An Improved of α-(Thioacylthio)methylphenyl-Ketones using Caesium Dithioates and a Convenient Synthesis of 2,4-Disubstituted 1,3-Thiazoles *via* the Ketones

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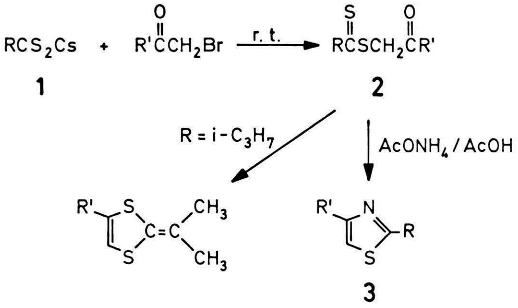
α-(Thiocylthio)methylphenylketones, 2,4-Disubstituted 1,3-Thiazoles, Caesium Dithioates

α-(Thioacylthio)methylphenylketones were found to be obtained in almost quantitative yields from caesium dithioates and *α*-phenacyl bromide. Refluxing of these ketones with ammonium acetate in gracial acetic acid affords the corresponding 2,4-disubstituted 1,3-thiazoles. While, the similar reaction of *α*-(thioisobutyrylthio)methylphenylketone gives the dithiafulvene (**4**).

α-(Thioaroylthio)methylarylketones (**2**) are known to be useful in synthesis of cyclic dithiolium compounds, especially meso ion compounds [1]. In general, the preparation of these aromatic ketones from *α*-bromoacetophenone and sodium dithioates leads to relatively low yields [2]. In the previous papers, we reported the preparation of a series of caesium dithioates (**1**) [3], which were found to react more readily with halotrimethylsilanes than the corresponding ammonium or sodium salts to give the corresponding silyl esters [4]. In this paper, we described an improved preparation of the ketones (**2**) by the use of caesium dithioates (**1**), and a convenient synthesis of 2,4-disubstituted-1,3-thiazoles (**3**) *via* (**2**).



As shown in Table I, the yields of **2** are substantially improved and almost quantitative. Preparation procedures are very easy. In order to extend the synthetic utility of **2**, the reactions of **2** with excess of ammonium acetate have been attempted according to the conditions, described by Dubs and Stuessi [5]. The results are summarized in Table II. The expected 1,3-thiazoles (**3**), indeed, can be obtained although the low yields. It is noted that the similar treatment of phenacyl dithioisobutyrate (**2e**) was led to only 2,2-isopropylidene-4-phenyl-1,3-dithiolene (**4**) in appreciable yield, formed by the hydrogen abstraction of *α*-position to the thiocarbonyl group. The structures of **2**, **3**, and **4** obtained here were established by IR, UV, Visible, ^{1}H NMR, and Mass spectral data and elemental analysis.

Experimental

Melting points were determined using a Yanagimoto micro melting point apparatus and are uncorrected. The IR spectra were measured on a JASCO grating IR spectrophotometer IR–G. The UV and Visible spectra were obtained from a Hitachi 124 spectrophotometer. The ^{1}H NMR spectra were recorded on a Hitachi R-24 (60 MHz) with tetramethylsilane as an internal standard. The mass spectra were taken on the Hitachi RMU-6M high resolution mass spectrometer. Elemental analyses were performed by the Elemental Analyses Centers of Kyoto and Nagoya Universities, or Wako Junyaku Co.

Materials

Piperidinium[1], caecium [2] and sodium dithiocarboxylates [5] were prepared according to the literatures. Phenacyl and 4-bromophenacyl bromides were reagent grade of Wako Junyaku Co.

Typical procedures for the preparation of the aliphatic and aromatic *α*-(thioacylthio)ketones (**2**), and 1,3-thiazoles (**3**) are described below.

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Table I. Yields and physical properties of α-(thioacylthio)methylphenylketones (**2**).

