Reactions of α-Oxoketenedithioacetals with Phenylmagnesium Bromide: Synthesis of Novel 1-Phenyl-1-methylthio-3-phenyl (or 2,3-Fused)-indenes and 2,3-Fused Heterocyclic-1,3-Diphenyl-2-alken-1-ones[1]

Gurdeep Singh, Hiriyakkanawar Ila*, Hiriyakkanawar Junjappa*

Department of Chemistry, North-Eastern Hill University, Bijni Complex, Bhagyakul,
Shillong - 793 003, Meghalaya, India

Novel substituted and 1-methylthio-1-phenylindenes have been synthesized by boron trifluoride etherate cyclocondensations of the corresponding carbinol acetals obtained by sequential 1,4 and 1,2 additions of phenylmagnesium bromide to α-oxoketenedithioacetals. Some of these indenes have been desulphurized to give the parent ring systems. Synthesis of novel 2,3-fused heterocyclic 1,3-diphenyl-alken-1-ones by boron trifluoride-ether catalyzed methanolysis of the corresponding carbinol acetals has also been described.

In our earlier studies we had reported[2] the reactions of few α-oxoketenedithioacetals **1**, with phenylmagnesium bromide, which undergo sequential 1,4 and 1,2-addition to give the corresponding alcohols **2**. Subsequent boron trifluoride etherate catalysed methanolysis of **2**, afforded the corresponding acyclic or cyclcic 1,3-diphenyl-2-alken-1-ones *via* 1,3-carbonyl transposition in good yields. In the present paper, we report the synthesis of substituted and fused indene derivatives by cyclodehydration of the alcohols **2** in the presence of boron trifluoride etherate in benzene.

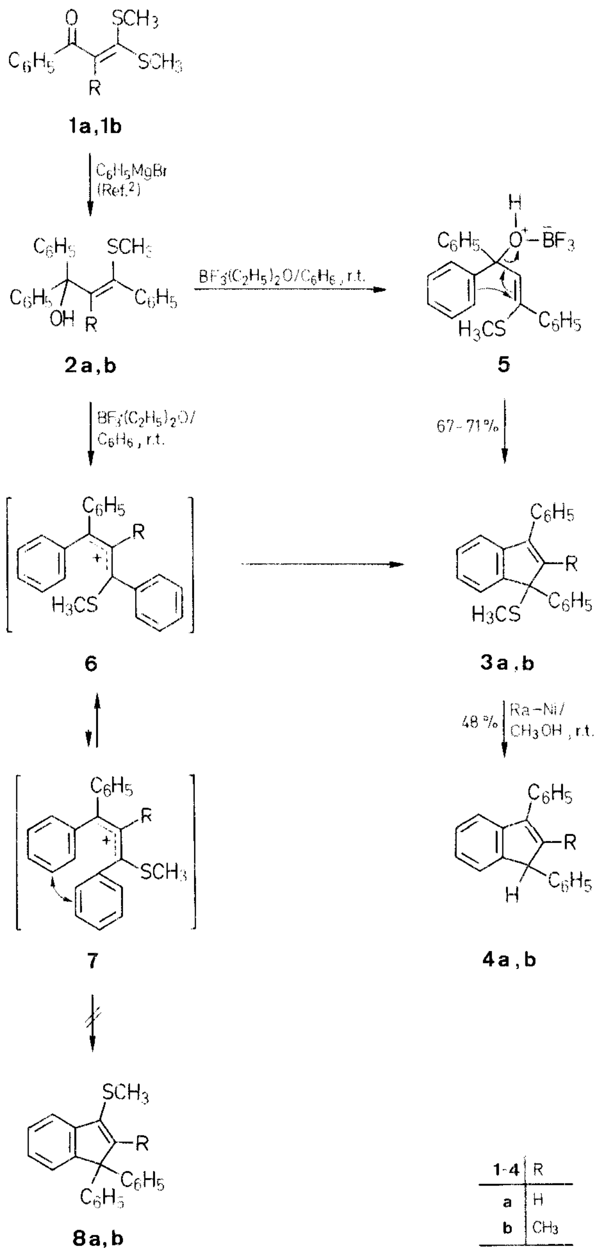
When the alcohol **2a** was refluxed with boron trifluoride etherate in dry benzene, the corresponding 1-methylthio-1,3 diphenylindene (**3a**) was obtained in 67 % yield. Subsequent desulphurization of **3a** in the presence of deactivated W_2-Raney nickel afforded 1,3-diphenylindene (**4a**) in 48 % yield (Scheme **A**)[3].

