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Studies on Hypolipidemic Agents. II. 3-(4-Phenoxybenzoyl)-propionic Acid Derivatives

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3-(4-Phenoxybenzoyl)propionic acids were prepared and tested for hypolipidemic activity in normal rats. A structure–activity relationship study showed that the 2-acetylthio derivative had hypolipidemic activity. Among these compounds, 2-acetylthio-[3-(4-chlorophenoxy)benzoyl]propionic acid possessed very potent activity.

Keywords——3-(4-phenoxybenzoyl)propionic acid derivative; 2-acetylthio-3-(4-phenoxybenzoyl)propionic acid derivative; structure–activity relationship; hypolipidemic activity

In the previous work,[1] we synthesized various derivatives of 3-aroylglycidic acid and found that 3-(4-phenoxybenzoyl)glycidic acid and 3-[4-(4-chlorophenoxy)benzoyl]glycidic acid have potent hypocholesterolemic activities. The present paper reports chemical modifications of the substituents at the 2-position of 3-(4-phenoxybenzoyl)propionic acids and the pharmacological activities of the resulting compounds.

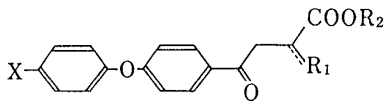
Chemistry

The 3-(4-phenoxybenzoyl)propionic acid derivatives listed in Tables I—IV were synthesized by the methods shown in Chart 1. 2-Substituted-3-(4-phenoxybenzoyl)propionic acids (II) were mostly obtained by the Michael addition reaction using the acrylic acids (I) (method A). The 2-oxo derivatives (**3**, **4**) were synthesized by condensation of acetophenones (III) with diethyl oxalate in the presence of NaH (method B).[2] Treatment of III with glyoxylic acid at 95 °C under reduced pressure provided the 2-hydroxy derivatives (**1**, **2**).[3] Compound **1** was converted to the 2-acetoxy derivatives (**14**) by reaction with acetyl chloride (method C). Ethyl 3-(4-phenoxybenzoyl)acrylates were reacted with isopropylisopropylideneamine followed by treatment with diluted hydrochloric acid to give the 2-acetonyl derivatives (**15**, **16**)[4] (method D).

Hydrolysis of the 2-acetylthio derivatives (**10**, **11**, **13**) prepared by method A gave the 2-mercapto derivatives (**21**, **22**, **23**), which were reacted with the olefins or the halogenated compounds to give **25**, **26**, **28**—**32** (method E).

3-(4-Phenoxybenzoyl)propionic acids (IV) were brominated at the 3-position[5] and reacted with potassium thioacetate to give the 3-acetylthio derivatives (**18**, **20**), which were treated with hydrazine to give the 3-mercapto derivatives (**17**, **19**) (method F). Ester and amide derivatives of 3-(4-phenoxybenzoyl)acrylic acids were prepared by the methods shown in Chart 2. The acrylic acids were reacted with dialkyl sulfates or alkyl halides in the presence of potassium carbonate to give the ester derivatives. The acrylic acids were also treated with isobutyl chloroformate and triethylamine in toluene, then reacted with the appropriate amine to give the amide derivatives.[6]

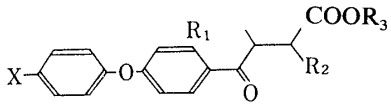
TABLE I. Physical and Biological Properties of 3-(4-Phenoxybenzoyl)propionic Acids



No.	X	R_1	R_2	Method[a]	mp (°C)	Re-crystn.[b] solvent	Formula	Hypolipidemic activity rank[c]		Liver weight[e] change (%)
								Cholesterol	Triglyceride	
1	H	OH	H	C	96—98	E–H	$C_{16}H_{14}O_5$	0	3	3.7
2	Cl	OH	H	C	132—133.5	E–H	$C_{16}H_{13}ClO_5$	1	0	7.2
3	H	O	C_2H_5	B	54—55	A–H	$C_{18}H_{16}O_5$	1	0	7.3
4	Cl	O	C_2H_5	B	53—56	A–H	$C_{18}H_{15}ClO_5$	1	0	8.9
5	Cl	OCH_3	H	A	79—81	E–H	$C_{17}H_{15}ClO_5$	0	0	37.2
6	H	OC_2H_5	C_2H_5	A	Oil[d]		$C_{20}H_{22}O_5$	1	1	46.7
7	Cl	OC_2H_5	C_2H_5	A	Oil[d]		$C_{20}H_{21}ClO_5$	5	1	46.7
8	H	Br	H	A	111—118 (dec.)	E–H	$C_{16}H_{13}BrO_4$	3	0	18.6
9	H	Cl	H	A	116—117 (dec.)	E–H	$C_{16}H_{13}ClO_4$	4	0	13.1
10	H	$SCOCH_3$	H	A	105.5—106.5	D–H	$C_{18}H_{16}O_5S$	2	2	0.9
11	H	$SCOCH_3$	C_2H_5	A	78—79	E–H	$C_{20}H_{20}O_5S$	1	2	11.1
12	Cl	$SCOCH_3$	H	A	91—94	E–H	$C_{18}H_{15}ClO_5S$	4	4	11.9
13	Cl	$SCOCH_3$	C_2H_5	A	75.5—77	E–H	$C_{20}H_{19}ClO_5S$	3	2	12.7

a) See Experimental. *b*) A=acetone, D=dichloromethane, E=ether, H=hexane. *c*) Reduction levels were calculated as percentages with respect to the control value; less than 15% reduction=0, 16—25% reduction=1, 26—35% reduction=2, 36—45% reduction=3, 46—55% reduction=4, more than 56% reduction=5. *d*) Purified by column chromatography. *e*) Liver weight increase calculated as a percentage with respect to the control value.

TABLE II. Physical and Biological Properties of 3-(4-Phenoxybenzoyl)propionic Acids



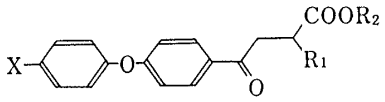
No.	X	R_1	R_2	R_3	Method[a]	mp (°C)	Re-crystn.[b] solvent	Formula	Hypolipidemic activity rank[c]	
									Cholesterol	Triglyceride
14	H	H	$OCOCH_3$	H	C	115.5—117.5	E–H	$C_{18}H_{16}O_6$	1	1
15	H	H	CH_2COCH_3	C_2H_5	D	Oil[d]		$C_{21}H_{22}O_5$	0	2
16	Cl	H	CH_2COCH_3	C_2H_5	D	Oil[d]		$C_{21}H_{21}ClO_5$	1	0
17	H	SH	H	H	F	98—99.5	A–H	$C_{16}H_{14}O_4S$	1	0
18	H	$SCOCH_3$	H	H	F	105—107	A–H	$C_{18}H_{16}O_5S$	0	0
19	Cl	SH	H	H	F	110—112	A–H	$C_{16}H_{13}ClO_4S$	1	0
20	Cl	$SCOCH_3$	H	H	F	101—103	E–H	$C_{18}H_{15}ClO_5S$	0	3

a—*d*) See footnotes in Table I.

