Chem. Pharm. Bull.
34(2) 540—549 (1986)

Monomethylation of Aromatic Rings by Friedel–Crafts Reaction with Chloromethyl Sulfide

YASUMITSU TAMURA,*[,a] HIROKAZU ANNOURA,[a] MASAHIRO FUJI,[a] MASAMI OKURA,[a] and HIROYUKI ISHIBASHI[b]

Faculty of Pharmaceutical Sciences, Osaka University,[a] 1–6, Yamada-oka, Suita, Osaka 565, Japan and Kyoto Pharmaceutical University,[b] Misasagi, Yamashina, Kyoto 607, Japan

(Received July 3, 1985)

A novel method for the introduction of a methyl group into aromatic rings is described. Friedel–Crafts reactions of ethyl α-(chloromethylthio)acetate (**3k**) and α-chloromethylthio-γ-butyrolactone (**3m**) with an arene in the presence of stannic chloride gave ethyl α-(arylmethylthio)-acetate (**6**) and α-arylmethylthio-γ-butyrolactone (**7**), respectively, which were easily converted to the corresponding methylated arene (**8**) by reductive desulfurization with Raney nickel or zinc dust–acetic acid.

Keywords——monomethylation; ethyl α-(chloromethylthio)acetate Friedel–Crafts reaction; α-chloromethylthio-γ-butyrolactone Friedel–Crafts reaction; ethyl α-(arylmethylthio)acetate; α-arylmethylthio-γ-butyrolactone; methylated arene; reductive desulfurization; Raney nickel; zinc dust–acetic acid

Introduction of a methyl group into an aromatic ring by Friedel–Crafts reaction with methyl halide is usually unsuccessful because the undesired polymethylation preferentially occurs as a side-reaction.[1] Recently, we have reported[2] that the Friedel–Crafts reaction of α-ethoxycarbonyl-α-(methylthio)methyl chloride (**1**) with arenes gives a high yield of ethyl α-(methylthio)arylacetate (**2**). If alkyl or aryl chloromethyl sulfide (**3**) could be successfully employed instead of **1**, the reaction would afford alkyl or aryl arylmethyl sulfide, which could be easily desulfurized to the methylated arene. Therefore, in order to develop a method for monomethylation of aromatic rings, we have examined the Friedel–Crafts reactions of various chloromethyl sulfides (**3a**—**m**) with benzene in the presence of stannic chloride. As a result, ethyl α-(chloromethylthio)acetate (**3k**) and α-chloromethylthio-γ-butyrolactone (**3m**) were found to be most reactive, giving high yields of ethyl α-(benzylthio)acetate (**4k**) and α-benzylthio-γ-butyrolactone (**4m**), respectively. The chloromethyl sulfides, **3k** and **3m**, were further shown to react with arenes other than benzene, giving ethyl α-(arylmethylthio)acetate (**6**) and α-arylmethylthio-γ-butyrolactone (**7**), respectively, which were easily converted to the corresponding methylated arene (**8**) by reductive desulfurization. Thus, the reactions appear to provide a general and useful method of introducing a methyl group into an aromatic ring. We present here a full account of these experiments with experimental details.[3]

Friedel–Crafts Reaction

The chloromethyl sulfides (**3b**—**m**) were prepared from the thiol and bromochloromethane by treatment with 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU) in acetonitrile[4] or with sodium in tetrahydrofuran (see Experimental). First, we carried out the Friedel–Crafts reactions of the chloromethyl sulfides (**3a**—**m**) with a 5-fold molar excess of benzene in the presence of stannic chloride and compared the yields of the benzyl sulfides (**4a**—**m**). The reactions of **3a**—**c**, in which the substituent R is methyl (*cf.* **3a**) or phenyl (*cf.* **3b**, **c**) with