No.	$RCS_2CH_2C(O)R'$ R	R′	Yield[a] [%]	Method[b]	M.p. [°C]	IR [cm^{-1}]	$\nu C{=}O$	$\nu C{=}S$	UV, Vis [cm^{-1}][c] λmax (log ε)	^1H NMR[d] δ [ppm]
2a	CH_3	4-BrC_6H_4	92 54 61	A B C	99–99.5	KBr	1673	1185	263(4.44) 306(4.02) 457(1.48)	2.80 (s, 3H, CH_3), 4.64 (s, 2H, CH_2), 7.30–7.83 (m, 4H, Ar)
2b	C_2H_5	C_6H_5	95 55	A C	oil	neat	1687	1202	306(3.75) 435(1.34)	1.32 (t, 3H, CH_3), 3.03 (q, 2H, CH_2), 4.70 (s, 2H, CH_2), 7.26–8.15 (m, 5H, Ar)
2c		4-BrC_6H_4	82 48	A B	44–44.3	KBr	1685	1207	262(4.32) 306(4.08) 450(1.51)	1.34 (t, 3H, CH_3), 3.04 (q, 2H, CH_2), 4.68 (s, 2H, CH_2), 7.45–7.95 (m, 4H, Ar)
2d	*n*-C_3H_7	4-BrC_6H_4	35	B	38–39	KBr	1688	1202	261(4.23) 306(4.00) 450(1.51)	0.94 (t, 3H, CH_3), 1.80 (m, 4H, CH_2), 4.65 (s, 2H, CH_2S), 7.45–7.95 (m, 4H, Ar)
2e	*i*-C_3H_7	C_6H_5	38	B	oil	neat	1690	1198	306(3.94) 447(1.54)	1.26 (d, 6H, CH_3), 3.43 (m, 1H, CH), 4.71 (s, 2H, CH_2), 7.26–8.15 (m, 5H, Ar)
2f		4-BrC_6H_4	46	B	38.5–40.2	KBr	1680	1189	262(4.29) 306(4.07) 450(1.62)	1.29 (d, 6H, CH_3), 3.44 (m, 1H, CH), 4.75 (s, 2H, CH_2), 7.56–8.05 (m, 4H, Ar)
2g	*cyclo*-C_6H_{11}	4-BrC_6H_4	56	B	94–95.5	KBr	1690	1202	261(4.23) 307(3.96) 452(1.57)	1.00–2.08 (m, 10H, *cyclo*-C_6H_{11}), 2.81–3.29 (m, 1H, *cyclo*-C_6H_{11}), 4.53 (s, 2H, CH_2), 7.81–7.93 (m, 4H, Ar)
2h	C_6H_5	C_6H_5	59	C	78.5–79.5	KBr	1685	1230	297(4.21) 496(2.12)	4.80 (s, 2H, CH_2), 7.00–8.10 (m, 10H, Ar)
2i		4-$CH_3C_6H_4$	37	B	109.5–111	KBr	1674	1230	298(4.23) 496(2.14)	2.26 (s, 3H, CH_3), 4.60 (s, 2H, CH_2), 7.00–8.10 (m, 9H, Ar)
2j		4-$CH_3OC_6H_4$	61	B	82.5–83.5	KBr	1673	1230	282(4.45) 497(2.15)	3.85 (s, 3H, CH_3O), 4.90 (s, 2H, CH_2), 6.95–8.02 (m, 9H, Ar)
2k		4-ClC_6H_4	53	B	88–89	KBr	1681	1240	298(4.25) 497(2.14)	4.79 (s, 2H, CH_2), 7.12–8.10 (m, 9H, Ar)
2l		4-BrC_6H_4	48	B	89.5–91	KBr	1690	1240	299(4.28) 496(2.16)	4.79 (s, 2H, CH_2), 7.10–8.05 (m, 9H, Ar)
2m	4-$CH_3C_6H_4$	C_6H_5	98 77	A C	108–109	KBr	1685	1230	314(4.32) 496(2.20)	2.22 (s, 3H, CH_3), 4.62 (s, 2H, CH_2), 7.02 (m, 9H, Ar)
2n		4-$CH_3C_6H_4$	64	B	123–125	KBr	1679	1230	314(4.33) 497(2.23)	2.23 (s, 3H, CH_3), 2.27 (s, 3H, CH_3), 4.59 (s, 2H, CH_2), 7.15 (m, 8H, Ar)
2o		4-$CH_3OC_6H_4$	57	B	124–126	KBr	1682	1236	313(4.37) 496(2.24)	2.30 (s, 3H, CH_3), 3.81 (s, 3H, CH_3O), 4.83 (s, 2H, CH_2), 7.05–8.10 (m, 8H, Ar)
2p		4-ClC_6H_4	58	B	109.5–111.5	KBr	1680	1230	315(4.36) 496(2.24)	2.30 (s, 3H, CH_3), 4.75 (s, 2H, CH_2), 7.05–7.84 (m, 8H, Ar)
2q		4-BrC_6H_4	61	B	117–118	KBr	1681	1240	314(4.35) 495(2.24)	2.35 (s, 3H, CH_3), 4.85 (s, 2H, CH_2), 7.20–8.15 (m, 8H, Ar)
2r	2-$CH_3OC_6H_4$	C_6H_5	66	C	85–91	KBr	1680	1240	318(4.02) 489(2.16)	3.75 (s, 3H, CH_3O), 4.81 (s, 2H, CH_2), 6.67–8.07 (m, 9H, Ar)