Biological Method

Five-week-old male rats (five rats per group) were used. After prefeeding for a week, the test compounds, which were prepared as a suspension in 0.2% sodium carboxymethylcellulose (CMCNa) solution, were orally administered to the rats at a daily dose of 100 mg/kg for 3 d. A 0.2% CMCNa solution was orally administered to rats in the control group. Eighteen hours

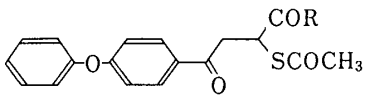
TABLE III. Physical and Biological Properties of 3-(4-Phenoxybenzoyl)propionic Acids



No.	X	R_1	R_2	mp (°C)	Recrystn.[b] solvent	Formula	Hypolipidemic activity rank[c]	
							Cholesterol	Triglyceride
21	H	SH	H	134—135	E–H	$C_{16}H_{14}O_4S$	2	0
22	H	SH	C_2H_5	46—47.5	E–H	$C_{18}H_{18}O_4S$	1	1
23	Cl	SH	C_2H_5	75.5—76.5	E–H	$C_{18}H_{17}ClO_4S$	3	2
24	H	SC_2H_5	C_2H_5	Oil[d]		$C_{20}H_{22}O_4S$	0	0
25	H	$S(CH_2)_2COCH_3$	C_2H_5	Oil[d]		$C_{22}H_{24}O_5S$	0	1
26	Cl	$SCOOCH_3$	C_2H_5	60—62	E–H	$C_{20}H_{20}O_6S$	2	0
27	Cl	$SCH_2COOC_2H_5$	C_2H_5	Oil[d]		$C_{22}H_{23}ClO_6S$	0	0
28	Cl	$S(CH_2)_2COOC_2H_5$	C_2H_5	Oil[d]		$C_{23}H_{25}ClO_6S$	0	0
29	H	$SCOC_2H_5$	C_2H_5	55—57	E–H	$C_{21}H_{22}O_5S$	1	1
30	H	$SCOC_6H_5$	C_2H_5	95—96	E	$C_{25}H_{22}O_5S$	0	1
31	H	$SCOCH(CH_3)_2$	C_2H_5	Oil[d]		$C_{22}H_{24}O_5S$	0	0
32	H	$SCO(CH_2)_4CH_3$	C_2H_5	Oil[d]		$C_{24}H_{28}O_5S$	0	1

b—*d*) See footnotes in Table I.

TABLE IV. Physical and Biological Properties of 3-(4-Phenoxybenzoyl)-2-acetylthiopropionic Acids



No.	R	mp (°C)	Recrystn.[b] solvent	Formula	Hypolipidemic activity rank[c]	
					Cholesterol	Triglyceride
33	OCH_3	59—61	E–H	$C_{19}H_{18}O_5S$	1	2
34	$OCH(CH_3)_2$	Oil[d]		$C_{21}H_{22}O_5S$	1	2
35	$O(CH_2)_4CH_3$	Oil[d]		$C_{23}H_{26}O_5S$	0	1
36	NH_2	155—157	A–H	$C_{18}H_{17}NO_4S$	0	0
37	$N(CH_3)_2$	105—106	E–H	$C_{20}H_{21}NO_4S$	1	2
38	$N(C_2H_5)_2$	36—38	E–H	$C_{22}H_{25}NO_4S$	1	1
39		129—131	D–H	$C_{22}H_{23}NO_5S$	0	1

b—*d*) See footnotes in Table I.

after the final drug administration, the rats were anesthetized with diethyl ether and their blood was collected. The lipid concentration in the serum was then determined with an autoanalyzer (Hitachi model 105).

Results and Discussion

The physical constants and biological data of the 3-(4-phenoxybenzoyl)propionic acid derivatives prepared in this work are shown in Tables I—IV. As shown in Table I,