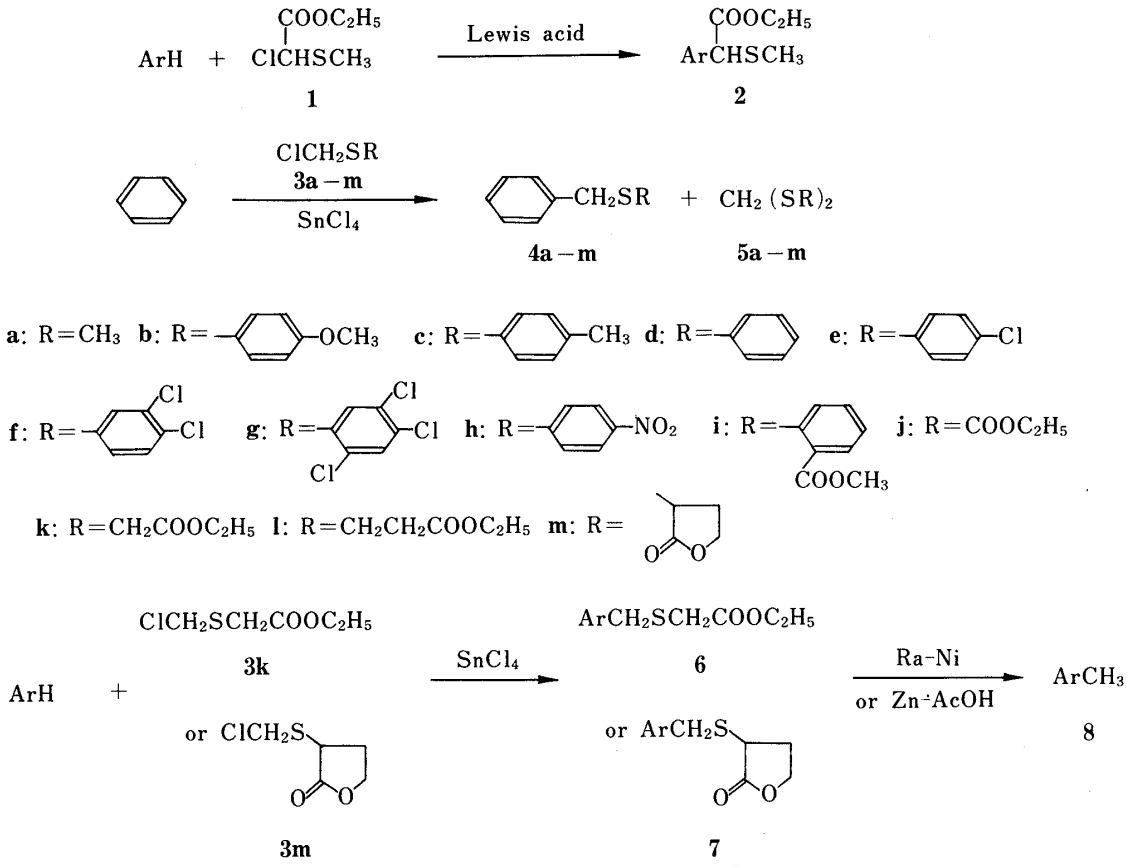


Chart 1

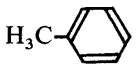
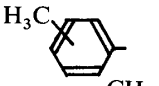
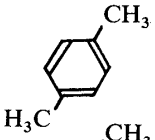
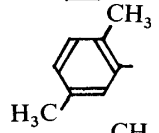
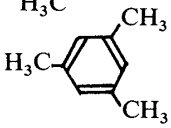
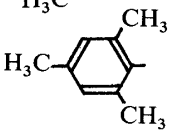
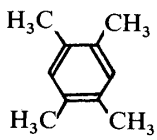
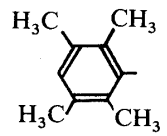
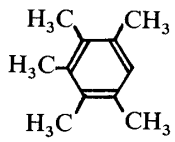
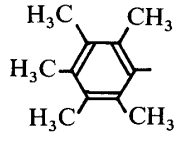
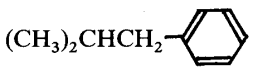
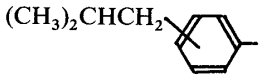
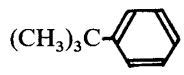
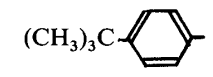
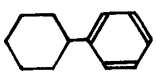
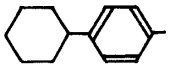
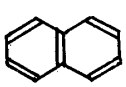
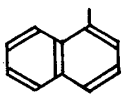
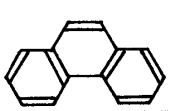
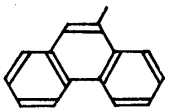
TABLE I. Friedel–Crafts Reactions of the Chloromethyl Sulfide (**3a**—**m**) with a Five-Fold Molar Excess or Equimolar Amount of Benzene

Chloromethyl sulfide No.	Product No.	Yield (%)	No.	Yield[a] (%)
3a	**4a**	—[c]	**5a**	—[b]
3b	**4b**	—[c]	**5b**	—[b]
3c	**4c**	—[c]	**5c**	—[b]
3d	**4d**	6[c]	**5d**	3
3e	**4e**	34[c]	**5e**	33
3f	**4f**	45[c]	**5f**	35
3g	**4g**	53[c]	**5g**	39
3h	**4h**	29[c]	**5h**	46
3i	**4i**	75[c]	**5i**	0
3i	**4i**	56[d]	**5i**	0
3j	**4j**	17[c]	**5j**	0[e]
3k	**4k**	94[c]	**5k**	0
3k	**4k**	83[d]	**5k**	0
3l	**4l**	86[c]	**5l**	0
3l	**4l**	70[d]	**5l**	0
3m	**4m**	99[c]	**5m**	0
3m	**4m**	91[d]	**5m**	0

a) Yield of **5** is based on 2 mol of **3**. *b*) A complex mixture. *c*) The reaction was carried out using a 5-fold molar excess of benzene. *d*) The reaction was carried out using an equimolar amount of benzene in dichloromethane. *e*) A considerable amount of the chloromethyl sulfide (**3j**) was recovered unchanged.

electron-donating groups such as CH_3 and CH_3O, did not give the expected products but yielded complex mixtures.[5] When R was phenyl (*cf.* **3d**) and phenyl (*cf.* **3e**—**h**) with electron-withdrawing groups such as Cl and NO_2, the reactions gave the benzyl sulfides (**4d**—**h**) accompanied with considerable amounts of dithioacetals (**5d**—**h**),[6] which would be formed by nucleophilic attack of the sulfur atom of **3** on the intermediary α-thiocarbocation[7] derived from **3**. The yields of **4d**—**h** are shown in Table I. In contrast, the reactions of **3i**—**m** possessing an ester moiety gave no dithioacetals but gave good yields (75—99%) of the benzyl sulfides (**4i**, **k**, **l**, and **m**) as sole products except in the case of **3j**. Next, we examined the reaction of **3i**, **k**, **l**, and **m** with an equimolar amount of benzene in dichloromethane. The results are summarized in Table I. Ethyl α-(chloromethylthio)acetate (**3k**) and α-

TABLE II. Friedel–Crafts Reactions of **3k** and **3m** with an Equimolar Amount of Arene

ArH	Product				
	Ar in **6** or **7**	No.	Yield (%)	No.	Yield (%)
		**6a**[a]	81	**7a**[a]	95
		**6b**	85	**7b**	90
		**6c**	86	**7c**	92
		**6d**	86	**7d**	92
		**6e**	86	**7e**	89
		**6f**[a]	85	**7f**[a]	91
		**6g**	86	**7g**	92
		**6h**	87	**7h**	94
		**6i**	85	**7i**	92
		**6j**	71	**7j**	84

a) A mixture of *o*- and *p*-isomers: **6a**, *o* : *p* = 2 : 5; **6f**, *o* : *p* = 1 : 5; **7a**, *o* : *p* = 2 : 5; **7f**, *o* : *p* = 1 : 5. The ratio was determined from the ^{1}H-NMR spectra.

chloromethylthio-γ-butyrolactone (**3m**), which possess an ester moiety at the γ-position to the reaction center, gave the benzyl sulfides, **4k** and **4m**, in 83 and 91% yields, respectively, and proved to be the most efficient reagents for the reaction. Although the reaction mechanism is obscure, these results suggest that the introduction of an ester moiety at the γ-position from the reaction center in **3** is responsible for suppressing the formation of **5** and increasing the yield of **4**. The structural assignments of **4** and **5** were made on the basis of their compositions and spectroscopic data (see Experimental).

To confirm the generality of this procedure, the reactions of **3k** and **3m** with substituted benzenes, naphthalene and phenanthrene were examined. Treatment of **3k** and **3m** with an equimolar amount of an arene in dichloromethane in the presence of stannic chloride afforded high yields of ethyl α-(arylmethylthio)acetate (**6**) and α-arylmethylthio-γ-butyrolactone (**7**), respectively. The results are summarized in Table II. It is noteworthy that no polyalkylated product is formed under the present conditions. The structural assignments of **6** and **7** were made on the basis of their composition and spectral data (see Tables IV and V).

Desulfurization

The compounds **6** and **7**, obtained by the above Friedel–Crafts reaction were easily converted to the corresponding methylated arene (**8**) by heating with Raney nickel in ethanol or zinc dust in acetic acid. Some examples of the desulfurization are given in Table III.

Table III. Desulfurization[a] of **6d, e, g, i, j** and **7d, e, j**

Sulfide	Product	
6 or **7**	No.	Yield (%)
6d	**8d**	82
6e	**8e**	80
6g	**8g**	85
6i	**8i**	95
6j	**8j**	97
7d	**8d**	93
7e	**8e**	89
7j	**8j**	91

a) Raney nickel for **6d, e, g, i, j** and zinc dust–acetic acid for **7d, e, j**.

