decarboxylation. This route provides the following distinct features: (i) Inexpensive and handy sodium ethoxide can be employed as a base; (ii) **1** is selectively produced without formation of 2,2-bis(methylthio)alkanoic acid due to masking the hydrogen at 2-position of **1** with ethoxycarbonyl group; (iii) all the reactions take place smoothly in ethanol at room temperature or in refluxing ethanol; and (iv) many methods are available for production of **3** and **4** to make this route widely applicable (*vide post*).

Results and Discussion

For preparation of alkyl- or aryl-substituted malonic esters (**3**), we employed three methods summarized in Scheme 2. When Y of **3** is an alkyl group or a 2-alkenyl group, the corresponding **3** is synthesized by the so-called malonic ester synthesis [Method A].[12] Ethoxycarbonylation of ethyl arylacetate with diethyl carbonate and sodium ethoxide gives the starting material (**3**) having an aryl group as Y [Method B].[13] The Michael reaction of diethyl malonate with ethyl 2-alkenoate can be utilized to afford **3** (Y=-CHR'CH_2COOEt) [Method C].[14]

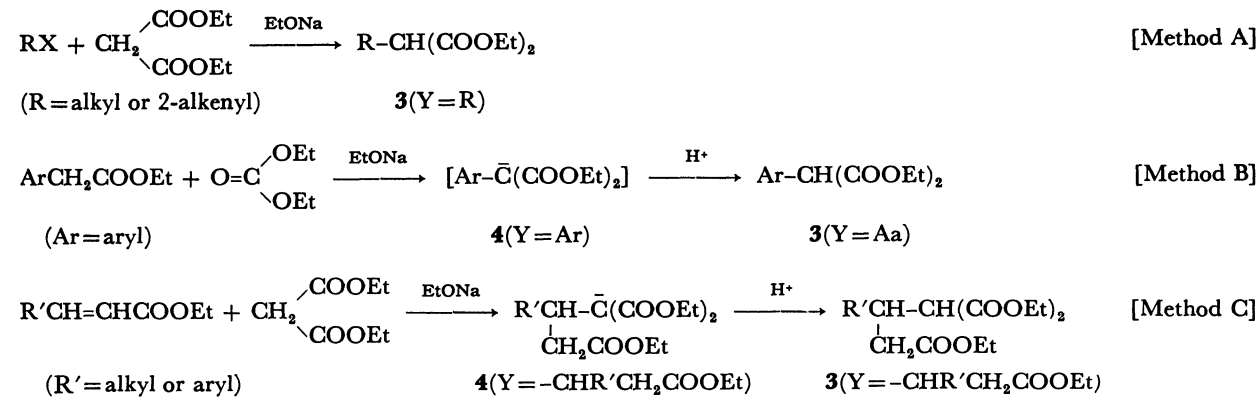
Conversion of the thus-obtained **3** into the corresponding **6** was accomplished by successive treatment with sodium ethoxide and with **5** in ethanol. To 0.47 M ethanolic solution (100 ml) of sodium ethoxide, were added **2a** (9.97 g : 33 mmol) and then **5** (5.30 g : 42 mmol),[15] and the resulting mixture was stirred at room temperature for 4 h. The usual workup followed by distillation afforded **6a** in 90% yield. In analogous manners, various derivatives (**6b—g**) of diethyl (methylthio)malonate were obtained. When *S*-phenyl benzenethiosulfonate (**7**)[15] was utilized instead of **5** in the above reactions, the corresponding phenylthio derivatives (**8a**, **8b**, and **8d**) were also produced in high yields. The results are given in Tables 1 and 2.