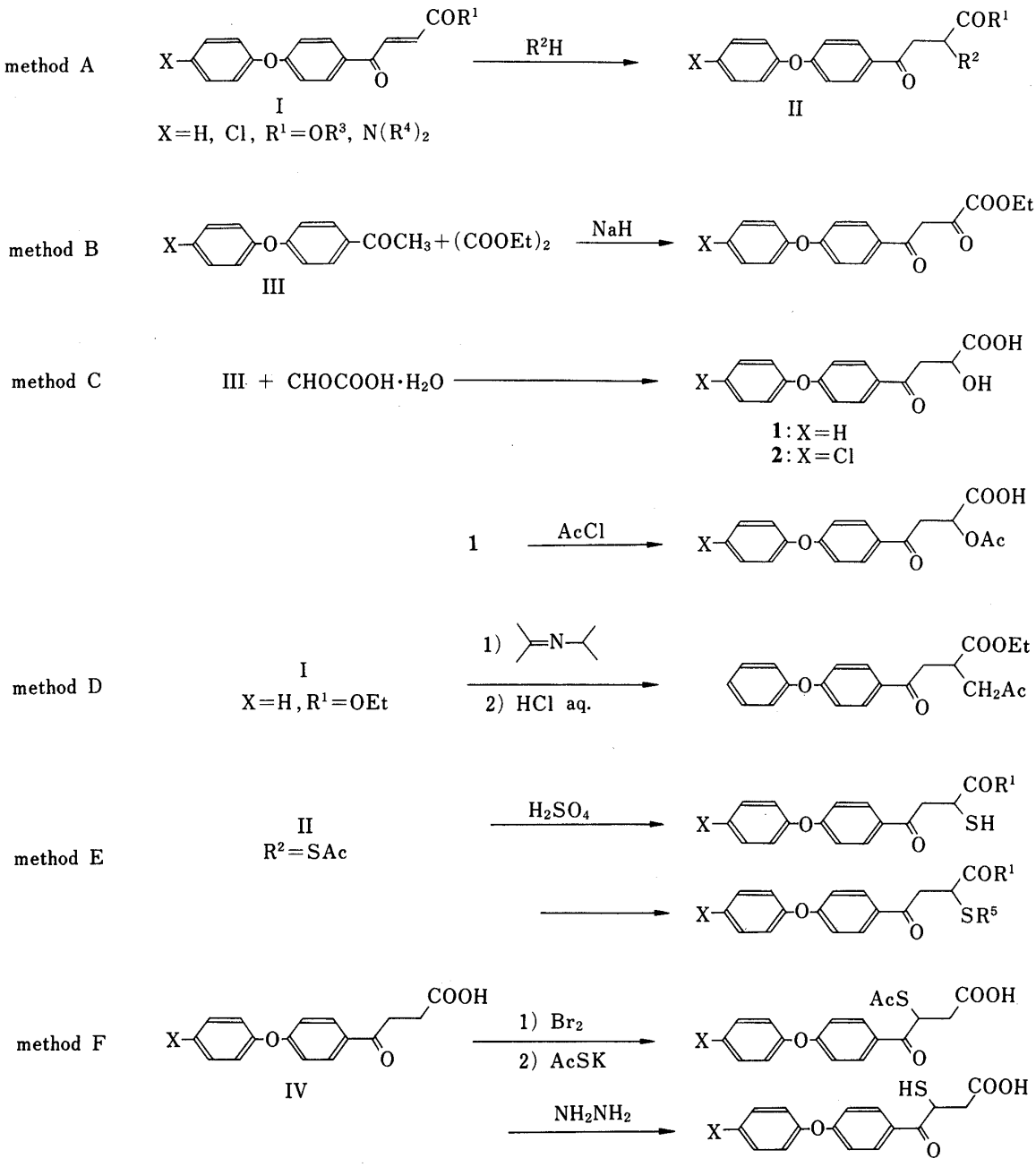


Chart 1

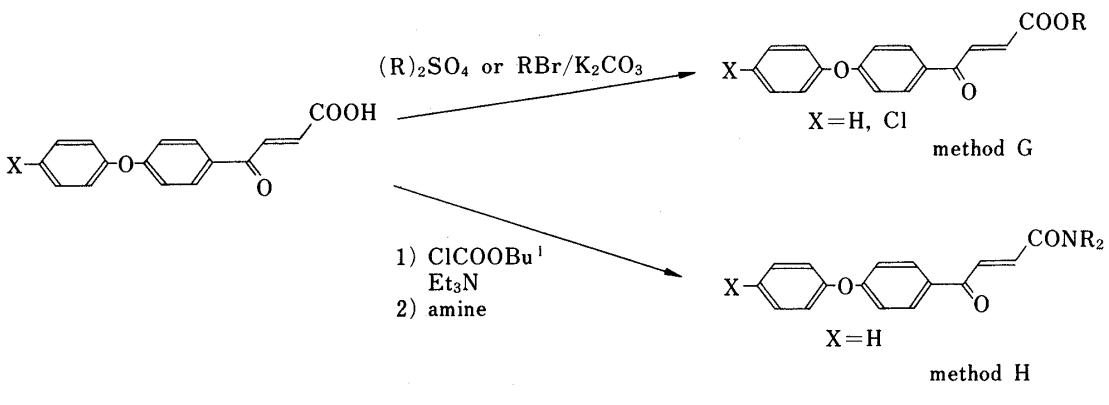


Chart 2

substitution at the 2-position in 3-(4-phenoxybenzoyl)propionic acids had a considerable influence on serum cholesterol-lowering activity. Compounds **7**—**10**, **12** and **13** showed strong activities. A comparison of the activities of the 2-acetylthio derivatives (**10**—**13**) suggests that the activity of the free acids is stronger than that of the ethyl ester, and that chloro substitution at the *para* position on the diphenyl ether increases the activity.

The 2-alkoxy derivatives (**5**—**7**) strongly increased liver weight, but the 2-acetylthio derivatives did not show such liver toxicity.

As shown in Table II, the 2-acetoxy derivative (**14**) and the 2-acetonyl derivatives (**15**, **16**) showed weaker activities. Because the 3-mercapto and 3-acetylthio derivatives (**17**—**20**) also showed weak activities, it was considered that substitution at the 3-position has little influence on the activity. The activities of the 2-mercapto, 2-alkylthio, and 2-acylthio derivatives are listed in Table III. The 2-mercapto derivatives (**21**—**23**) were found to be as active as the 2-acetylthio derivatives (**10**, **11**, **13**), but the other derivatives did not show especially strong activities. In comparisons with compound **10**, the ester and amide derivatives of **10** listed in Table IV showed weaker activities.

Experimental

All the melting points are uncorrected. Infrared (IR) spectra were measured with a JASCO DS-301 spectrophotometer. Nuclear magnetic resonance (NMR) spectra were taken at 200 MHz with tetramethylsilane (TMS) as an internal standard on a Varian XL-200 spectrometer, in $CDCl_3$ unless otherwise noted. The chemical shifts are expressed as ppm downfield from TMS. The following abbreviations are used: s = singlet; d = doublet; t = triplet; q = quartet; m = multiplet and br = broad. The unit (Hz) of coupling constants (J Hz) is omitted. Lipid concentrations in serum were estimated by the enzyme method (Daitest Series Kit, Dai-ichi Co., Ltd., Tokyo).

Method A——3-[4-(4-Chlorophenoxy)benzoyl]-2-methoxypropionic Acid (**5**): A solution of NaOMe (1.6 g) in MeOH (20 ml) was added to a stirred solution of 3-[4-(4-chlorophenoxy)benzoyl]acrylic acid[2] (3.0 g) in MeOH (50 ml). The mixture was stirred for an additional 6 h at room temperature and the MeOH was removed under reduced pressure. The residue was dissolved in H_2O, and the whole was acidified with 10% HCl aq. and extracted with AcOEt. The extract was washed with H_2O, dried ($MgSO_4$) and concentrated. The residue was purified by column chromatography on silica gel using Et_2O–hexane (1 : 1, v/v) as an eluent, and recrystallized from Et_2O–hexane to give **5** (1.58 g, 47.7%), mp 79—81 °C. IR ν_{max}^{KBr} cm^{-1}: 2500, 1660. NMR (acetone-d_6) δ: 3.32 (1H, dd, J = 16 and 4), 3.42 (3H, s), 3.49 (1H, dd, J = 16 and 6), 4.40 (1H, dd, J = 6 and 4), 7.10—8.12 (9H, m). *Anal.* Calcd for $C_{17}H_{15}ClO_5$: C, 60.99; H, 4.52. Found: C, 60.72; H, 4.64.

Ethyl 2-Ethoxy-3-(4-phenoxybenzoyl)propionate (**6**): A solution of ethyl 3-(4-phenoxybenzoyl)acrylate (10.0 g) and conc. H_2SO_4 (1.2 ml) in EtOH (50 ml) was refluxed for 7 h, then the EtOH was removed under reduced pressure. The residue was dissolved in Et_2O, and the solution was washed with H_2O, dried ($MgSO_4$) and concentrated. The residue was purified by column chromatography on silica gel using Et_2O–hexane (1 : 5, v/v) as an eluent to give **6** as an oil (5.89 g, 51.0%). IR ν_{max}^{neat} cm^{-1}: 1740, 1680. NMR δ: 1.19 (3H, t, J = 7), 1.28 (3H, t, J = 7), 3.30 (1H, dd, J = 18 and 5), 3.46 (1H, dd, J = 18 and 7), 3.58 (1H, dq, J = 12 and 7), 3.77 (1H, dq, J = 12 and 7), 4.25 (2H, q, J = 7), 4.54 (1H, dd, J = 7 and 5), 6.97—7.50 (7H, m), 7.96 (2H, d, J = 8). *Anal.* Calcd for $C_{20}H_{22}O_5$: C, 70.16; H, 6.48. Found: C, 70.39; H, 6.49. Compound **7** was similarly prepared.

Ethyl 3-[4-(4-Chlorophenoxy)benzoyl]-2-ethoxypropionate (**7**). Oil. Yield 64.3% IR ν_{max}^{neat} cm^{-1}: 1740, 1680. NMR δ: 1.19 (3H, t, J = 7), 1.29 (3H, t, J = 7), 3.30 (1H, dd, J = 18 and 15), 3.45 (1H, dd, J = 18 and 7), 3.58 (1H, dq, J = 12 and 7), 3.76 (1H, dq, J = 12 and 7), 4.53 (1H, dd, J = 7 and 5), 7.00 (2H, q, J = 8), 7.02 (2H, d, J = 8), 7.37 (2H, d, J = 8), 7.96 (2H, d, J = 8). *Anal.* Calcd for $C_{20}H_{21}ClO_5$: C, 63.75; H, 5.62. Found: C, 63.52; H, 5.68.