Table I (continued).

No.	$RCS_2CH_2C(O)R'$ R	R′	Yield[a] [%]	Meth-ods[b]	M.p. [°C]	IR [cm^{-1}]	$\nu C{=}O$	$\nu C{=}S$	UV, Vis [cm^{-1}][c] λmax (log ε)	^1H NMR[d] δ [ppm]
2s	$4\text{-}CH_3OC_6H_4$	C_6H_5	95 58	A B	122–123	KBr	1688	1240	338(4.62)	3.90 (s, 3H, CH_3O), 4.86 (s, 2H, CH_2), 6.63–8.23 (m, 9H, Ar)
2t	$4\text{-}ClC_6H_4$	C_6H_5	97 59	A C	117–120	KBr	1677	1240	307(4.32) 500(2.24)	4.90 (s, 2H, CH_2), 7.18–8.28 (m, 9H, Ar)
2u		$4\text{-}CH_3C_6H_4$	53	B	104.5–106	KBr	1673	1230	308(4.32) 498(2.23)	2.41 (s, 3H, CH_3), 4.90 (s, 2H, CH_2), 7.12–8.15 (m, 8H, Ar)
2v	$4\text{-}ClC_6H_4$	$4\text{-}CH_3OC_6H_4$	81	A	138–140	KBr	1667	1230	291(4.43) 500(2.25)	3.82 (s, 3H, CH_3O), 4.80 (s, 2H, CH_2), 6.95–8.05 (m, 8H, Ar)
2w		$4\text{-}ClC_6H_4$	54	B	119–120	KBr	1686	1230	308(4.38) 500(2.25)	4.75 (s, 2H, CH_2), 7.10–8.05 (m, 8H, Ar)
2x		$4\text{-}BrC_6H_4$	65	B	109–110	KBr	1680	1230	308(4.35) 499(2.16)	4.78 (s, 2H. CH_2), 7.12–8.05 (m, 8H, Ar)
2y	$1\text{-}C_{10}H_7$	C_6H_5	68	B	78.5–80	KBr	1691	1245	–	4.95 (s, 2H, CH_2), 7.20–8.08(m, 12H, Ar)

[a] The isolated yield; [b] the starting dithio salt: A = caesium dithioate, B = piperidinium dithioate, and C = sodium dithioate; [c] THF; [d] $CDCl_3$.

Table I (continued).