Generally, Friedel–Crafts alkylation tends to result in polyalkylation, so that dialkylated and higher alkylated by-products are formed.[1] The only practical way of preventing such additional reactions is to keep the arene in large excess. This procedure is practical with benzene and other inexpensive compounds often used as solvents, but it is impractical with substituted benzenes, which are more expensive.

The Friedel–Crafts reactions of **3k** and **3m** using an equimolar amount of arene appear to provide a practical method to introduce a methyl group into an aromatic ring through reductive desulfurization of the products.

Experimental

All melting points and boiling points are uncorrected. The infrared (IR) spectra were recorded on a JASCO IRA-1 spectrometer. The proton nuclear magnetic resonance (^{1}H-NMR) spectra were measured on a Hitachi R-20 (60 MHz) or a R-22 (90 MHz) spectrometer with tetramethylsilane as an internal standard. Low- and high-resolution mass spectra (MS) were obtained with Hitachi RMU-6D and JEOL LMS D-300 instruments with a direct inlet system at 70 eV.

Materials——Chloromethyl methyl sulfide (**3a**) is commercially available. Other chloromethyl sulfides (**3b—m**) were prepared as follows.

General Procedure for Chloromethyl Aryl Sulfides (3b—i)——The procedure was essentially analogous to that

reported by Ono *et al.*[4] A solution of the thiol (0.012 mol) and DBU (1.99 g, 0.013 mol) in acetonitrile (7 ml) was added to bromochloromethane (24 g, 0.19 mol) at 0 °C and the mixture was stirred for 1 h at the same temperature. After being warmed up to room temperature, the mixture was stirred for a further 1 h and poured into ice-water (5 ml). The organic layer was separated and dried over magnesium sulfate. After evaporation of the solvent, the residue was purified by distillation under reduced pressure (in the case of **3b**—**f**) or by flash column chromatography on silica gel (Merck Kieselgel 60; 230—400 mesh) with *n*-hexane–benzene (1 : 1) as an eluent (in the case of **3g**—**i**) to give the chloromethyl sulfide (**3**). Yields, boiling or melting points (recrystallization solvent), and spectral and analytical data are given below.

Chloromethyl *p*-Methoxyphenyl Sulfide (**3b**): This compound was prepared from *p*-methoxythiophenol in 46% yield (1.05 g) as a colorless oil, bp 120—121 °C/5 mmHg (lit.[8] 144—146 °C/15 mmHg). ^{1}H-NMR ($CDCl_3$) δ: 7.50 (2H, d, J=9.0 Hz, ArH), 6.88 (2H, d, J=9.0 Hz, ArH), 4.83 (2H, s, SCH_2Cl), 3.80 (3H, s, OCH_3).

Chloromethyl *p*-Tolyl Sulfide (**3c**): This compound was prepared from *p*-thiocresol in 45% yield (0.93 g) as a colorless oil, bp 113—114 °C/10 mmHg (lit.[4] 67—68 °C/0.7 mmHg). ^{1}H-NMR ($CDCl_3$) δ: 7.38 (2H, d, J=8.0 Hz, ArH), 7.10 (2H, d, J=8.0 Hz, ArH), 4.86 (2H, s, SCH_2Cl), 2.35 (3H, s, Ar-CH_3).

Chloromethyl Phenyl Sulfide (**3d**): This compound was prepared from thiophenol in 65% yield (1.90 g) as a colorless oil, bp 110—112 °C/18 mmHg (lit.[4] 55—60 °C/0.4 mmHg). ^{1}H-NMR ($CDCl_3$) δ: 7.65—7.20 (5H, m, ArH), 4.90 (2H, s, SCH_2Cl).

Chloromethyl *p*-Chlorophenyl Sulfide (**3e**): This compound was prepared from *p*-chlorothiophenol in 35% yield (0.81 g) as a colorless oil, bp 110—112 °C/17 mmHg (lit.[4] 90—91 °C/1.5 mmHg). ^{1}H-NMR ($CDCl_3$) δ: 7.39 (4H, br s, ArH), 4.92 (2H, s, SCH_2Cl).

Chloromethyl 3,4-Dichlorophenyl Sulfide (**3f**): This compound was prepared from 3,4-dichlorothiophenol in 65% yield (1:77 g) as a colorless oil, bp 142—145 °C/5 mmHg (lit.[9] 159—164 °C/15 mmHg). ^{1}H-NMR ($CDCl_3$) δ: 7.56 (1H, br s, ArH), 7.36 (2H, br s, ArH), 4.90 (2H, s, SCH_2Cl).

Chloromethyl 2,4,5-Trichlorophenyl Sulfide (**3g**): This compound was prepared from 2,4,5-trichlorothiophenol in 44% yield (1.38 g) as white crystals, mp 60—62 °C (*n*-hexane–benzene) (lit.[10] 59.5—61 °C). ^{1}H-NMR ($CDCl_3$) δ: 7.64 (1H, s, ArH), 7.53 (1H, s, ArH), 4.95 (2H, s, SCH_2Cl).

Chloromethyl *p*-Nitrophenyl Sulfide (**3h**): This compound was prepared from *p*-nitrothiophenol in 34% yield (0.83 g) as pale yellow crystals, mp 62—64 °C (*n*-hexane–benzene) (lit.[11] 63.4—64 °C). IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 1345 (NO_2). ^{1}H-NMR ($CDCl_3$) δ: 8.18 (2H, d, J=8.0 Hz, ArH), 7.55 (2H, d, J=8.0 Hz, ArH), 5.03 (2H, s, SCH_2Cl).

Methyl 2-(Chloromethylthio)benzoate (**3i**): This compound was prepared from methyl 2-mercaptobenzoate[12] in 53% yield (1.38 g) as white crystals, mp 77.5—78 °C (*n*-hexane–dichloromethane). IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 1715 (C=O). ^{1}H-NMR ($CDCl_3$) δ: 8.05—7.05 (4H, m, ArH), 5.00 (2H, s, SCH_2Cl), 3.90 (3H, s, OCH_3). *Anal.* Calcd for $C_9H_9ClO_2S$: C, 49.89; H, 4.19. Found: C, 49.85; H, 4.04.