2-Acetylthio-3-(4-phenoxybenzoyl)propionic Acid (**10**): 3-(4-Phenoxybenzoyl)acrylic acid[7] (10.0 g) and thioacetic acid (2.7 ml) were dissolved in CH_2Cl_2 (200 ml), then the mixture was stirred for 4 h at room temperature. The mixture was concentrated and the residue was purified by column chromatography on silica gel using CH_2Cl_2–hexane (1 : 1, v/v) as an eluent, then recrystallized from CH_2Cl_2–hexane to give **10** (11.3 g, 87.7%), mp 105—106.5 °C. IR ν_{max}^{KBr} cm^{-1}: 2500, 1705, 1700, 1680. NMR δ: 2.38 (3H, s), 3.55 (1H, dd, J = 16 and 4), 3.67 (1H, dd, J = 16 and 6), 4.77 (1H, dd, J = 6 and 4), 6.98—7.50 (7H, m), 7.93 (2H, d, J = 8), 9.13 (1H, br s). *Anal.* Calcd for $C_{18}H_{16}O_5S$: C, 62.78; H, 4.68. Found: C, 62.86; H, 4.70. Compounds **8**, **9**, **11**—**13**, **24**, **27**, **33**—**39** were similarly prepared.

2-Bromo-3-(4-phenoxybenzoyl)propionic Acid (**8**): mp 111—118 °C (dec.) (from Et_2O–hexane). Yield 56.8% IR ν_{max}^{KBr} cm^{-1}: 2500, 1690, 1660. NMR δ: 3.49 (1H, dd, J = 18 and 6), 3.91 (1H, dd, J = 18 and 7), 4.74 (1H, dd, J = 7 and 6), 6.85—8.05 (9H, m), 11.47 (1H, s). *Anal.* Calcd for $C_{16}H_{13}BrO_4$: C, 55.05; H, 3.75. Found: C, 54.76; H, 3.95.

2-Chloro-3-(4-phenoxybenzoyl)propionic Acid (**9**): mp 116—117 °C (dec.) (from Et_2O–hexane). Yield 76.4%. IR ν_{max}^{KBr} cm^{-1}: 2500, 1725, 1675. NMR δ: 3.45 (1H, dd, $J=18$ and 6), 3.80 (1H, dd, $J=18$ and 7), 4.82 (1H, dd, $J=7$ and 6), 6.82—8.00 (8H, m), 9.90 (1H, s). *Anal.* Calcd for $C_{16}H_{13}ClO_4$: C, 63.07; H, 4.30. Found: C, 63.34; H, 4.49.

Ethyl 2-Acetylthio-3-(4-phenoxybenzoyl)propionate (**11**): mp 78—79 °C (from Et_2O–hexane). Yield 93.2%. IR ν_{max}^{KBr} cm^{-1}: 1725, 1705, 1670. NMR δ: 1.26 (3H, t, $J=7$), 2.38 (3H, s), 3.53 (1H, dd, $J=18$ and 5), 3.66 (1H, dd, $J=18$ and 7), 4.23 (2H, q, $J=7$), 4.72 (1H, dd, $J=6$ and 4), 6.96—7.48 (7H, m), 7.95 (2H, d, $J=8$). *Anal.* Calcd for $C_{20}H_{20}O_5S$: C, 64.50; H, 5.41. Found: C, 64.28; H, 5.54.

2-Acetylthio-3-[4-(4-chlorophenoxy)benzoyl]propionic Acid (**12**): mp 91.5—94 °C (from Et_2O–hexane). Yield 92.5%. IR ν_{max}^{KBr} cm^{-1}: 2500, 1700, 1670. NMR δ: 2.39 (3H, s), 3.54 (1H, dd, $J=16$ and 4), 3.68 (1H, dd, $J=16$ and 6), 4.77 (1H, dd, $J=6$ and 4), 7.02 (2H, d, $J=8$), 7.03 (2H, d, $J=8$), 7.39 (2H, d, $J=8$), 7.95 (2H, d, $J=8$), 10.40 (1H, br s). *Anal.* Calcd for $C_{18}H_{15}ClO_5S$: C, 57.07; H, 3.99. Found: C, 57.19; H, 4.00.

Ethyl 2-Acetylthio-3-[4-(4-chlorophenoxy)benzoyl]propionate (**13**): mp 75.5—77 °C (from Et_2O–hexane). Yield 93.2%. IR ν_{max}^{KBr} cm^{-1}: 1720, 1705. NMR δ: 1.26 (3H, t, $J=7$). 2.37 (3H, s), 3.51 (1H, dd, $J=16$ and 4), 3.69 (1H, dd, $J=16$ and 6), 4.21 (2H, q, $J=7$), 4.71 (1H, dd, $J=6$ and 4), 7.05 (2H, d, $J=8$), 7.07 (2H, d, $J=8$), 7.07 (2H, d, $J=8$), 7.37 (2H, d, $J=8$), 7.95 (2H, d, $J=8$). *Anal.* Calcd for $C_{20}H_{19}ClO_5S$: C, 59.04; H, 4.71. Found: C, 59.02; H, 4.66.

Ethyl 2-Ethylthio-3-(4-phenoxybenzoyl)propionate (**24**): Oil. Yield 97.1%. IR ν_{max}^{neat} cm^{-1}: 1740, 1680. NMR δ: 1.30 (3H, t, $J=7$), 1.32 (3H, t, $J=7$), 2.77 (2H, m), 3.28 (1H, dd, $J=18$ and 4), 3.70 (1H, dd, $J=18$ and 8), 3.89 (1H, dd, $J=8$ and 4), 4.25 (2H, q, $J=7$), 6.97—7.50 (7H, m), 7.97 (2H, d, $J=8$). *Anal.* Calcd for $C_{20}H_{22}O_4S$: C, 67.01: H, 6.19. Found: C, 66.84; H, 6.32.

Ethyl 3-[4-(4-Chlorophenoxyl)benzoyl]-2-ethoxycarbonylmethylthiopropionate (**27**): Oil. Yield 91.0%. IR ν_{max}^{neat} cm^{-1}: 1710, 1680. NMR δ: 1.29 (6H, t, $J=7$), 3.32 (1H, dd, $J=18$ and 4), 3.35 (1H, d, $J=16$), 3.67 (1H, d, $J=16$), 3.70 (1H, dd, $J=18$ and 10), 4.01 (1H, dd, $J=10$ and 4), 4.10 (2H, q, $J=7$), 4.11 (2H, q, $J=7$), 7.02 (4H, d, $J=9$), 7.27 (2H, d, $J=9$), 7.96 (2H, d, $J=9$). *Anal.* Calcd for $C_{22}H_{23}ClO_6S$: C, 58.60; H, 5.14. Found: C, 58.51; H, 5.39.