The corresponding 2-methylindenes **3b** and **4b** were also obtained in good yields when the dithioacetal **1b** was subjected to the same reaction sequence.

The reaction was next extended to the synthesis of fused indene derivatives **3c–g**. Thus when the alcohol **2c** derived from the dithioacetal of 1-tetralone was treated with boron trifluoride etherate in benzene, the condensed polycyclic indene **3c** was obtained in 54 % yield (Scheme **B**). The indene **3c** underwent desulphurization to give the corresponding benzofluorene derivative **4c** in 29 % yield (Scheme **B**). Similarly the heterocyclic ketenedithioacetals **1d** and **1f–h** afforded the corresponding methylthio substituted indenes **3d–g** in 68–76 % over all yields, under indentical conditions. While the benzoxepinoindene **3g** underwent smooth disulphurization to give **4d** in 61 % yield, the fused indene **3d** derived from benzothiopyrone yielded **4b**, apparently by simultaneous desulphurization of methylthio group and the ring sulphur atom (Scheme **B**).

The alcohols **2d–h** derived from the respective heterocyclic ketenedithioacetals **1d–h** were subjected to boron trifluoride etherate catalysed methanolysis to afford the corresponding heterocyclic 1,3-diphenyl alk-1-enylketones **9a–e** respectively in good yields (Scheme **B**).

The α-oxoketenedithioacetals **1i** and **1j** derived from acyclic aliphatic ketones underwent only 1,2-addition with phenylmagnesium bromide to afford the corresponding alcohol acetals **10a** and **10b** respectively in nearly quantitative yields.

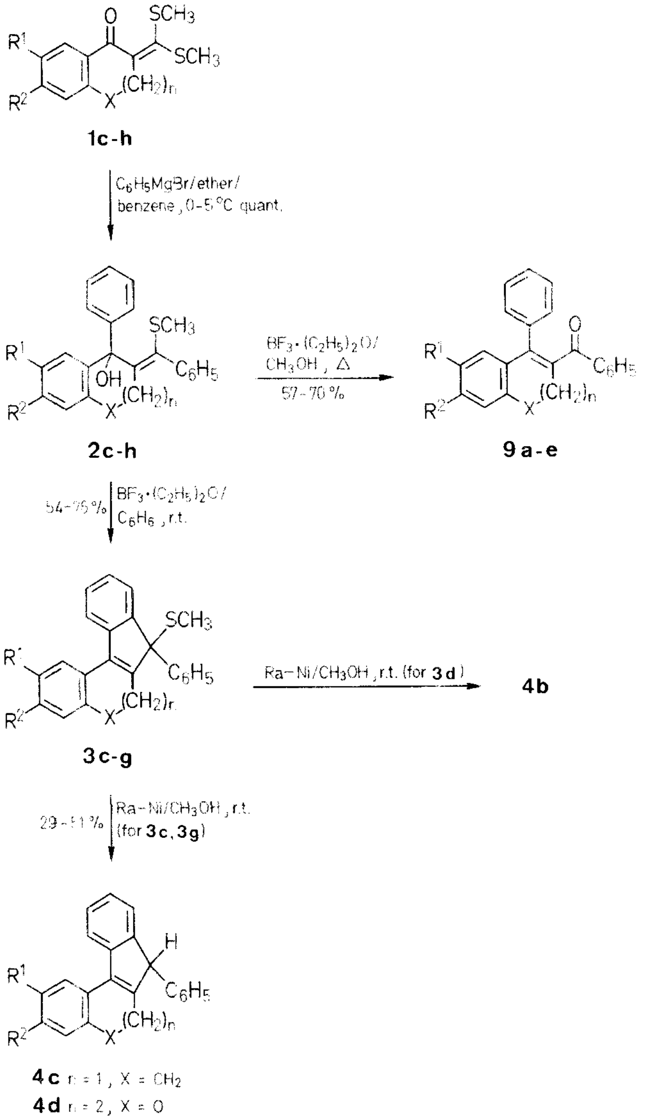


Scheme **A**

Subsequent cyclization of the alcohol acetal **10a** gave the corresponding 1,1-bismethylthio-2,3-dimethyl indene (**11a**) in 66 % yield (Scheme **C**), whereas the alcohol acetal **10b** afforded the indene **12** in 61 % yield, formed by rearrangement of indene **11b** (Scheme **C**).