As shown in Scheme 2, the carbanion (**4**, Y=Ar) is



a: Y=*n*-$C_{10}H_{21}$-, b: Y=$PhCH_2$-, c: Y=*n*-$C_5H_{11}CH$=$CHCH_2$-, d: Y=Ph,
e: Y=-CH_2CH_2COOEt [Y'=-CH_2CH_2COOH], f: Y=-CHCH$_2$COOEt [Y'=-CHCH$_2$COOH]
g: Y=-CHCH$_2$COOEt [Y'=-CHCH$_2$COOH]
Ph Ph

Scheme 1.



Scheme 2. Preparation of the starting material (**3**)

intermediately formed in Method B. Hence, we examined whether a "one-pot" reaction is feasible for preparation of **6** (Y=Ar) from ethyl arylacetate. Ethyl phenylacetate (16 mmol) and a large excess of diethyl carbonate (15 ml) were added to an ethanolic solution (15 ml) of sodium ethoxide (1.2 equiv.) and the mixture was heated under slow removal of ethanol and diethyl carbonate to afford an insoluble carbanion (**4d**). Then, tetrahydrofuran (50 ml) and **5** (1.3 mol-equiv.) were added to this reaction system and the resulting mixture was stirred at room temperature for 3 h to give **6d** in 92% yield. Analogously, **8d** was given in 90% yield, starting from ethyl phenylacetate and **7**.

Method C of Scheme 2 also suggests that **6** having $-CHR'CH_2COOEt$ as Y can be produced in one flask from ethyl 2-alkenoate by direct treatment of the carbanion **4** (Y=$-CHR'CH_2COOEt$), which is formed in the reaction of ethyl 2-alkenoate with the carbanion of diethyl malonate, with **5**. After a solution containing ethyl 2-alkenoate, diethyl malonate (1—1.2 equiv.), and sodium ethoxide (1—2.2 equiv.) in ethanol was stirred at room temperature or refluxing temperature, **5** (1—2.7 equiv.) was added and the resulting mixture was further stirred at room temperature. The usual workup gave **6f** and **6g** in 67 and 72% yields, respectively. However, preparation of **6e** using this "one-pot" procedure was found to be less effective because the Michael addition of diethyl malonate to ethyl acrylate was always accompanied with formation of diethyl bis[2-(ethoxycarbonyl)ethyl]malonate to lower the yield of the carbanion **4e**. In this case, it is recommended that **3e** is once isolated by distillation and then subjected to the reaction with **5** in the presence of sodium ethoxide in ethanol as mentioned above from a viewpoint of obtaining **6e** in a pure form.

Transformation of **6** into the desired **1** was easily achieved by alkaline hydrolysis. When **6** was treated with excess potassium hydroxide in refluxing ethanol, hydrolysis of the ethoxycarbonyl groups and decarboxylation took place simultaneously to give **1**. However, it should be noted that **6g** afforded ethyl cinnamate and/or cinnamic acid by cleavage of a C–C bond (the retro-Michael reaction) when the hydrolysis was carried out in refluxing ethanol. This was overcome by performing the hydrolysis at room temperature followed by heating at the final stage to form **1g** in 93% yield. 2-(Phenylthio)alkanoic acid (**9**) was also produced in a good yield by alkaline hydrolysis of **8**. These results are also summarized in Tables 1 and 2.

For preparation of **1d**, benzyl cyanide could be employed as a starting material instead of ethyl phenylacetate. Ethoxycarbonylation of benzyl cyanide with diethyl carbonate in the presence of sodium ethoxide gave sodium salt (**10**) of ethyl α-cyanophenylacetate. After the precipitated **10** was again dissolved by addition of tetrahydrofuran to the reaction system, **5** was added and the resulting mixture was stirred at room temperature for 4 h to afford ethyl α-cyano-α-(methylthio)-