Methyl 2-Acetylthio-3-(4-phenoxybenzoyl)propionate (**33**): mp 59—61 °C (from Et_2O–hexane). Yield 81.3%. IR ν_{max}^{KBr} cm^{-1}: 1725, 1670. NMR δ: 2.38 (3H, s), 3.56 (1H, dd, $J=18$ and 5), 3.66 (1H, dd, $J=18$ and 7), 3.76 (3H, s), 4.74 (1H, dd, $J=7$ and 5), 6.94—7.50 (7H, m), 7.94 (2H, d, $J=8$). *Anal.* Calcd for $C_{19}H_{18}O_5S$: C, 63.67; H, 5.06. Found: C, 63.49; H, 5.12.

Isopropyl 2-Acetylthio-3-(4-phenoxybenzoyl)propionate (**34**): Oil. Yield 93.8%. IR ν_{max}^{neat} cm^{-1}: 1730, 1690. NMR δ: 1.22 (3H, d, $J=6$), 1.25 (3H, d, $J=6$), 2.37 (3H, s), 3.51 (1H, dd, $J=17$ and 4), 3.66 (1H, dd, $J=17$ and 8), 4.67 (1H, dd, $J=8$ and 4), 5.05 (1H, m), 6.96—7.48 (7H, m), 8.01 (2H, d, $J=8$). *Anal.* Calcd for $C_{21}H_{22}O_5S$: C, 65.27; H, 5.74. Found: C, 65.19; H, 6.00.

n-Pentyl 2-Acetylthio-3-(4-phenoxybenzoyl)propionate (**35**): Oil. Yield 94.9%. IR ν_{max}^{neat} cm^{-1}: 1735, 1685. NMR δ: 0.83 (3H, m), 1.30 (4H, m), 1.63 (2H, m), 2.38 (3H, s), 3.52 (1H, dd, $J=18$ and 5), 3.66 (1H, dd, $J=18$ and 8), 4.14 (2H, t, $J=6$), 4.72 (1H, dd, $J=8$ and 5), 6.95—7.48 (7H, m), 7.94 (2H, d, $J=8$). *Anal.* Calcd for $C_{23}H_{26}O_5S$: C, 66.64; H, 6.32. Found: C, 66.40; H, 6.42.

2-Acetylthio-3-(4-phenoxybenzoyl)propionamide (**36**): mp 155—157 °C (from acetone–hexane). Yield 57.0%. IR ν_{max}^{KBr} cm^{-1}: 1690, 1670, 1655. NMR δ: 2.41 (3H, s), 3.32 (1H, dd, $J=18$ and 5), 3.77 (1H, dd, $J=18$ and 9), 4.70 (1H, dd, $J=9$ and 5), 5.38 (1H, br s), 6.38 (1H, br s), 6.99—7.47 (7H, m), 7.96 (2H, d, $J=9$). *Anal.* Calcd for $C_{18}H_{17}NO_4S$: C, 62.96; H, 4.99; N, 4.08. Found: C, 62.87; H, 5.19; N, 3.94.

2-Acetylthio-*N*,*N*-dimethyl-3-(4-phenoxybenzoyl)propionamide (**37**): mp 105—106 °C (from Et_2O–hexane). Yield 98.2%. IR ν_{max}^{KBr} cm^{-1}: 1690, 1670, 1650. NMR δ: 2.39 (3H, s), 2.99 (3H, s), 3.17 (1H, dd, $J=18$ and 4), 3.22 (3H, s), 4.01 (1H, dd, $J=18$ and 12), 5.07 (1H, dd, $J=12$ and 4), 6.98—7.96 (9H, m). *Anal.* Calcd for $C_{20}H_{21}NO_4S$: C, 64.67; H, 5.70; N, 3.77. Found: C, 64.64; H, 5.77; N, 3.74.

2-Acetylthio-*N*,*N*-diethyl-3-(4-phenoxybenzoyl)propionamide (**38**): mp 36—38 °C (from Et_2O–hexane). Yield 75.5%. IR ν_{max}^{KBr} cm^{-1}: 1680, 1660, 1630. NMR δ: 1.12 (3H, t, $J=7$), 1.36 (3H, t, $J=7$), 2.40 (3H, s), 3.17 (1H, dd, $J=18$ and 4), 3.26—3.56 (4H, m), 4.02 (1H, dd, $J=18$ and 10), 4.99 (1H, dd, $J=10$ and 4), 6.98—7.48 (7H, m), 7.96 (2H, d, $J=9$). *Anal.* Calcd for $C_{22}H_{25}NO_4S$: C, 66.14; H, 6.31; N, 3.51. Found: C, 66.12; H, 6.55; N, 3.36.

N-[2-Acetylthio-3-(4-phenoxybenzoyl)propionyl]morpholine (**39**): mp 129—131 °C (from CH_2Cl_2–hexane). Yield 80.7%. IR ν_{max}^{KBr} cm^{-1}: 1690, 1660, 1640. NMR δ: 2.39 (3H, s), 3.18 (1H, dd, $J=18$ and 4), 3.65—3.89 (8H, m), 4.01 (1H, dd, $J=18$ and 11), 5.05 (1H, dd, $J=11$ and 4), 6.98—7.46 (7H, m), 7.94 (2H, d, $J=8$). *Anal.* Calcd for $C_{22}H_{23}NO_5S$: C, 63.90; H, 5.61; N, 3.39. Found: C, 69.09; H, 5.88; N, 3.18.

Method B——Ethyl 2-Oxo-3-(4-phenoxybenzoyl)propionate (**3**): A portion of 55% NaH (1.2 g) was added to a stirred solution of 4-phenoxyacetophenone[8] (5.0 g) in dimethylformamide (DMF) (30 ml) and the stirring was continued for 30 min. Diethyl oxalate (4.2 g) was added dropwise to the mixture, which was then stirred for an additional 6 h at room temperarure. The mixture was poured into ice-water, then the whole was acidified with 10% HCl aq and extracted with AcOEt. The extract was washed with H_2O, dried ($MgSO_4$) and concentrated. The residue was purified by column chromatography on silica gel using acetone–hexane (1 : 10, v/v) as an eluent, and recrystallized from acetone–hexane to give **3** (2.4 g, 33.2%), mp 54—55 °C. IR ν_{max}^{KBr} cm^{-1}: 1740, 1600. NMR δ: 3.36 (3H, t, $J=7$), 4.35 (2H, q, $J=7$), 6.85—8.05 (9H, m), 6.94 (2H, s). *Anal.* Calcd for $C_{18}H_{16}O_5$: C, 69.22; H, 5.16. Found: C, 69.08; H, 5.25.

Compound **4** was similarly prepared.

Ethyl 3-[4-(4-Chlorophenoxy)benzoyl]-2-oxopropionate (**4**): mp 53—56 °C (from acetone–hexane). Yield 31.7%. IR ν_{max}^{KBr} cm^{-1}: 1730, 1600. NMR δ: 1.36 (3H, t, J=7), 4.34 (2H, q, J=7), 6.93 (2H, s), 6.83—7.10 (4H, m), 7.30 (2H, d, J=8), 7.90 (2H, q, J=8). *Anal.* Calcd for $C_{18}H_{15}ClO_5$: C, 62.35; H, 4.36. Found: C, 62.43; H, 4.50.