No.	$RCS_2CH_2C(O)R'$ R	R′	Formula (mol. weight)		Elemental analyses [%] C	H	S
2a	CH_3	$4\text{-}BrC_6H_4$	$C_{10}H_9OS_2Br$	Calcd	41.53	3.14	22.17
			(289.21)	Found	41.71	3.22	22.32
2b	C_2H_5	C_6H_5	$C_{11}H_{12}OS_2$	Calcd	58.89	5.39	
			(224.34)	Found	58.70	5.42	
2d	$n\text{-}C_3H_7$	$4\text{-}BrC_6H_4$	$C_{12}H_{13}OS_2Br$	Calcd	45.43	4.13	
			(317.27)	Found	45.61	4.09	
2e	$i\text{-}C_3H_7$	C_6H_5	$C_{12}H_{14}OS_2$	Calcd	60.47	5.92	26.90
			(238.37)	Found	60.73	6.06	27.09
2g	*cyclo*-C_6H_{11}	$4\text{-}BrC_6H_4$	$C_{15}H_{17}OS_2Br$	Calcd	50.42	4.80	
			(357.33)	Found	50.48	4.97	
2h	C_6H_5	C_6H_5	$C_{15}H_{12}OS_2$	Calcd	66.14	4.44	
			(272.39)	Found	66.23	4.56	
2m	$4\text{-}CH_3C_6H_4$	C_6H_5	$C_{16}H_{14}OS_2$	Calcd	67.09	4.93	22.39
			(286.41)	Found	67.32	4.87	22.62
2r	$2\text{-}CH_3OC_6H_4$	C_6H_5	$C_{16}H_{14}O_2S_2$	Calcd	63.55	4.67	
			(302.41)	Found	63.85	4.81	
2t	$4\text{-}ClC_6H_4$	C_6H_5	$C_{15}H_{11}OS_2Cl$	Calcd	58.72	3.61	
			(306.85)	Found	58.83	3.70	
2y	$1\text{-}C_{10}H_7$	C_6H_5	$C_{19}H_{14}OS_2$	Calcd	70.77	4.38	
			(322.45)	Found	70.94	4.49	

α-(Thioacetylthio)-4-bromoacetophenone (**2a**)

Caesium dithioacetate (0.54 g, 2.4 mmol) and 4-bromophenacyl bromide (0.67 g, 2.4 mmol) were stirred in dichloromethane (20 ml) at room temperature for 1 h. After washing of the reaction mixture with water, the dichloromethane layer was dried over anhydrous sodium sulfate. Evaporation of the solvent under the reduced pressure and recrystallization of the resulting residue from *n*-hexane gave 0.64 g (92%) of **2a**.

α-(4-Methoxythiobenzoylthio)-acetophenone (**2s**)

Caesium dithio-4-methoxybenzoate (0.74 g, 2.3 mmol) and phenacyl bromide (0.5 g, 2.5 mmol) were stirred in dichloromethane (20 ml) at room

Table II. Yields and physical properties of 2,4-disubstituted 1,3-thiazoles (**3**).

No.	2-R, 5-R′-Thiazole R	 R′	Yield [%]	M.p. [°C]	IR [cm^{-1}]^a νC=N	UV, Vis [nm]^b λmax (log ε)	^{1}H NMR^c δ
3a	CH_3	4-BrC_6H_4	35	135–136.5	1500	273(4.23)	2.70 (s, 3H, CH_3), 7.13–7.30 (m, 1H, CH), 7.35–7.83 (m, 4H, Ar)
3b	C_2H_5		16	82.5–84	1494	273(4.30)	1.35 (t, 3H, CH_3), 3.02 (q, 2H, CH_2), 7.15–7.27 (m, 1H, CH), 7.30–7.80 (m, 4H, Ar)
3c	*cyclo*-C_6H_{11}		41	88.2–89	1489	273(3.91)	0.90–2.42 (m, 10H, CH_2), 2.72–3.20 (m, 1H, CH), 7.10–7.20 (m, 1H, CH), 7.24–7.85 (m, 4H, Ar)
3d	C_6H_5	C_6H_5	40	95–95.5	1483	251(4.25) 314(3.89)	7.05–7.55 (m, 6H, Ar and Thiazole ring-H), 7.65–8.11 (m, 5H, Ar)
3e	4-$CH_3C_6H_4$		26	129.5–130	1483	255(4.33) 314(4.02)	2.85 (s, 3H, CH_3), 7.06–7.18 (m, 1H, CH), 7.20–7.52 (m, 5H, Ar), 7.74–8.10 (m, 4H, Ar)
3f	4-$CH_3OC_6H_4$		27	98.5–99.5	1490	262(4.65) 314(4.46)	3.81 (s, 3H, CH_3), 7.23–7.50 (m, 6H, Ar and Thiazole ring-H), 7.70–8.10 (m, 4H, Ar)
3g	4-ClC_6H_4	C_6H_5	37	104–105	1479	256(4.46) 315(4.05)	7.15–7.55 (m, 6H, Ar) and 7.70–8.05 (m, 4H, Ar)

^{a} KBr; ^{b} CH_2Cl_2; ^{c} $CDCl_3$.