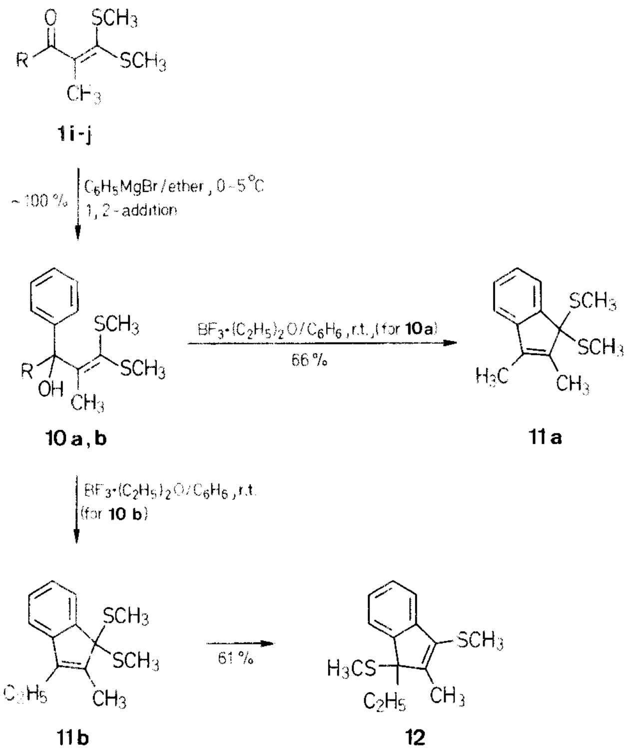
The mechanism of the formation of indenes **3** (or **11**) from **2** involves either concerted elimination and cyclization of the borate complex **5** or *via* allyl cation **6** formed by cleavage of the carbon-oxygen bond[4]. (Scheme **A**).

The complete absence of isomeric indenes **8** in the reaction mixture implicates that the cation **6** does not exist in equilibrium with another conformer cation **7** probably due to flagpole interaction between the bulkier phenyl groups[5]. In the ^{1}H-NMR spectrum of all the indenes **3a–g**, the signal due to the methylthio group appeared between $\delta = 1.5$ to 1.63 ppm (Table 1) indicating that it is attached to a sp^3 carbon[6], while methylthio group attached to a sp^2 carbon generally appear above $\delta = 2.00$ ppm.



Compounds	R^1	R^2	X	n
1-3c	H	H	CH$_2$	1
1-3d, 9a	H	H	S	1
1-2e, 9b	H	CH$_3$	S	1
1-2f, 3e, 9c	H	CH$_3$	S	2
1-2g, 3f, 9d	CH$_3$	H	S	2
1-2h, 3g, 9e	H	H	O	2

Scheme **B**



	R
1i, 10a	CH$_3$
1j; 10b	C$_2$H$_5$

Scheme **C**

Indenes have been prepared by a number of cycloalkylation procedures[3,7,8], involving phenyl substituted diols or alkenes as starting materials. They are generally prepared by treating Grignard or organolithium reagents with an appropriate indanone followed by dehydration of the resulting indanols. Recently high yield and regioselective methods for the synthesis of substituted indenes have been developed by acid catalysed cyclodehydration of the phenyl substituted allyl alcohols[3,5] or by pyrolysis of the corresponding magnesium alkoxides[4]. The latter methods consist of large structural flexibility, since a wide variety of phenyl substituted allyl alcohols or their magnesium alkoxides can be prepared by reaction of Grignard reagents with substituted α,β-unsaturated ketones. The present reaction provides a simple procedure for the preparation of previously unreported substituted and fused 1-methylthio-1-phenylindenes, which could also be desulphurized to the parent ring systems. Further, the alcohols **2** could be utilized for the synthesis of novel heterocyclic 1,3-diphenylenones **9** by subjecting them to methanolysis.