Table 1. Yields of **6** and **1**

3 (Y)	**3** → **6**[a]				**6** → **1**[a]		
	EtONa (equiv.)	**5** (equiv.)	Temp (Time/h)	Yield/%	KOH (equiv.)	Temp(Time/h)	Yield/%
3a (n-$C_{10}H_{21}$–)	1.4	1.3	r.t.(4)	90	3.7	reflux(3)	74
3b ($PhCH_2$–)	1.2	1.2	r.t.(4)	70	4.3	reflux(4)	74
3c (n-$C_5H_{11}CH$=$CHCH_2$–[b])	1.5	1.6	r.t.(5)	88	3.9	reflux(6)	87
3d (Ph)	1.2	1.3	r.t.(3)	92[c]	4.1	reflux(3)	79
3e ($-CH_2CH_2COOEt$)	2.1	2.5	r.t.(16)	73	8.9	reflux(3)	82
3f ($-CH(CH_3)CH_2COOEt$)	1.5	1.5	r.t.(4.5)	77	8.2	reflux(4)	71
3g ($-CH(Ph)CH_2COOEt$)	1.6	2.2	r.t.(18)	75	10.0	r.t.(17) → reflux(5)	93

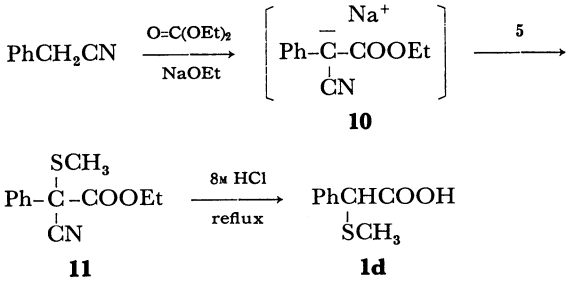
a) In EtOH. b) The (*E*)-isomer was used in this reaction. By an NMR analysis (100 MHz and proton-decoupling), the presence of the corresponding (*Z*)-isomers was not observed in the products **6** and **1**. c) The carbanion (**4**) was obtained by the reaction of ethyl phenylacetate with diethyl carbonate (see Text). This value indicates an overall yield from ethyl phenylacetate.

TABLE 2. YIELDS OF **8** AND **9**

3(Y)	3 → 8[a]				8 → 9[a]		
	EtONa (equiv.)	7 (equiv.)	Temp/°C(Time/h)	Yield/%	KOH (equiv.)	Temp(Time/h)	Yield/%
3a (n-$C_{10}H_{21}$–)	1.0	1.0	r.t.(4) → 50(11)	90	5.2	reflux(2)	77
3b ($PhCH_2$–)	1.1	1.2	r.t.(2) → 50(23)	(83)[b]	4.0	reflux(2)	76[c]
3d (Ph)	1.2	1.3	r.t.(2) → 50(33)	90[d]	5.0	reflux(3)	86

a) In EtOH. b) Contaminated with a small amount of inseparable and unidentified product(s). c) The overall yield from **3**. d) See the footnote (c) of Table 1.

phenylacetate (**11**) in 82% yield. Alkaline hydrolysis of **11** resulted in formation of a complex mixture containing ethyl α-cyanophenylacetate, benzoic acid, and ethyl benzoate. However, transformation of **11** into **1d** was successively accomplished by acidic hydrolysis with 8 M hydrochloric acid to produce the expected **1d** in 76% yield.



Furthermore, direct conversion of **6** into the ethyl ester (**2**) was examined by retro-ethoxycarbonylation. When a mixture of **6** and sodium ethoxide (about 5 equiv.) was stirred in ethanol, the corresponding **2** was produced (**2a** 93%; **2b** 77%; **2c** 76%; **2d** 80%).

Thus, we have established a convenient method for preparation of 2-(methylthio)alkanoic acids, 2-(phenylthio)alkanoic acids, and their esters. Finally, it should be noted that the present method can be suitably applied to selective synthesis of 3-substituted 2-(methylthio)-pentanedioic acids starting from ethyl 2-alkenoates, which is not achieved by the already-mentioned known methods for making **1** and **2**.