Table II (continued).

No.	2-R, 5-R′-Thiazole R	 R′	Formula (mol. weight)		Elemental analyses [%] C	 H	 N	 S
3a	CH_3	4-BrC_6H_4	$C_{10}H_8NSBr$	Calcd	47.26	3.17	5.51	12.62
			(254.15)	Found	47.19	3.25	5.68	12.90
3b	C_2H_5		$C_{11}H_{10}NSBr$	Calcd	49.26	3.76	5.22	
			(268.18)	Found	49.60	3.83	5.36	
3c	*cyclo*-C_6H_{11}		$C_{15}H_{16}NS$	Calcd	74.34	6.61	5.78	
			(242.32)	Found	74.51	6.83	5.91	
3d	C_6H_5	C_6H_5	$C_{15}H_{11}NS$	Calcd	75.92	4.67	5.90	
			(237.32)	Found	76.11	4.80	6.03	
3e	4-$CH_3C_6H_4$		$C_{16}H_{13}NS$	Calcd	76.46	5.21	5.57	
			(251.35)	Found	76.39	5.37	5.63	
3f	4-$CH_3OC_6H_4$		$C_{16}H_{13}NOS$	Calcd	71.89	4.90	5.25	11.99
			(267.35)	Found	72.01	4.93	5.41	11.78
3g	4-ClC_6H_4	C_6H_5	$C_{15}H_{10}NSCl$	Calcd	66.29	3.71	5.15	
			(271.77)	Found	66.47	3.86	5.33	

temperature for 1 h. The reaction mixture was washed with water (*ca.* 100 ml) and the solvent was evaporated under the reduced pressure. The resulting residue was recrystallized from methanol below —30 °C to give 0.70 g (95%) of **2s**.

2-(4-Methylphenyl)-4-phenyl-1,3-thiazole (**3e**)

α-(4-Methylthiobenzoylthio)acetophenone (**2m**) (0.34 g, 2 mmol) and ammonium acetate (6 mmol) were refluxed in gracial acetic acid (10 ml) for 5 h (10 min for the aliphatic derivatives). The reaction mixture was neutralized with an aqueous 10% solution of sodium hydroxide and then was extracted with *n*-hexane (20 ml). The *n*-hexane layer was washed with water and dried over anhydrous sodium sulfate. Evaporation of the solvent and then recrystallization of the resulting residue from methanol gave 0.24 g (26%) of **3e**.

2,2-Isopropylidene-4-phenyl-1,3-dithiolene (**4**)

α-(Thioisobutyrylthio)acetophenone (**2f**) 2.4 g, 10 mmol) and ammonium acetate (2.3 g, 30 mmol) were refluxed in gracial acetic acid (6 ml) for 10 min. The reaction mixture was neutralized with an aqueous saturated solution of sodium hydroxide and then extracted with *n*-hexane (20 ml). The *n*-hexane layer was washed with water and dried over anhydrous sodium sulfate. Evaporation of the solvent *in vacuo*, and silica gel column chromatography [Wako Gel C-200, *n*-hexane:benzene (9:1)] of the resulting oily residue gave 0.11 g (5%) of **4** with pale yellow crystals, m.p. 78 ~ 78.5 °C and 0.7 g of an unidentified oily substance.

$C_{12}H_{12}S_2$ (220.12)

Found	C. 65.51	H 5.27	S 29.10,
Calcd	C. 65.41	H 5.49	S 29.10.

MS (70 eV) *m/e* 220 (47% M$^+$), 205 (100%); UV, Visible (CH_2Cl_2): $\lambda_{\max} = 254$ nm ($\log \varepsilon = 4.31$), 377 ($\log \varepsilon = 3.65$); IR (KBr): ν(cm^{-1}): 1618 (C=C), 1600 (arom. C=C); ^{1}H NMR: $CDCl_3$ δ(ppm): 1.70 (s, 3H, C$\underline{H}_3$); 1.74 (s, 3H, C$\underline{H}_3$); 6.34 (s, H, $\underline{H}$C=C); 7.11 ~ 7.45 (m, 5H, Ar).

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