Method C——2-Hydroxy-3-(4-phenoxybenzoyl)propionic Acid (**1**): A mixture of 4-phenoxyacetophenone[8] (21.2 g) and glyoxylic acid hydrate (9.2 g) was stirred at 95 °C under reduced pressure (9 mmHg) for 2 h. After cooling, the mixture was dissolved in 5% K_2CO_3 aq., and washed with AcOEt. The aqueous layer was acidified with 10% HCl aq., and the whole was extracted with AcOEt. The extract was washed with H_2O, dried ($MgSO_4$) and concentrated. The residue was purified by column chromatography on silica gel using Et_2O–hexane (1 : 1, v/v) as an eluent, and recrystallized from Et_2O–hexane to give **1** (15.2 g, 53.2%), mp 96—98 °C. IR ν_{max}^{KBr} cm^{-1}: 3050, 2500, 1730, 1680. NMR δ: 3.52 (2H, d, J=6), 4.18 (1H, t, J=6), 6.50—8.00 (11H, m). *Anal.* Calcd for $C_{16}H_{14}O_5$: C, 67.13; H, 4.93. Found: C, 67.01; H, 5.06.

Compound **2** was similarly prepared.

3-[4-(4-Chlorophenoxy)benzoyl]-2-hydroxypropionic Acid (**2**): mp 132—133.5 °C (from Et_2O–hexane). Yield 54.4%. IR ν_{max}^{KBr} cm^{-1}: 3100, 2500, 1730, 1680. NMR (acetone-d_6) δ: 3.45 (2H, d, J=5), 4.50 (1H, br s), 4.71 (1H, t, J=5), 7.07—8.15 (9H, m). *Anal.* Calcd for $C_{16}H_{13}ClO_5$: C, 59.92; H, 4.08. Found: C, 59.78; H, 4.15.

2-Acetoxy-3-(4-phenoxybenzoyl)propionic Acid (**14**): A solution of acetyl chloride (0.34 ml) in Et_2O (20 ml) was added dropwise to a stirred and ice-cooled solution of compound **1** (1.38 g) and pyridine (0.39 ml) in Et_2O (30 ml). After being stirred for 1 h at room temperature, the mixture was washed with 10% HCl aq. and H_2O, then dried ($MgSO_4$) and concentrated. The residue was purified by column chromatography on silica gel using Et_2O–hexane (1 : 1, v/v) as an eluent, and recrystallized from Et_2O–hexane to give **14** (0.85 g, 53.7%), mp 115.5—117.5 °C. IR ν_{max}^{KBr} cm^{-1}: 2500, 1770, 1740, 1660. NMR δ: 2.09 (3H, s), 3.51 (2H, d, J=6), 5.67 (1H, t, J=6), 6.75—8.00 (9H, m), 9.40 (1H, br s). *Anal.* Calcd for $C_{18}H_{16}O_6$: C, 65.85; H, 4.91. Found: C, 65.63; H, 5.03.

Method D——Ethyl 2-Acetonyl-3-(4-phenoxybenzoyl)propionate (**15**): Isopropylisopropylideneamine[9] (2.76 g) was added to a stirred solution of ethyl 3-(4-phenoxybenzoyl)acrylate[7] (4.0 g) in acetone (40 ml), and the stirring was continued for 3 h at room temperature. The 6 N HCl aqueous solution (20 ml) was added to the mixture, and the whole was stirred for 15 h at room temperature. Et_2O was added, and the mixture was washed with H_2O, dried ($MgSO_4$) and concentrated. The residue was purified by column chromatography on silica gel using Et_2O–hexane (1 : 2, v/v) as an eluent to give **15** as an oil (3.0 g, 63.2%). IR ν_{max}^{neat} cm^{-1}: 1730, 1677. NMR δ: 1.24 (3H, t, J=7), 2.82 (1H, dd, J=17 and 6), 3.01 (1H, dd, J=17 and 4), 3.25 (1H, dd, J=18 and 8), 3.44 (2H, m), 4.17 (2H, q, J=7), 7.02 (2H, d, J=8), 7.08 (2H, d, J=8), 7.24 (1H, q, J=8), 7.42 (2H, t, J=8), 7.96 (2H, d, J=8). *Anal.* Calcd for $C_{21}H_{22}O_5$: C, 71.17; H, 6.26. Found: C, 71.16; H, 6.33.

Compound **16** was similarly prepared.

Ethyl 2-Acetonyl-3-[4-(4-chlorophenoxy)benzoyl]propionate (**16**): Oil. Yield 65.4%. IR ν_{max}^{neat} cm^{-1}: 1735, 1680. NMR δ: 1.21 (3H, t, J=7), 2.16 (3H, s), 2.78 (1H, dd, J=17 and 5), 2.98 (1H, dd, J=17 and 6), 3.22 (1H, dd, J=18 and 8), 3.42 (2H, m), 4.13 (2H, q, J=7), 6.98 (2H, d, J=8), 7.00 (2H, d, J=8), 7.34 (2H, d, J=8), 7.94 (2H, d, J=8). *Anal.* Calcd for $C_{21}H_{21}ClO_5$: C, 64.87; H, 5.44. Found: C, 64.81; H, 5.58.

Method E——2-Mercapto-3-(4-phenoxybenzoyl)propionic Acid (**21**): A mixture of compound **10** (3.44 g), AcOH (20 ml), conc. H_2SO_4 (2 ml) and H_2O (6 ml) was refluxed for 2 h, then AcOH was distilled off under reduced pressure. The residue was dissolved in AcOEt, and the whole was washed with H_2O, dried ($MgSO_4$) and concentrated. The residue was purified by column chromatography on silica gel using Et_2O–hexane (1 : 2, v/v) as an eluent and recrystallized from Et_2O–hexane to give **21** (1.87 g, 61.9%) mp 134—135 °C. IR ν_{max}^{KBr} cm^{-1}: 2560, 1700, 1665. NMR (d_6-acetone) δ: 2.68 (1H, d, J=9), 3.48 (1H, dd, J=18 and 5), 3.73 (1H, dd, J=18 and 7), 3.96 (1H, dd, J=7 and 5), 7.03—7.55 (7H, m), 7.38 (1H, s), 8.08 (2H, d, J=8). *Anal.* Calcd for $C_{16}H_{14}O_4S$: C, 63.56; H, 4.67. Found: C, 63.54; H, 4.70.

Compounds **22** and **23** were similarly prepared.

Ethyl 2-Mercapto-3-(4-phenoxybenzoyl)propionate (**22**): mp 46—47.5 °C (from Et_2O–hexane). Yield 82.1%. IR ν_{max}^{KBr} cm^{-1}: 2540, 1735, 1662. NMR δ: 1.30 (3H, t, J=7), 2.26 (1H, d, J=9), 3.42 (1H, dd, J=18 and 5), 3.68 (1H, dd, J=18 and 8), 3.96 (1H, td, J=8 and 5), 4.25 (2H, q, J=7), 6.97—7.50 (7H, m), 7.96 (2H, d, J=8). *Anal.* Calcd for $C_{18}H_{18}O_4S$: C, 65.44; H, 5.50. Found: C, 65.37; H, 5.56.