General Procedure for Chloromethyl Alkyl Sulfides (3j—m)——A solution of the thiol (0.02 mol) in dry tetrahydrofuran (2 ml) was added dropwise to a stirred suspension of sodium hydride (60% dispersion in oil; 0.8 g, 0.02 mol) in dry tetrahydrofuran (12 ml) at room temperature. After being stirred for 1 h at the same temperature, the resulting suspension of sodium salt was added portionwise over 15 min to bromochloromethane (13 g, 0.1 mol) at 0 °C, then the mixture was stirred for 1 h at this temperature. Sodium bromide that precipitated was removed by filtration, and then unreacted bromochloromethane was evaporated off *in vacuo*. The residue was distilled under reduced pressure to afford the chloromethyl sulfide (**3**). Yields, boiling points, and spectral and analytical data are given below.

Ethyl (Chloromethylthio)formate (**3j**): This compound was prepared from Bender's salt ($KSCOOC_2H_5$)[13] in 25% yield (0.77 g) as a colorless oil, bp 63 °C/15 mmHg. IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 1730 (C=O). ^{1}H-NMR ($CDCl_3$) δ: 4.88 (2H, s, SCH_2Cl), 4.35 (2H, q, J=7.2 Hz, OCH_2CH_3), 1.35 (3H, t, J=7:2 Hz, OCH_2CH_3). *Anal.* Calcd for $C_4H_7ClO_2S$: C, 31.07; H, 4.56. Found: C, 30.94; H, 4.64.

Ethyl α-(Chloromethylthio)acetate (**3k**): This compound was prepared from ethyl thioglycolate in 59% yield (1.2 g) as a colorless oil, bp 100—105 °C/15 mmHg. IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 1730 (C=O). ^{1}H-NMR ($CDCl_3$) δ: 4.84 (2H, s, SCH_2Cl), 4.22 (2H, q, J=7.2 Hz, OCH_2CH_3), 3.45 (2H, s, SCH_2CO), 1.30 (3H, t, J=7.2 Hz, OCH_2CH_3). *Anal.* Calcd for $C_5H_9ClO_2S$: C, 35.61; H, 5.38. Found: C, 35.81; H, 5.37.

Ethyl β-(Chloromethylthio)propionate (**3l**): This compound was prepared from ethyl β-mercaptopropionate[14] in 52% yield (2.24 g) as a colorless oil, bp 92—96 °C/4 mmHg. IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 1730 (C=O). ^{1}H-NMR ($CDCl_3$) δ: 4.75 (2H, s, SCH_2Cl), 4.18 (2H, q, J=7.2 Hz, OCH_2CH_3), 3.15—2.50 (4H, m, SCH_2CH_2CO), 1.27 (3H, t, J=7.2 Hz, OCH_2CH_3). Exact mass Calcd for $C_6H_{11}{}^{35}ClO_2S$: 182.0166. Found: 182.0159. Exact mass Calcd for $C_6H_{11}{}^{37}ClO_2S$: 184.0139. Found: 184.0159.

α-Chloromethylthio-γ-butyrolactone (**3m**): This compound was prepared from α-mercapto-γ-butyrolactone[15] in 60% yield (2.01 g) as a colorless oil, bp 140—145 °C/5 mmHg. IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 1775 (C=O). ^{1}H-NMR ($CDCl_3$) δ: 5.22 (1H, d, J=12 Hz, SCH_2Cl), 4.67 (1H, d, J=12 Hz, SCH_2Cl), 4.55—4.25 (2H, m, OCH_2CH_2–), 3.88 (1H, dd, J= 8.7, 6.2 Hz, SCHCO), 3.00—2.59 (1H, m, OCH_2CH_2–), 2.40—2.00 (1H, m, OCH_2CH_2–). *Anal.* Calcd for $C_5H_7ClO_2S$: C, 36.04; H, 4.54. Found: C, 36.21; H, 4.24.

General Procedure for Friedel–Crafts Reaction of Alkyl or Aryl Chloromethyl Sulfide (3) with Arene——a)

TABLE IV. Physical Properties and Spectral Data for Ethyl α-(Arylmethylthio)acetate (**6**)

Compd. No.	mp (°C) (solvent)	Analysis (%) Calcd (Found) C	H	Formula	IR $\nu_{max}^{CHCl_3}$ cm^{-1}	^{1}H-NMR ($CDCl_3$) δ
6a	Oil	64.25 (64.61	7.19 7.25)	$C_{12}H_{16}O_2S$	1725	7.16 (4H, s, ArH), 4.18 (2H, q, J=7.2 Hz, OCH_2CH_3), 3.84 (2/5×2H, s, SCH_2Ar), 3.78 (3/5 2H, s, SCH_2Ar), 3.07 (2/5×2H, s, SCH_2CO), 3.03 (3/5×2H, s, SCH_2CO), 2.39 (2/5×3H, s, Ar-CH_3), 2.33 (3/5×3H, s, Ar-CH_3), 1.28 (3H, t, J=7.2 Hz, OCH_3CH_3)
6b	Oil	65.51 (65.59	7.61 7.81)	$C_{13}H_{18}O_2S$	1725	7.02 (3H, s, ArH), 4.20 (2H, q, J=7.2 Hz, OCH_2CH_3), 3.81 (2H, s, SCH_2Ar), 3.11 (2H, s, SCH_2CO), 2.34 (3H, s, Ar-CH_3), 2.30 (3H, Ar-CH_3), 1.30 (3H, t, J=7.2 Hz, OCH_2CH_3)
6c	Oil	66.63 (66.77	7.99 8.11)	$C_{14}H_{20}O_2S$	1725	6.82 (2H, s, ArH), 4.22 (2H, q, J=7.2 Hz, OCH_2CH_3), 3.91 (2H, s, SCH_2Ar), 3.22 (2H, s, SCH_2CO), 2.38 (6H, s, Ar-CH_3×2), 2.24 (3H, s, Ar-CH_3), 1.31 (3H, t, J=7.2 Hz, OCH_2CH_3)
6d	51—52 (H_2O–CH_3OH)	67.62 (67.37	8.23 8.43)	$C_{15}H_{22}O_2S$	1725	6.88 (1H, s, ArH), 4.16 (2H, q, J=7.2 Hz, OCH_2CH_3), 3.97 (2H, s, SCH_2Ar), 3.24 (2H, s, SCH_2CO), 2.28 (6H, s, Ar-CH_3×2), 2.22 (6H, s, Ar-CH_3×2), 1.32 (3H, t, J=7.2 Hz, OCH_2CH_3)
6e	64.5—66 (CH_3OH)	68.53 (68.14	8.63 8.78)	$C_{16}H_{24}O_2S$	1725	4.23 (2H, q, J=7.2 Hz, OCH_2CH_3), 3.97 (2H, s, SCH_2Ar), 3.35 (2H, s, SCH_2CO), 2.44 (6H, s, Ar-CH_3×2), 2.31 (9H, s, Ar-CH_3×3), 1.30 (3H, t, J=7.2 Hz, OCH_2CH_3)
6f	Oil	67.62 (67.85	8.23 8.47)	$C_{15}H_{22}O_2S$	1725	7.30—6.80 (4H, m, ArH), 4.17 (2H, q, J=7.2 Hz, OCH_2CH_3), 3.88 (1/5×2H, s, SCH_2Ar), 3.80 (4/5×2H, s, SCH_2Ar), 3.11 (1/5×2H, s, SCH_2CO), 3.05 (4/5×3H, s, SCH_2CO), 2.46 [2H, d, J=6.6 Hz, $(CH_3)_2CHCH_2$–], 2.10—1.60 [1H, m, $(CH_3)_2CHCH_2$–], 1.28 (3H, t, J=7.2 Hz, OCH_2CH_3), 0.90 [6H, d, J=6.6 Hz, $(CH_3)_2CHCH_2$–]
6g	Oil	67.62 (67.82	8.23 8.47)	$C_{15}H_{22}O_2S$	1725	7.29 (4H, s, ArH), 4.17 (2H, q, J=7.2 Hz, OCH_2CH_3), 3.80 (2H, s, SCH_2Ar), 3.05 (2H, s, SCH_2CO), 1.31 [9H, s, $(CH_3)_3C$–], 1.28 (3H, s, t, J=7.2 Hz, OCH_2CH_3]
6h	Oil	69.82 (69.82	8.27 8.41)	$C_{17}H_{24}O_2S$	1725	7.18 (4H, br s, ArH), 4.19 (2H, q, J=7.2 Hz, OCH_2CH_3), 3.78 (2H, s, SCH_2Ar), 3.05 (2H, s, SCH_2CO), 2.80—1.10 (14H, m, OCH_2CH_3, *cyclo*-C_6H_{11})
6i	Oil	69.20 (69.34	6.20 6.21)	$C_{15}H_{16}O_2S$	1725	8.10—7.00 (7H, m, ArH), 4.29 (2H, s, SCH_2Ar), 4.18 (2H, q, J=7.2 Hz, OCH_2CH_3), 3.07 (2H, s, SCH_2CO), 1.26 (3H, t, J=7.2 Hz, OCH_2CH_3)
6j	Oil	73.53 (73.34	5.85 5.82)	$C_{19}H_{18}O_2S$	1725	8.80—7.00 (9H, m, ArH), 4.33 (2H, s, SCH_2Ar), 4.20 (2H, q, J=7.2 Hz, OCH_2CH_3), 3.11 (2H, s, SCH_2CO), 1.28 (3H, t, J=7.2 Hz, OCH_2CH_3)