Experimental

Synthesis of ***6a***. *Typical Procedure*: To a 0.47 M ethanolic solution (100 ml) of sodium ethoxide, were successively added **3a** (9.967 g, 33 mmol) and **5** (5.297 g, 42 mmol), and the resulting mixture was stirred at room temperature for 4 h. After addition of water (100 ml), the mixture was extracted with diethyl ether (50 ml × 3). The organic layer was dried (Na_2SO_4) and evaporated *in vacuo*. Distillation of the residue gave 10.374 g of **6a** as a colorelss oil: bp 145—148 °C/1 mmHg (1 mmHg≈133.322 Pa); NMR ($CDCl_3$): δ 0.75—1.05 (3H, broad t), 1.15—1.40 (24H, broad), 2.10 (3H, s), and 4.24 (4H, q, J=7 Hz); IR (neat): 1730 cm^{-1}.

Found: C, 62.71; H, 10.06; S, 9.25%. Calcd for $C_{18}H_{34}O_4S$: C, 62.39; H, 9.89; S, 9.25%.

In analogous manners using the conditions given in Tables 1 and 2, the following compounds were synthesized.

6b: A colorless oil which was purified by column chromatography on silica gel using hexane–benzene (1 : 1) as an eluent followed by a short-path distilation (bath temperature: 120 °C/3 mmHg); NMR ($CDCl_3$): δ 1.21 (6H, t, J=7 Hz), 2.15 (3H, s), 3.43 (2H, s), 4.21 (4H, q, J=7 Hz), and 7.21 (s, 5H); IR (neat): 1730 cm^{-1}.

Found: C, 60.90; H, 6.72%. Calcd for $C_{15}H_{20}O_4S$: C, 60.79; H, 6.80%.

6c: A colorless oil; bp 103—103.5 °C/4 mmHg; NMR ($CDCl_3$): δ 0.78—0.91 (3H, broad t), 1.13—1.56 (6H, m), 1.28 (6H, t, J=7 Hz), 1.80—2.24 (2H, m), 2.11 (3H, s), 2.74 (2H, d, J=6 Hz), 4.23 (4H, q, J=7 Hz), 5.40 (1H,dt, J=15.5 and 6 Hz), and 5.52 (1H, dt, J=15.5 and 6 Hz); IR (neat): 1730 cm^{-1}.

Found: C, 60.70; H, 8.84%. Calcd for $C_{16}H_{28}O_4S$: C, 60.71; H, 8.94%.

6e: A colorless oil; bp 108—109 °C/1 mmHg; NMR ($CDCl_3$): δ 1.27 (3H, t, J=7 Hz), 1.30 (6H, t, J=7 Hz), 2.07 (3H, s), 2.30 (4H, s), 4.13 (2H, q, J=7 Hz), and 4.25 (4H, q, J=7 Hz); IR (neat): 1725 cm^{-1}.

Found: C, 51.18; H, 7.21%. Calcd for $C_{13}H_{22}O_6S$: C, 50.96; H, 7.23%.

6f: A colorless oil; bp 114.5—117 °C/0.5 mmHg; NMR ($CDCl_3$): δ 1.14 (3H, d, J=6 Hz), 1.25 (3H, t, J=7 Hz), 1.29 (6H, t, J=7 Hz), 2.14 (3H, s), 2.3—3.2 (3H, m), 4.14 (2H, q, J=7 Hz), and 4.26 (4H, q, J=7 Hz); IR (neat): 1725 cm^{-1}.

Found: C, 52.23; H, 7.48%. Calcd for $C_{14}H_{24}O_6S$: C, 52.48; H, 7.54%.

6g: Colorless crystals; mp 62—63 °C (from hexane); NMR (CCl_4): δ 1.02 (3H, t, J=7 Hz), 1.18 (3H, t, J=7 Hz), 1.25 (3H, t, J=7 Hz), 2.14 (3H, s), 2.80—3.25 (2H, m), 3.85—4.40 (7H, m), and 7.0—7.4 (5H, m); IR (KBr): 1725 cm^{-1}.