Reaction of 1 with Phenylmagnesium bromide; General Procedure:
To an ice cooled (0–5°C) solution of phenylmagnesium bromide [0.03 mol, prepared from magnesium (0.8 g) and bromobenzene (3.81 g)] in dry ether (60 ml), **1** (0.01 mol) in benzene (15 ml) is added dropwise over a period of 2 min and stirred for 30 min (1.5 h for **2b**). It is then decomposed with saturated solution of ammonium chloride (30 ml), extracted with ether (3 × 60 ml), washed with water (60 ml), dried with sodium sulfate and evaporated to give crude alcohols **2a–h** and **10a–b** in near quantitative yields, which are used without purification for further transformations.

Table 1. Methylthio Substituted Indenes (**3a–g**) Prepared

Starting Alcohol	Product No.	Yield [%]	m.p. [°C]	Molecular Formula[a]	IR (KBr/Film)[b] ν [cm^{-1}]	^{1}H-NMR (CCl$_4$)[c] δ [ppm]	M.S. m/e (M$^+$-47) (100%)
2a	**3a**	67	oil	$C_{22}H_{18}S$ (314.5)	1600 (C=C), 1498	1.5 (s, 3H, $SC\underline{H}_3$); 6.35 (s, 1H, =CH); 6.92–7.64 (m, 14H_{arom})	267
2b	**3b**	71	oil	$C_{23}H_{20}S$ (328.5)	1600 (C=C), 1498	1.50 (s, 3H, $SC\underline{H}_3$); 1.9 (s, 3H, CH_3); 7.0–7.51 (m, 14H_{arom})	281
2c	**3c**	54	oil	$C_{24}H_{20}S$ (340.5)	1600 (C=C), 1499	1.40 (s, 3H, $SC\underline{H}_3$); 2.19–2.87 [m, 4H, $(C\underline{H}_2)_2$]; 7.01–8.95 (m, 13H_{arom})	293
2d	**3d**	72	oil	$C_{23}H_{18}S_2$ (358.5)	1605 (C=C), 1495	1.46 (s, 3H, $SC\underline{H}_3$); 3.5 (s, 2H, $SC\underline{H}_2$); 6.70–7.84 (m, 13H_{arom})	311
2f	**3e**	76	125–126	$C_{25}H_{22}S_2$ (386.6)	1602 (C=C), 1495	1.62 (s, 3H, $SC\underline{H}_3$); 2.38 (s, 3H, CH_3); 2.45–2.68 (m, 2H, $SCH_2C\underline{H}_2$); 3.10–3.35 (m, 2H, $SC\underline{H}_2CH_2$); 7.0–7.52 (m, 12H_{arom})	339
2g	**3f**	71	131–132	$C_{25}H_{22}S_2$ (386.6)	1604 (C=C), 1498	1.63 (s, 3H, $SC\underline{H}_3$); 2.43 (s, 3H, CH_3); 2.41–2.64 (m, 2H, $SCH_2C\underline{H}_2$); 3.08–3.40 (m, 2H, $SC\underline{H}_2CH_2$); 7.07–7.84 (m, 12H_{arom})	339
2h	**3g**	68	116	$C_{24}H_{20}OS$ (356.5)	1600 (C=C), 1495	1.49 (s, 3H, $SC\underline{H}_3$); 2.8 (t, 2H, J = 6.5 Hz, $OCH_2C\underline{H}_2$); 4.41 (t, 2H, $OC\underline{H}_2CH_2$); 7.06–8.15 (m, 13H_{arom})	309

[a] Satisfactory microanalyses obtained: C ±0.39, H ±0.28.

[b] Recorded on a Perkin-Elmer 297 spectrometer.

[c] Recorded at 90 MHz on a varian EM-390 spectrometer.