TABLE V. Physical Properties and Spectral Data for α-Arylmethylthio-γ-butyrolactone (7)

Compd. No.	mp (°C) (solvent)	Analysis (%) Calcd (Found) C	H	Formula	IR $\nu_{max}^{CHCl_3}$ cm^{-1}	^{1}H-NMR ($CDCl_3$) δ
7a	Oil	64.85 (65.14	6.35 6.35)	$C_{11}H_{12}O_2S$	1770	7.23 (2/5×4H, s, ArH), 7.18 (3/5×4H, s, ArH), 4.55—4.18 (2H, m, $OC\underline{H}_2CH_2$–), 4.13 (2/5×1H, d, J=13.5 Hz, SCH_2Ar), 4.10 (3/5×1H, d, J=13.5 Hz, SCH_2Ar), 3.84 (3/5×1H, d, J=13.5 Hz, SCH_2Ar), 3.75 (2/5×1H, d, J=13.5 Hz, SCH_2Ar), 3.37 (2/5×1H, dd, J=8.7, 4.2 Hz, SCHCO), 3.30 (3/5×1H, dd, J=8.7, 4.2 Hz, SCHCO), 2.90—1.75 (2H, m, $OCH_2C\underline{H}_2$–), 2.40 (2/5×3H, s, Ar-CH_3), 2.33 (3/5×3H, s, Ar-CH_3)
7b	Oil	66.08 (66.36	6.83 6.87)	$C_{12}H_{14}O_2S$	1770	7.13 (1H, s, ArH), 7.02 (2H, br s, ArH), 4.47—4.15 (2H, m, $OC\underline{H}_2CH_2$–), 4.08 (1H, d, J=12.0 Hz, SCH_2Ar), 3.82 (1H, d, J=12.0 Hz, SCH_2Ar), 3.39 (1H, dd, J=8.4, 4.8 Hz, SCHCO), 2.87—1.75 (2H, m, $OCH_2C\underline{H}_2$–), 2.35 (3H, s, Ar-CH_3), 2.29 (3H, s, Ar-CH_3)
7c	Oil	67.18 (67.34	7.25 7.38)	$C_{13}H_{16}O_2S$	1770	6.83 (2H, s, ArH), 4.60—4.21 (2H, m, $OC\underline{H}_2CH_2$–), 4.18 (1H, d, J=10.8 Hz, SCH_2Ar), 3.94 (1H, d, J=10.8 Hz, SCH_2Ar), 3.54 (1H, dd, J=8.4, 4.8 Hz, SCHCO), 2.90—1.75 (2H, m, $OCH_2C\underline{H}_2$–), 2.38 (6H, s, Ar-CH_3×2), 2.24 (3H, s, Ar-CH_3)
7d	108—109 (CH_3OH)	68.13 (67.85	7.64 7.63)	$C_{14}H_{18}O_2S$	1770	6.88 (1H, s, ArH), 4.55—4.20 (2H, m, $OC\underline{H}_2CH_2$–), 4.23 (1H, d, J=10.8 Hz, SCH_2Ar), 3.97 (1H, d, J=10.8 Hz, SCH_2Ar), 3.56 (1H, dd, J=8.4, 4.8 Hz, SCHCO), 2.90—1.80 (2H, m, $OCH_2C\underline{H}_2$–), 2.29 (6H, s, Ar-CH_3×2), 2.22 (6H, s, Ar-CH_3×2)