Found: C, 59.75; H, 6.82%. Calcd for $C_{19}H_{26}O_6S$: C, 59.66; H, 6.85%.

8a: A colorless oil which was purified by column chromatography on silica gel using benzene as an eluent followed by a short-path distillation (bath temperature: 180 °C/1.5 mmHg); NMR ($CDCl_3$): δ 0.65—1.00 (3H, broad t), 1.0—2.1 (24H, broad), 4.16 (4H, q, J=7 Hz), and 7.22—7.60 (5H, broad s).

Found: C, 67.70; H, 9.09%. Calcd for $C_{23}H_{36}O_4S$: C, 67.61; H, 8.88%.

Synthesis of ***9b*** *from* ***3b*** via ***8b***. To a 0.37 M ethanolic solution (20 ml) of sodium ethoxide, were added **3b** (1.656 g, 6.62 mmol) and **7** (2.010 g, 8.04 mmol), and the resulting mixture was stirred at room temperature for 2 h and at 50 °C for 23 h. After addition of water (20 ml) and extraction with diethyl ether (50 ml × 3), the organic layer was dried (Na_2SO_4), evaporated, and subjected to column chromatography on silica gel to give an oil (1.974 g) which was shown by NMR and TLC analyses to consist mainly of **8b**. However, the impurities could not be separated from **8b** by repeated chromatography.

The oil (0.709 g, about 1.98 mmol) was dissolved in ethanol (10 ml) and, after addition of potassium hydroxide (444 mg, 7.92 mmol), the resulting mixture was refluxed for 2 h. After

water (20 ml) was added, the mixture was acidified to pH 2 with 2 M hydrochloric acid and extracted with diethyl ether (50 ml×3). The extract was dried (Na_2SO_4), evaporated, and separated by column chromatography on silica gel using ethyl acetate as an eluent to give **9b** (465 mg) in 76% overall yield from **3b** as a colorless oil, which was further purified by a short-path distillation (bath temperature: 180 °C/1 mmHg); NMR ($CDCl_3$): δ 3.13 (2H, d, J=7 Hz) 3.85 (1H, t, J=7 Hz), 7.12—7.54 (10H, broad), and 11.06 (1H, s); IR (neat): 3300—2500 and 1715 cm^{-1}.

Found: C, 70.11; H, 5.58%. Calcd for $C_{15}H_{14}O_2S$: C, 69.74; H, 5.46%.

Synthesis of ***6d*** *from Ethyl Phenylacetate. Typical Procedure*: To a 1.27 M ethanolic solution (15 ml) of sodium ethoxide, were added ethyl phenylacetate (2.630 g, 16 mmol) and diethyl carbonate (15 ml), and the resulting mixture was heated under slow removal of ethanol and diethyl carbonate through the top of the Vigreux column equipped on the reaction flask. After diethyl carbonate (9 ml) was removed, the mixture was cooled to an ambient temperature. Then, tetrahydrofuran (50 ml) and **5** (2.620 g, 20.8 mmol) were added and the resulting mixture was stirred at room temperature for 3 h. After addition of water (30 ml) and extraction with diethyl ether (50 ml×3), the extract was dried (Na_2SO_4), evaporated, and distilled *in vacuo* to give **6d** (4.160 g, 92% yield) as a colorless oil: bp 130—132 °C/1 mmHg; NMR ($CDCl_3$): δ 1.24 (6H, t, J=7 Hz), 1.97 (3H, s), 4.28 (4H, q, J=7 Hz), and 7.2—7.8 (5H, broad); IR (neat): 1725 cm^{-1}.

Found: C, 59.64; H, 6.35%. Calcd for $C_{14}H_{18}O_4S$: C, 59.55; H, 6.43%.

In analogous manners, **8d** and **11** were synthesized.