Ethyl 3-[4-(4-Chlorophenoxy)benzoyl]-2-mercaptopropionate (**23**): mp 75.5—76.5 °C (from Et_2O–hexane). Yield 76.1%. IR ν_{max}^{KBr} cm^{-1}: 2540, 1735, 1665. NMR δ: 1.30 (3H, t, J=7), 2.26 (1H, d, J=9), 3.41 (1H, dd, J=18 and 5), 3.68 (1H, dd, J=18 and 7), 3.96 (1H, m), 4.24 (2H, q, J=7), 7.00 (2H, d, J=8), 7.02 (2H, d, J=8), 7.37 (2H, d, J=8), 7.96 (2H, d, J=8). *Anal.* Calcd for $C_{18}H_{17}ClO_4S$: C, 59.26; H, 4.70. Found: C, 59.14; H, 4.76.

Ethyl 2-(3-Oxobutylthio)-3-(4-phenoxybenzoyl)propionate (**25**): A solution of compound **22** (990 mg) and methyl vinyl ketone (250 mg) in DMF (10 ml) was stirred for 3 h at room temperature. The solution was suspended with H_2O, and extracted with AcOEt. The extract was washed with H_2O, dried ($MgSO_4$) and concentrated. The residue was purified by column chromatography on silica gel using Et_2O–hexane (1 : 1, v/v) as an eluent to give **25** as an oil (1.14 g, 94.9%). IR ν_{max}^{neat} cm^{-1}: 1720, 1675. NMR δ: 1.29 (3H, t, J=7), 2.19 (3H, s), 2.75—2.84 (2H, m), 2.93—3.00 (2H, m), 2.25 (1H, dd, J=18 and 5), 3.66 (1H, dd, J=18 and 10), 3.86 (1H, dd, J=10 and 5), 4.23 (2H, q, J=7),

6.99—7.45 (2H, d, J=9). *Anal.* Calcd for $C_{22}H_{24}O_5S$: C, 65.98; H, 6.04. Found: C, 65.86; H, 6.18.

Compound **28** was similarly prepared.

Ethyl 3-[4-(4-Chlorophenoxy)benzoyl]-2-(2-ethoxycarbonylethylthio)propionate (**28**): Oil. Yield 28.2%. IR ν_{max}^{neat} cm^{-1}: 1780, 1675. NMR δ: 1.26 (3H, t, J=7), 1.29 (3H, t, J=7), 2.66 (2H, m), 3.00 (2H, m), 3.24 (1H, dd, J=18 and 4), 3.67 (1H, dd, J=18 and 10), 3.87 (1H, dd, J=10 and 4), 4.15 (2H, q, J=7), 4.22 (2H, q, J=7), 6.99 (2H, d, J=8), 7.01 (2H, d, J=8), 7.36 (2H, d, J=8), 7.95 (2H, d, J=8). *Anal.* Calcd for $C_{23}H_{25}ClO_6S$: C, 59.41; H, 5.42. Found: C, 59.32; H, 5.34.

Ethyl 3-[4-(4-Chlorophenoxy)benzoyl]-2-methoxycarbonylthiopropionate (**26**): Methyl chlorocarbonate (0.56 g) was added dropwise to a stirred and ice-cooled solution of **22** (1.82 g) and pyridine (0.5 ml) in Et_2O (50 ml). After being stirred for 3 h at room temperature, the mixture was washed with H_2O, dried ($MgSO_4$) and concentrated. The residue was recrystallized from Et_2O–hexane to give **26** (1.07 g, 50.8%), mp 60—62 °C. IR ν_{max}^{KBr} cm^{-1}: 1720, 1675. NMR δ: 2.28 (3H, t, J=7), 3.57 (1H, dd, J=18 and 5), 3.78 (1H, dd, J=18 and 7), 3.85 (3H, s), 4.25 (2H, q, J=7), 4.56 (1H, dd, J=7 and 5), 7.01 (4H, d, J=8), 7.38 (2H, d, J=8), 7.97 (2H, d, J=8). *Anal.* Calcd for $C_{20}H_{19}ClO_6S$: C, 56.81; H, 4.53. Found: C, 56.94; H, 4.66.

Compounds **29**—**32** were similarly prepared.

Ethyl 3-(4-Phenoxybenzoyl)-2-propionylthiopropionate (**29**): mp 55—57 °C (from Et_2O–hexane). Yield 89.4%. IR ν_{max}^{KBr} cm^{-1}: 1730, 1710, 1670. NMR δ: 1.19 (3H, t, J=7), 1.26 (3H, t, J=7), 2.62 (2H, q, J=7), 3.52 (1H, dd, J=18 and 5), 3.66 (1H, dd, J=18 and 7), 4.21 (2H, q, J=7), 4.71 (1H, dd, J=7 and 5), 6.96—7.48 (7H, m), 7.94 (2H, d, J=8). *Anal.* Calcd for $C_{21}H_{22}O_5S$: C, 65.27; H, 5.74. Found: C, 65.29; H, 5.69.

Ethyl 2-Benzoylthio-3-(4-phenoxybenzoyl)propionate (**30**): mp 95—96 °C (from Et_2O). Yield 51.2%. IR ν_{max}^{KBr} cm^{-1}: 1730, 1670. NMR δ: 1.26 (3H, t, J=7), 3.65 (1H, dd, J=18 and 5), 3.77 (1H, dd, J=18 and 7), 4.25 (2H, q, J=7), 4.94 (1H, dd, J=7 and 5), 6.96—7.66 (10H, m), 7.97 (4H, m). *Anal.* Calcd for $C_{25}H_{22}O_5S$: C, 69.11; H, 5.10. Found: C, 69.02; H, 5.15.

Ethyl 2-Isobutyrylthio-3-(4-phenoxybenzoyl)propionate (**31**): Oil. Yield 86.7%. IR ν_{max}^{neat} cm^{-1}: 1735, 1680. NMR δ: 0.89 (9H, m), 2.79 (1H, heptet, J=6), 3.52 (1H, dd, J=17 and 5), 3.68 (1H, dd, J=17 and 8), 4.22 (2H, q, J=7), 4.70 (1H, dd, J=8 and 5), 6.98—7.48 (7H, m), 7.96 (2H, d, J=8). *Anal.* Calcd for $C_{22}H_{24}O_5S$: C, 65.98; H, 6.04. Found: C, 65.70; H, 5.97.

Ethyl 2-Hexanoylthio-3-(4-phenoxybenzoyl)propionate (**32**): Oil. Yield 79.7%. IR ν_{max}^{neat} cm^{-1}: 1735, 1680. NMR δ: 0.89 (3H, m), 1.27 (3H, t, J=7), 1.30 (4H, m), 1.69 (2H, m), 2.60 (2H, t, J=7), 3.51 (1H, dd, J=17 and 4), 3.67 (1H, dd, J=17 and 8), 4.22 (2H, q, J=7), 4.72 (1H, dd, J=8 and 4), 6.96—7.48 (7H, m), 7.95 (2H, d, J=8). *Anal.* Calcd for $C_{24}H_{28}O_5S$: C, 67.27; H, 6.59. Found: C, 67.27; H, 6.51.