7e	102—103.5 (CH_3OH)	69.04 (68.97	7.97 7.99)	$C_{15}H_{20}O_2S$	1770	4.55—4.20 (2H, m, $OC\underline{H}_2CH_2$–), 4.25 (1H, d, J=10.8 Hz, SCH_2Ar), 3.97 (1H, d, J=10.8 Hz, SCH_2Ar), 3.56 (1H, dd, J=8.4, 4.8 Hz, SCHCO), 2.89—1.75 (2H, m, $OCH_2C\underline{H}_2$–), 2.33 (6H, s, Ar-CH_3 × 2), 2.20 (9H, Ar-CH_3 × 3)
7f	Oil	68.13 (68.01	7.64 7.62)	$C_{14}H_{18}O_2S$	1770	7.45—6.95 (4H, m, ArH), 4.55—4.10 (2H, m, $OC\underline{H}_2CH_2$–), 4.13 (1/5 × 1H, d, J=13.2 Hz, SCH_2Ar), 4.11 (4/5 × 1H, d, J=13.2 Hz, SCH_2Ar), 3.76 (1H, d, J=13.2 Hz, SCH_2Ar), 3.33 (1/5 × 1H, dd, J=8.4, 4.8 Hz, SCHCO), 3.31 (4/5 × 1H, dd, J=8.4, 4.8 Hz, SCHCO), 2.95—1.70 [3H, m, $OC\underline{H}_2CH_2$–, $(CH_3)_2C\underline{H}CH_2$–], 2.47 [2H, d, J=7.2 Hz, $(CH_3)_2CHC\underline{H}_2$–], 0.94 [1/5 × 6H, d, J=6.0 Hz, $(CH_3)_2CHC\underline{H}_2$–], 0.89 [4/5 × 6H, d, J=6.0 Hz, $(CH_3)_2CHC\underline{H}_2$–]
7g	Oil	68.13 (68.25	7.64 7.79)	$C_{14}H_{18}O_2S$	1770	7.23 (4H, br s, ArH), 4.50—4.10 (2H, m, $OC\underline{H}_2CH_2$–), 4.10 (1H, d, J=13.2 Hz, SCH_2Ar), 3.74 (1H, d, J=13.2 Hz, SCH_2Ar), 3.31 (1H, dd, J=7.8, 4.8 Hz, SCHCO), 2.85—1.75 (2H, m, $OCH_2C\underline{H}_2$–), 1.30 [9H, s, $(CH_3)_3C$–]
7h	Oil	70.32 (70.16	7.64 7.65)	$C_{16}H_{20}O_2S$	1770	7.30 (2H, d, J=8.4 Hz, ArH), 7.11 (2H, d, J=8.4 Hz, ArH), 4.45—4.09 (2H, m, $OC\underline{H}_2CH_2$–), 4.08 (1H, d, J=13.2 Hz, SCH_2Ar), 3.73 (1H, d, J=13.2 Hz, SCH_2Ar), 3.28 (1H, dd, J=8.4, 4.8 Hz, SCHCO), 2.85—1.05 (13H, m, $OCH_2C\underline{H}_2$–, *cyclo*-C_6H_{11})
7i	Oil	258.0698[a] (258.0705)		$C_{15}H_{14}O_2S$	1770	8.31—7.18 (7H, m, ArH), 4.59 (1H, d, J=13.8 Hz, SCH_2Ar), 4.45—4.17 (2H, m, $OC\underline{H}_2CH_2$–), 4.33 (1H, d, J=13.8 Hz, SCH_2Ar), 3.37 (1H, dd, J=8.4, 4.8 Hz, SCHCO), 2.85—1.70 (2H, m, $OCH_2C\underline{H}_2$–)
7j	Oil	308.0868[a] (308.0868)		$C_{19}H_{16}O_2S$	1770	8.80—7.10 (9H, m, ArH), 4.55 (1H, d, J=13.8 Hz, SCH_2Ar), 4.55—3.92 (2H, m, $OC\underline{H}_2CH_2$–), 4.29 (1H, d, J=13.8 Hz, SCH_2Ar), 3.29 (1H, dd, J=8.4, 4.8 Hz, SCHCO), 2.70—1.60 (2H, m, $OCH_2C\underline{H}_2$–)

a) High-resolution MS (M^+).

Reaction using 5-fold molar excess of benzene; Stannic chloride (391 mg, 1.5 mmol) was added to a stirred solution of **3** (1.5 mmol) in dry benzene (0.67 ml, 7.5 mmol) at room temperature under a nitrogen stream. After being stirred for 1 h, the mixture was poured into ice-water (3 ml) and extracted with benzene (5 ml × 3). The combined extracts were washed with aqueous sodium chloride (3 ml) and dried over magnesium sulfate. The solvent was evaporated off *in vacuo* to give a residue, which was chromatographed on silica gel (Merck Kieselgel 60; 70—200 mesh) with *n*-hexane–benzene (1 : 4) as an eluent to afford **4** and **5**. The results are summarized in Table I. Boiling or melting points (recrystallization solvent), and spectral and analytical data are given below.

b) Reaction using an equimolar amount of benzene and other arenes; Stannic chloride (391 mg, 1.5 mmol) was added to a stirred solution of **3** (1.5 mmol) and benzene (117 mg, 1.5 mmol) in dry dichloromethane (0.67 ml) at room temperature under a nitrogen stream. After being stirred for 1 h, the mixture was worked up in the same manner as described above in a) to give **4**. The results are summarized in Table I. The similar reaction of **3k** and **3m** with other arenes afforded **6** and **7**, respectively. The results are listed in Table II. The physical properties and spectral data of the products are given in Tables IV and V.

Benzyl Phenyl Sulfide (**4d**): White crystals, mp 39.5—40.7 °C (*n*-hexane) (lit.[16] 40—41 °C). ^{1}H-NMR ($CDCl_3$) δ: 7.26 (10H, s, ArH), 4.10 (2H, s, SCH_2Ar). MS *m/z*: 200 (M^+).

Benzyl *p*-Chlorophenyl Sulfide (**4e**): White crystals, mp 51.5—52 °C (methanol) (lit.[17] 52—53 °C). ^{1}H-NMR ($CDCl_3$) δ: 7.25 (4H, s, ArH), 7.20 (5H, s, ArH), 4.06 (2H, s, SCH_2Ar). MS *m/z*: 234 (M^+).

Benzyl 3,4-Dichlorophenyl Sulfide (**4f**): A colorless oil, bp 165 °C/1.5 mmHg (lit.[18] 225 °C/25 mmHg). ^{1}H-NMR ($CDCl_3$) δ: 7.35—7.08 (3H, m, ArH), 7.25 (5H, s, ArH), 4.06 (2H, s, SCH_2Ar). MS *m/z*: 269 (M^+).

Benzyl 2,4,5-Trichlorophenyl Sulfide (**4g**): White crystals, mp 120.5—121.7 °C (*n*-hexane) (lit.[19] 118—119 °C). ^{1}H-NMR ($CDCl_3$) δ: 7.39 (1H, s, ArH), 7.27 (5H, s, ArH), 7.23 (1H, s, ArH), 4.09 (2H, s, SCH_2Ar). MS *m/z*: 304 (M^+).

Benzyl *p*-Nitrophenyl Sulfide (**4h**): White crystals, mp 124.2—125.7 °C (*n*-hexane) (lit.[20] 123 °C). IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 1345 (NO_2). ^{1}H-NMR ($CDCl_3$) δ: 8.02 (2H, d, J=8.8 Hz, ArH), 7.30 (5H, s, ArH), 7.27 (2H, d, J=8.8 Hz, ArH), 4.23 (2H, s, SCH_2Ar). MS *m/z*: 245 (M^+).