8d: A colorless oil which was purified by column chromatography on silica gel using benzene as an eluent followed by a shortpath distillation (bath temperature: 180 °C/2 mmHg); NMR ($CDCl_3$): δ 1.50 (6H, t, J=7 Hz), (4H, q, J=7 Hz), and 7.0—7.75 (10H, broad); IR (neat): 1750 and 1730 (sh) cm^{-1}.

Found: C, 66.13; H, 5.88%. Calcd for $C_{19}H_{20}O_4S$: C, 66.26; H, 5.85%.

11; A colorless oil; bp 131 °C/3 mmHg; NMR ($CDCl_3$): δ 1.29 (3H, t, J=7 Hz), 2.25 (3H, s), 4.28 (2H, q, J=7 Hz), and 7.3—7.85 (5H, broad); IR (neat): 2250 and 1750 cm^{-1}.

Found: C, 61.33; H, 5.59; N, 5.98%. Calcd for $C_{12}H_{13}NO_2S$: C, 61.25; H, 5.59; N, 5.95%.

Hydrolysis of ***6a***. *Typical Procedure*: To a solution of **6a** (2.007 g, 5.80 mmol) in ethanol (20 ml), was added potassium hydroxide (1.208 g, 21.6 mmol), and the resulting mixture was refluxed for 3 h. Then, water (30 ml) was added and the mixture was acidified below pH 2 with 3 M hydrochloric acid. After extraction with diethyl ether (30 ml ×3), the extract was dried (Na_2SO_4), evaporated, and subjected to column chromatography on silica gel using ethyl acetate as an eluent to give **1a** (1.059 g, 74% yield) as a colorless oil which was further purified by a short-path distillation (bath temperature: 145—148 °C/0.1 mmHg); NMR ($CDCl_3$): δ 0.75—1.10 (3H, broad t), 1.10—1.40 (18H, broad), 2.20 (3H, s), 3.19 (1H, t, J=8 Hz), and 10.77 (1H, s); IR (neat): 3300—2500 and 1715 cm^{-1}.

Found: C, 63.54; H, 10.81%. Calcd for $C_{13}H_{26}O_2S$: C, 63.34; H, 10.64%.

In analogous manners using the conditions given in Tables 1 and 2, the following compounds were obtained.

1b: A colorless oil which was purified by column chromatography on silica gel using ethyl acetate as an eluent followed by a short-path distillation (bath temperature: 150 °C/2 mmHg); NMR ($CDCl_3$): δ 2.19 (3H, s), 2.80—3.60 (3H, m), 7.20 (5H, s), and 8.92 (1H, s); IR (neat): 3300—2400 and 1700 cm^{-1}.

Found: C, 61.15; H, 6.32%. Calcd for $C_{10}H_{12}O_2S$: C, 61.20; H, 6.16%.

1c: A colorless oil which was purified by column chromatography on silica gel using benzene-hexane (2 : 1) as an eluent followed by a short-path distillation (bath temperature: 168—170 °C/0.08 mmHg); NMR ($CDCl_3$): δ 0.75—1.06 (3H, broad t), 1.10—1.55 (6H, m), 1.81—2.17 (2H, m), 2.18 (3H, s), 1.94—2.55 (2H, m), 3.20 (1H, t, J=7.5 Hz), 5.40 (1H, dt, J=15.5 and 6 Hz), 5.52 (1H, dt, J=15.5 and 6 Hz), and 10.4 (1H, broad); IR (neat): 3300—2500 and 1715 cm^{-1}.

Found: C, 60.99; H, 9.24%. Calcd for $C_{11}H_{20}O_2S$: C, 61.06; H, 9.34%.

1d: Colorless crystals which were obtained by column chromatography on silica gel using dichloromethane as an eluent; mp 76—77 °C; NMR ($CDCl_3$): δ 2.09 (3H, s), 4.50 (1H, s), 7.2—7.6 (5H, broad), and 10.98 (1H, s); IR (KBr): 3200—2700 and 1690 cm^{-1}.