Method F——3-Acetylthio-3-(4-phenoxybenzoyl)propionic Acid (**18**): A solution of Br_2 (5.7 g) in $CHCl_3$ (20 ml) was added dropwise to a stirred solution of 3-(4-phenoxybenzoyl)propionic acid[2] (27.1 g) in $CHCl_3$ (150 ml). The mixture was stirred for an additional 3 h at room temperature, and $CHCl_3$ was removed under reduced pressure. The residue was dissolved in Et_2O and the whole was washed with H_2O, dried ($MgSO_4$) and concentrated. The residue was dissolved in DMF (40 ml), and AcSK (3.53 g) was added to the solution under stirring. The stirring was continued for 3.5 h at room temperature, and the mixture was suspended in H_2O. The whole was extracted with AcOEt, and the extract was washed with H_2O, dried ($MgSO_4$) and concentrated. The residue was purified by column chromatography on silica gel with acetone–hexane (1 : 10, v/v) as an eluent and recrystallized from acetone–hexane to give **18** (26.0 g, 75.6%), mp 105—107 °C. IR ν_{max}^{KBr} cm^{-1}: 2500, 1700, 1695, 1660. NMR δ: 2.63 (3H, s), 2.78 (1H, dd, J=8 and 4), 3.32 (1H, dd, J=8 and 6), 5.49 (1H, dd, J=6 and 4), 6.99 (2H, d, J=8), 7.09 (2H, d, J=8), 7.22 (1H, t, J=8), 7.42 (2H, d, J=8), 7.96 (2H, d, J=8). *Anal.* Calcd for $C_{18}H_{16}O_5S$: C, 62.78; H, 4.68. Found: C, 62.59; H, 4.82.

Compound **20** was similarly prepared.

3-Acetylthio-3-[4-(4-chlorophenoxy)benzoyl]propionic Acid (**20**): mp 101—103 °C (from Et_2O–hexane). Yield 51.5%. IR ν_{max}^{KBr} cm^{-1}: 2500, 1740—1670. NMR δ: 2.37 (3H, s), 2.80 (1H, dd, J=16 and 5), 3.34 (1H, dd, J=16 and 8), 5.49 (1H, dd, J=8 and 5), 6.60 (1H, br s), 6.96—7.10 (4H, m), 7.38 (2H, d, J=9), 7.96 (2H, d, J=9). *Anal.* Calcd for $C_{18}H_{15}ClO_5S$: C, 57.07; H, 3.99. Found: C, 57.03; H, 4.15.

3-Mercapto-3-(4-phenoxybenzoyl)propionic Acid (**17**): An 80% N_2H_4 aqueous solution (0.99 g) was added to a stirred and ice-cooled solution of **18** (3.65 g) in THF (35 ml). The mixture was stirred for 30 min at room temperature and THF was removed under reduced pressure. The residue was suspended in H_2O and the whole was extracted with AcOEt. The extract was washed with H_2O, dried ($MgSO_4$) and concentrated. The residue was purified by column chromatography on silica gel using Et_2O–hexane (1 : 5, v/v) as an eluent and recrystallized from acetone–hexane to give **17** (1.64 g, 51.5%), mp 98—99.5 °C. IR ν_{max}^{KBr} cm^{-1}: 3400, 2540, 1705, 1665. NMR δ: 2.02 (1H, d, J=10), 2.94 (1H, dd, J=17 and 6), 3.30 (1H, dd, J=17 and 9), 4.56 (1H, m), 7.03 (2H, d, J=8), 7.09 (2H, d, J=8), 7.24 (1H, t, J=8), 7.42 (2H, t, J=8), 8.00 (2H, d, J=8). *Anal.* Calcd for $C_{16}H_{16}O_4S$: C, 63.56; H, 4.67. Found: C, 63.52; H, 4.84.

Compound **19** was similarly prepared.

3-[4-(4-Chlorophenoxy)benzoyl]-3-mercaptopropionic Acid (**19**): mp 110—112 °C (from acetone–hexane). Yield 62.4%. IR ν_{max}^{KBr} cm^{-1}: 3400, 2500, 1695, 1670. NMR δ: 2.03 (1H, d, J=11), 2.95 (1H, dd, J=18 and 5), 3.32 (1H, dd, J=18 and 7), 4.56 (1H, ddd, J=11, 7 and 5), 7.03 (2H, d, J=9), 7.04 (2H, d, J=9), 7.39 (2H, d, J=9), 8.02 (2H, d, J=9). *Anal.* Calcd for $C_{16}H_{13}ClO_4S$: C, 57.06; H, 3.89. Found: C, 57.11; H, 3.80.

Preparation of the Ester Derivatives of 3-(4-Phenoxybenzoyl)acrylic Acids——A typical example is given to illustrate the general procedure. Ethyl 3-(4-phenoxybenzoyl)acrylate: 3-(4-Phenoxybenzoyl)acrylic acid (5.36 g) and Et_2SO_4 (3.68 g) was dissolved in DMF (30 ml), then K_2CO_3 (1.36 g) was added under stirring. The mixture was stirred for an additional 3 h at room temperature, then suspended in H_2O and the whole was extracted with Et_2O. The extract was washed with H_2O, dried ($MgSO_4$) and concentrated. The residue was recrystallized from Et_2O–hexane to give ethyl 3-(4-phenoxybenzoyl)acrylate (4.36 g, 73.7%), mp 50—53.5 °C (lit.[7] mp 46 °C).

The following compounds were similarly prepared. Methyl 3-(4-phenoxybenzoyl)acrylate: mp 88—90 °C (from benzene–hexane) (lit.[7] mp 93 °C), 93.2%. Isopropyl 3-(4-phenoxybenzoyl)acrylate: mp 71.5—72 °C (from Et_2O–hexane), 75.4%. *n*-Pentyl 3-(4-phenoxybenzoyl)acrylate: Oil, 61.7%. Ethyl 3-[4-(4-chlorophenoxy)benzoyl]acrylate: mp 57—58 °C (from Et_2O–hexane), 92.3%.

Preparation of the Amide Derivatives of 3-(4-Phenoxybenzoyl)acrylic Acid——A typical example is given to illustrate the general procedure. 3-(4-Phenoxybenzoyl)acrylamide: Isobutyl chloroformate (0.8 ml) was added to a stirred solution of 3-(4-phenoxybenzoyl)acrylic acid (1.3 g) and Et_3N (0.7 ml) in toluene (15 ml) at −5 °C, and the stirring was continued at −5 °C for 30 min. A 28% NH_3 aqueous solution (0.4 ml) was added dropwise to the mixture and the whole was stirred at room temperature for 2 h. The mixture was dissolved in AcOEt, and the solution was washed with 5% Na_2CO_3 aq., dried ($MgSO_4$) and concentrated. The residue was recrystallized from acetone–hexane to give 3-(4-phenoxybenzoyl)acrylamide (1.06 g, 81.8%), mp 165 °C (dec.).

The following compounds were similarly prepared. *N*,*N*-Dimethyl-3-(4-phenoxybenzoyl)acrylamide: mp 118—120 °C (from AcOEt–hexane), 73.8%. *N*,*N*-Diethyl-3-(4-phenoxybenzoyl)acrylamide: mp 67—68 °C (from acetone–hexane), 90.4%. *N*-[3-(4-Phenoxybenzoyl)acryloyl]morpholine: mp 94.5—95.5 °C (from CH_2Cl_2–hexane), 62.4%.

References and Notes

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