Methyl 2-(Benzylthio)benzoate (**4i**): White crystals, mp 67.3—68 °C (methanol) (lit.[21] 67 °C). IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 1710 (C=O). ^{1}H-NMR ($CDCl_3$) δ: 7.95—6.89 (9H, m, ArH), 4.10 (2H, s, SCH_2Ar), 3.89 (3H, s, OCH_3). MS *m/z*: 258 (M^+).

Ethyl (Benzylthio)formate (**4j**): A colorless oil. IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 1705 (C=O). ^{1}H-NMR ($CDCl_3$) δ: 7.31 (5H, s, ArH), 4.28 (2H, q, J=7.2 Hz, $OC\underline{H}_2CH_3$), 4.10 (2H, s, SCH_2Ar), 1.30 (3H, t, J=7.2 Hz, $OCH_2C\underline{H}_3$). Exact mass Calcd for $C_{10}H_{12}O_2S$: 196.0559. Found: 196.0572.

Ethyl α-(Benzylthio)acetate (**4k**): A colorless oil, bp 116—119 °C/2 mmHg. IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 1725 (C=O). ^{1}H-NMR ($CDCl_3$) δ: 7.31 (5H, s, ArH), 4.18 (2H, q, J=7.2 Hz, $OC\underline{H}_2CH_3$), 3.83 (2H, s, SCH_2Ar), 3.06 (2H, s, SCH_2CO), 2.18 (3H, t, J=7.2 Hz, $OCH_2C\underline{H}_3$) MS *m/z*: 210 (M^+). *Anal.* Calcd for $C_{11}H_{14}O_2S$: C, 62.82; H, 6.71. Found: C, 62.70; H, 6.73.

Ethyl β-(Benzylthio)propionate (**4l**): A colorless oil, bp 110 °C/0.3 mmHg (lit.[22] 134—136 °C/1.7 mmHg). IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 1725 (C=O). ^{1}H-NMR ($CDCl_3$) δ: 7.30 (5H, m, ArH), 4.14 (2H, q, J=7.2 Hz, $OC\underline{H}_2CH_3$), 3.73 (2H, s, SCH_2Ar), 2.75—2.45 (4H, m, SCH_2CH_2CO), 1.25 (3H, t, J=7.2 Hz, $OCH_2C\underline{H}_3$). MS *m/z*: 224 (M^+).

α-Benzylthio-γ-butyrolactone (**4m**): A colorless oil, bp 192 °C/1.2 mmHg (lit.[23] 137—140 °C/0.03 mmHg). IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 1770 (C=O). ^{1}H-NMR ($CDCl_3$) δ: 7.23 (5H, m, ArH), 4.20 (2H, m, $OC\underline{H}_2CH_2$–), 4.06 (1H, d, J= 13.5 Hz, SCH_2Ar), 3.70 (1H, d, J=13.5 Hz, SCH_2Ar), 3.23 (1H, dd, J=8.0, 5.0 Hz, SCHCO), 2.70—2.20 (1H, m, $OCH_2C\underline{H}_2$–), 2.13—1.75 (1H, m, $OCH_2C\underline{H}_2$–). MS *m/z*: 208 (M^+).

Bis(phenylthio)methane (**5d**): A colorless oil, bp 180—182 °C/5 mmHg (lit.[4] 132 °C/0.3 mmHg). ^{1}H-NMR ($CDCl_3$) δ: 7.27 (10H, m, ArH), 4.25 (2H, s, SCH_2S). MS *m/z*: 232 (M^+).

Bis(*p*-chlorophenylthio)methane (**5e**): White crystals, mp 41—42 °C (*n*-hexane). ^{1}H-NMR ($CDCl_3$) δ: 7.29 (8H, s, ArH), 4.25 (2H, s, SCH_2S). MS *m/z*: 301 (M^+). *Anal.* Calcd for $C_{13}H_{10}Cl_2S_2$: C, 51.83; H, 3.35. Found: C, 51.83; H, 3.29.

Bis(3,4-dichlorophenylthio)methane (**5f**): White crystals, mp 56—57 °C (*n*-hexane). ^{1}H-NMR ($CDCl_3$) δ: 7.47 (2H, d, J=1.8 Hz, ArH), 7.33 (2H, s, ArH), 7.25 (2H, d, J=1.8 Hz, ArH), 4.29 (2H, s, SCH_2S). MS *m/z*: 370 (M^+). *Anal.* Calcd for $C_{13}H_8Cl_4S_2$: C, 42.19; H, 2.18. Found: C, 42.21; H, 2.03.

Bis(2,4,5-trichlorophenylthio)methane (**5g**): White crystals, mp 146—147 °C (*n*-hexane) (lit.[24] 143—144 °C). ^{1}H-NMR ($CDCl_3$) δ: 7.56 (2H, s, ArH), 7.50 (2H, s, ArH), 4.26 (2H, s, SCH_2S). MS *m/z*: 439 (M^+).

Bis(*p*-nitrophenylthio)methane (**5h**): Pale yellow crystals, mp 179—180 °C (benzene) (lit.[24] 177—179 °C). IR ν_{max}^{KCl} cm^{-1}: 1340 (NO_2). ^{1}H-NMR (DMSO-d_6) δ: 8.16 (4H, d, J=8.4 Hz, ArH), 7.61 (4H, d, J=8.4 Hz, ArH), 5.05 (2H, s, SCH_2S). MS *m/z*: 322 (M^+).

General Procedure for Desulfurization of 6 and 7——a) Raney nickel (W-1; 2 g) was added to a solution of **6** (1 mmol) in ethanol (50 ml) and the mixture was refluxed for 4 h. Raney nickel was removed by filtration through a Celite column and then the solvent was evaporated off to give **8**.

b) Zinc dust (650 mg) was added to a solution of **7** (0.75 mmol) in acetic acid (3 ml) and the resulting mixture was heated with vigorous stirring at 100—110 °C for 3 h, then cooled. Water (20 ml) and dichloromethane (30 ml) were

added and the inorganic materials were filtered off. The organic layer was separated and the aqueous layer was further extracted with dichloromethane (2 × 10 ml). The combined organic layer was dried over magnesium sulfate and the solvent was evaporated off to give a residue, which was purified by column chromatography on silica gel (Merck Kieselgel 60; 70—200 mesh) with *n*-hexane–benzene (1 : 1) as an eluent to afford **8**. Some examples of the desulfurization are shown in Table III. Boiling or melting points (recrystallization solvent) and spectroscopic data of the products are given below.