Found: C, 59.34; H, 5.49%. Calcd for $C_9H_{10}O_2S$: C, 59.32; H, 5.53%.

1e: Colorless crystals; mp 62.5—63 °C (from benzene); NMR (d_6-DMSO): δ 1.83 (2H, m), 2.04 (3H, s), 2.28 (2H, t, J=8 Hz), 3.18 (1H, t, J=8 Hz), and 12.4 (2H, broad); IR (KBr): 3500—2500 and 1695 cm^{-1}.

Found: C, 40.61; H, 5.56%. Calcd for $C_6H_{10}O_4S$: C, 40.44; H, 5.65%.

1f: Colorless crystals; mp 132—134 °C (from dichloromethane–benzene); NMR (d_6-DMSO): δ 1.04 (3H, d, J= 6 Hz), 2.06 (3H, s), 2.24 (3H, m), 3.16 (1H, diffused d, J=7 Hz), and 12.36 (2H, broad); IR (KBr): 3300—2500 and 1700 cm^{-1}.

Found: C, 43.99; H, 6.30%. Calcd for $C_7H_{12}O_4S$: C, 43.73; H, 6.29%.

1g: Colorless crystals; mp 187—188 °C (from dichloromethane); NMR (d_6-DMSO): δ 2.14 (3H, s), 2.9—3.7 (4H, m), 7.28 (5H, s), and 12.2 (2H, broad); IR (KBr): 3300—2500 and 1700 cm^{-1}.

Found: C, 56.41; H, 5.51%. Calcd for $C_{12}H_{14}O_4S$: C, 56.67; H, 5.54%.

9a: A colorless oil which was purified by column chromatography on silica gel using ethyl acetate as an eluent followed by a short-path distillation (bath temperature: 195 °C/1 mmHg); NMR ($CDCl_3$): δ 0.62—1.03 (3H, broad t), 1.03—1.55 (18H, broad), 3.60 (1H, t, J=7 Hz), 7.15—7.58 (5H, broad), and 10.95 (1H, s); IR (neat): 3400—2400 and 1710 cm^{-1}.

Found: C, 70.15; H, 9.35%. Calcd for $C_{18}H_{28}O_2S$: C, 70.09; H, 9.15%.

9d: Colorless crystals which were obtained by column chromatography on silica gel using ethyl acetate as an eluent and subjected to an elemental analysis; mp 100 °C; NMR ($CDCl_3$): δ 4.88 (1H, s), 7.1—7.55 (10H, broad), and 11.08 (1H, s); IR (KBr): 3200—2400 and 1690 cm^{-1}.

Found: C, 68.58; H, 4.97%. Calcd for $C_{14}H_{12}O_2S$: C, 68.83; H, 4.95%.

Hydrolysis of ***11***. A mixture of **11** (947 mg, 4.0 mmol) and 8 M hydrochloric acid was refluxed for 12 h. After addition of water (50 ml) and extraction with diethyl ether (100 ml×3), the organic layer was dried (Na_2SO_4), evaporated, and subjected to column chromatography on silica gel using dichloromethane as an eluent to afford colorless crystals (558 mg, 76% yield) which were identified with **1d** by their IR and NMR spectra.

Production of ***2a*** *from* ***6a***. *Typical Procedure*: To a 0.66 M ethanolic solution of sodium ethoxide, was added **6a** (432 mg, 1.25 mmol) and the resulting solution was stirred

at room temperature for 88 h and at 50 °C for 5 h. After addition of water (20 ml) and extraction with diethyl ether (50 ml×3), the extract was dried (Na_2SO_4), evaporated, and subjected to column chromatography on silica gel using benzene–hexane (1 : 1) as an eluent to give **2a** (317 mg, 93% yield) as a colorless oil which was further purified by a short-path distillation (bath temperature: 145 °C/3 mmHg); NMR ($CDCl_3$): δ 0.70—1.10 (3H, broad t), 1.15—1.45 (21H, broad), 2.15 (3H, s), 3.18 (1H, t, J=7 Hz), and 4.22 (2H, q, J=7 Hz); IR (neat): 1725 cm^{-1}.

Found: C, 65.89; H, 10.77%. Calcd for $C_{15}H_{30}O_2S$: C, 65.64; H, 11.02%.

In analogous manners, **6b**, **6c**, and **6d** were converted to **2b**, **2c**, and **2d**, respectively.

2b: A colorless oil; NMR ($CDCl_3$): δ 1.13 (3H, t, J=7 Hz), 2.10 (3H, s), 2.85—3.50 (3H, m), 4.08 (2H, q, J=7 Hz), and 7.20 (5H, s); IR (neat): 1725 cm^{-1}. These data were in complete accordance with those of an authentic specimen prepared by esterification of **1b** (hydrogen chloride/ethanol).

2c: A colorless oil which was purified by column chromatography on silica gel using benzene–hexane (1 : 2) as an eluent followed by short-path distillation (bath temperature: 118—123 °C/0.03 mmHg); NMR ($CDCl_3$): δ 0.69—1.05 (3H, broad t), 1.10—1.59 (6H, m), 1.28 (3H, t, J=7 Hz), 1.74—2.85 (4H, m), 2.14 (3H, s), 3.19 (1H, dd, J=7 and 9 Hz), 4.19 (2H, q, J=7 Hz), 5.40 (1H, dt, J=15.5 and 6 Hz), and 5.52 (1H, dt, J=15.5 and 6 Hz); IR (neat): 1730 cm^{-1}.

Found: C, 63.88; H, 9.72%. Calcd for $C_{13}H_{24}O_2S$: C, 63.88; H, 9.92%.

2d: A colorless oil; NMR ($CDCl_3$): δ 1.20 (3H, t, J=7 Hz), 2.05 (3H, s), 4.15 (2H, q, J=7 Hz), 4.49 (1H, s), and 7.16—7.55 (5H, broad); IR (neat): 1735 cm^{-1}. These data were completely identical with those of an authentic sample prepared by esterification of **1d** (hydrogen chloride/ethanol).

*Preparation of **6f** from Ethyl Crotonate in One-pot Reaction.*
To a 0.63 M ethanolic solution of sodium ethoxide, were added diethyl malonate (1.695 g, 10.0 mmol) and ethyl crotonate (1.223 g, 10.0 mmol), and the resulting solution was refluxed for 2 h. Then, the mixture was cooled to room temperature and **5** (3.363 g, 27 mmol) was added. The mixture was stirred at room temperature for 39 h and refluxed for 1 h. After addition of water (80 ml) and extraction with dichloromethane (70 ml×3), the extract was dried (Na_2SO_4) and evaporated to give an oil (4.688 g) which was shown by GLC analysis using *trans*-stilbene as an internal standard to contain 2.25 g (67% yield) of **6f**.

*Preparation of **6g** from Ethyl Cinnamate in One-pot Reaction.*
To a 0.91 M ethanolic solution of sodium ethoxide, were added diethyl malonate (7.986 g, 50 mmol) and ethyl cinnamate (8.924 g, 50 mmol), and the resulting mixture was stirred at room temperature for 25 h. Then, **5** (7.153 g, 56 mmol) was added and the mixture was stirred at room temperature for 21 h. After addition of water (100 ml) and extraction with dichloromethane (100 ml×3), the extract was dried (Na_2SO_4) and evaporated to give a pale yellow oil containing crystals (21.353 g) which was shown by GLC analysis to contain 13.6 g (72% yield) of **6g**. By recrystallization from hexane, 8.628 g of **6g** was isolated in a pure form.

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