Pentamethylbenzene (**8d**): White crystals, mp 51—52 °C (ethanol) (lit.[25] 52.2—53.1 °C). ^{1}H-NMR ($CDCl_3$) δ: 6.81 (1H, s, ArH), 2.22 (9H, s, Ar-CH_3 × 3), 2.16 (6H, s, Ar-CH_3 × 2).

Hexamethylbenzene (**8e**): White crystals, mp 165—166.5 °C (ethanol) (lit.[25] 164.3—164.8 °C). ^{1}H-NMR ($CDCl_3$) δ: 2.30 (18H, s, Ar-CH_3 × 6).

4-*tert*-Butyltoluene (**8g**): A colorless oil, bp 76 °C/10 mmHg (lit.[26] 191.5 °C/740 mmHg). ^{1}H-NMR ($CDCl_3$) δ: 7.27 (2H, d, J=8.4 Hz, ArH), 7.05 (2H, d, J=8.4 Hz, ArH), 2.29 (3H, s, Ar-CH_3), 1.29 [9H, s, -$C(CH_3)_3$].

1-Methylnaphthalene (**8i**): A viscous oil, mp (picrate) 139—140 °C (ethanol) [lit.[27] (picrate) 140—141 °C]. ^{1}H-NMR ($CDCl_3$) δ: 7.95—7.05 (7H, m, ArH), 2.60 (3H, s, Ar-CH_3).

9-Methylphenanthrene (**8j**): White crystals, mp 91—93 °C (methanol) (lit.[28] 91—92.5 °C). ^{1}H-NMR ($CDCl_3$) δ: 8.78—8.30 (2H, m, ArH), 8.10—7.27 (7H, m, ArH), 2.74 (3H, s, Ar-CH_3).

References and Notes

1) C. C. Price, "Organic Reactions," Vol. III, ed. by R. Adams, John Wiley and Sons, Inc., New York, 1946, p. 1; G. Baddeley, *Quart. Rev.* (London), **8**, 355 (1954); M. Tashiro, *Yuki Gosei Kagaku Kyokai Shi*, **36**, 426 (1978).
2) Y. Tamura, H.-D. Choi, H. Shindo, and H. Ishibashi, *Chem. Pharm. Bull.*, **30**, 915 (1982).
3) A part of this study has been reported as a brief communication: Y. Tamura, T. Tsugoshi, H. Annoura, and H. Ishibashi, *Synthesis*, **1984**, 326.
4) N. Ono, H. Miyake, T. Saito, and A. Kaji, *Synthesis*, **1980**, 952.
5) Gross has reported that the Friedel–Crafts reaction of chloromethyl methyl sulfide (**3a**) with a large excess of benzene (used as a solvent) in the presence of titanium tetrachloride gives only 35% yield of benzyl methyl sulfide (**4a**): H. Gross and G. Matthey, *Chem. Ber.*, **97**, 2606 (1964).
6) The similar transformation of 2-chloro-1,3-dithiane has been observed under thermal conditions: C. G. Kruse, N. L. J. M. Broekhof, A. Wijsman, and A. van der Gen, *Tetrahedron Lett.*, **1977**, 885; and also see: H. Bohme and W. Krack, *Justus Liebigs Ann. Chem.*, **1977**, 51.
7) Y. Tamura and H. Ishibashi, *Yuki Gosei Kagaku Kyokai Shi*, **40**, 658 (1982); B. M. Trost and T. Sato, *J. Am. Chem. Soc.*, **107**, 719 (1985), and references cited therein.
8) F. G. Bordwell and B. M. Pitt, *J. Am. Chem. Soc.*, **77**, 572 (1955).
9) H. J. Barber, R. F. Fuller, M. B. Green, and H. T. Zwartouw, *J. Appl. Chem.*, **3**, 266 (1953).
10) N. V. Philips' Gloeilampenfabrieken Neth. Appl. Patent 6611689 (1968) [*Chem. Abstr.*, **70**, 114804*r* (1969)].
11) J. Hayami, N. Tanaka, S. Kurabayashi, Y. Kotani, and A. Kaji, *Bull. Chem. Soc. Jpn.*, **44**, 3091 (1971).
12) A. E. Sopchik and C. A. Kingsbury, *J. Chem. Soc., Perkin Trans. 2*, **1979**, 1058.
13) C. Bender, *Ann. Chem. Pharm.*, **148**, 137 (1868).
14) P. Karrer and H. Shimid, *Helv. Chim. Acta*, **27**, 124 (1944).
15) K. Tanaka, H. Uneme, N. Yamagishi, R. Tanikaga, and A. Kaji, *Bull. Chem. Soc. Jpn.*, **53**, 2910 (1980).
16) H. Hauptmann and B. Wladislaw, *J. Am. Chem. Soc.*, **72**, 710 (1950).
17) J. Degani, M. Tiecco, and A. Tundo, *Gazz. Chim. Ital.*, **92**, 1213 (1962) [*Chem. Abstr.*, **58**, 13830*d* (1963)].
18) S. M. Dandin, H. B. Bhat, G. H. Kulkarni, H. S. S. Iyenger, P. B. Sattur, and K. S. Nargund, *J. Karnatak Univ.*, **1**, 64 (1956) [*Chem. Abstr.*, **52**, 8071*g* (1958)].
19) N. G. Clark, J. E. Cranham, D. Greenwood, J. R. Marshall, and H. A. Stevenson, *J. Sci. Food Agric.*, **8**, 566 (1957) [*Chem. Abstr.*, **52**, 4544*e* (1958)].
20) W. R. Waldron and E. E. Reid, *J. Am. Chem. Soc.*, **45**, 2399 (1923).
21) F. Gialdi, R. Ponci, and A. Baruffini, *Farmaco Ed. Sci.*, **15**, 856 (1960) [*Chem. Abstr.*, **55**, 21040*c* (1961)].
22) J. L. Szabo and E. T. Stiller, *J. Am. Chem. Soc.*, **70**, 3667 (1948).
23) A. F. Wagner, U. S. Patent 2842588 (1958) [*Chem. Abstr.*, **53**, 228*d* (1959)].
24) R. F. Brookes, J. E. Cranham, W. A. Cummings, D. Greenwood, B. S. Jackson, and H. A. Stevenson, *J. Sci. Food Agric.*, **8**, 31 (1957) [*Chem. Abstr.*, **51**, 9629*e* (1957)].
25) L. I. Smith and F. H. MacDougall, *J. Am. Chem. Soc.*, **51**, 3001 (1929).
26) W. J. Heinzelman and B. B. Corson, *J. Org. Chem.*, **22**, 25 (1957).
27) O. L. Baril and E. S. Hauber, *J. Am. Chem. Soc.*, **53**, 1087 (1931).
28) C. K. Bradsher and R. W. H. Tess, *J. Am. Chem. Soc.*, **61**, 2184 (1939).