Table 2. β-Phenyl-α,β-unsaturated Ketones **9a–e** Prepared

Starting Alcohol	Product	Refluxing Time (h)	Yield [%]	m.p. (°C)	Molecular Formula[a]	IR (KBr)[b] ν [cm^{-1}]	^{1}H-NMR (CDCl$_3$)[c] δ [ppm]	M.S. m/e (M$^+$)
2d	**9a**	10	62	110	$C_{22}H_{16}OS$ (328.4)	1655 (C=O), 1603 (C=C)	3.7 (s, 2H, $SC\underline{H}_2$); 6.86–7.56 (m, 14H_{arom})	328
2e	**9b**	8	67	156	$C_{23}H_{18}OS$ (342.5)	1652 (C=O), 1601 (C=C)	2.2 (s, 3H, CH_3); 3.7 (s, 2H, $SC\underline{H}_2$); 6.71 (s, 1H_{arom}); 7.0–7.44 (m, 10H_{arom})	342
2f	**9c**	6	62	162–163	$C_{24}H_{20}OS$ (356.5)	1659 (C=O), 1603 (C=C)	2.4 (s, 3H, CH_3); 2.76 (t, 2H, J = 6.5 Hz, $SCH_2C\underline{H}_2$); 3.49 (t, 2H, J = 7 Hz, $SC\underline{H}_2CH_2$); 6.74–7.31 (m, 10H_{arom}); 7.61 (s, 1H_{arom}); 7.93–8.1 (m, 2H_{arom})	356
2g	**9d**	8	70	184–185	$C_{24}H_{20}OS$ (356.5)	1655 (C=O), 1603 (C=C)	2.22 (s, 3H, CH_3); 2.7 (t, 2H, J = 6.5 Hz, $SCH_2C\underline{H}_2$); 3.44 (t, 2H, J = 6 Hz, $SC\underline{H}_2CH_2$); 6.73 (s, 1H_{arom}); 6.95–7.32 (m, 9H_{arom}); 7.55–8.1 (m, 3H_{arom})	356
2h	**9e**	8	57	121	$C_{23}H_{18}O_2$ (326.4)	1642 (C=O), 1598 (C=C)	2.78 (t, 2H, J = 6 Hz, $OCH_2C\underline{H}_2$); 4.65 (t, 2H, J = 6.5 Hz, $OC\underline{H}_2CH_2$); 6.95–7.4 (m, 12H_{arom}); 7.7–7.88 (m, 2H_{arom})	326

[a] Satisfactory microanalyses obtained: C ±0.43, H ±0.18.

[b] Recorded on a Perkin Elmer 297 spectrometer.

[c] Recorded at 90 MHz on a Varian EM-390 spectrometer.

Boron Trifluoride Etherate Catalysed Cyclodehydration of 2 and 10; General Procedure:

Boron trifluoride etherate (1 ml) is added to a solution of the alcohol **2** in benzene (60 ml) and the reaction mixture is stirred for 1 h at room temperature, (refluxed for 45 min in case of **2a**). It is then poured over saturated sodium bicarbonate solution (50 ml), extracted with benzene (2 × 50 ml), washed with water (50 ml), dried with sodium sulfate and evaporated to give crude **3a–g**, which are further purified by column chromatography over silica gel (hexane as eluant) either as oils or crystalline solids (Table 1). Under similar reaction conditions, the alcohols **10a** and **10b** are cyclized to give the indenes **11** and **12** respectively.

1,1-Bis(methylthio),2-3-dimethylindene (11): isolated as an orange oil; yield: 66%.

$C_{13}H_{16}S_2$	calc.	C 66.10	H 6.77
(236.4)	found	66.33	6.84

IR (Film): ν = 1602, 1500 cm^{-1}.

^{1}H-NMR (CDCl$_3$): δ = 1.24 (s, 3 H, CH$_3$); 1.47 (s, 3 H, CH$_3$); 2.13 (s, 3 H, CH$_3$); 2.31 (s, 3 H, CH$_3$); 7.12–7.53 ppm (m, 4 H$_{\text{arom}}$).

1,3-Bis(methylthio)-1-ethyl-2-methylindene (**12**): isolated as an orange oil; yield: 61 %.

$C_{14}H_{18}S_2$	calc.	C 67.20	H 7.20
(250.4)	found	67.41	7.41

IR (Film): ν = 1602, 1463 cm^{-1}.

^{1}H-NMR (CDCl$_3$): δ = 0.42 (t, 3 H, J = 7 Hz, CH$_2$C$\underline{\text{H}}_3$); 1.25 (s, 3 H, SCH$_3$); 1.83 (q, 2 H, J = 7 Hz, C$\underline{\text{H}}_2$CH$_3$); 2.09 (s, 3 H, SCH$_3$); 2.31 (s, 3 H, CH$_3$); 7.0–7.45 ppm (m, 4 H$_{\text{arom}}$).

M.S.: m/e = 250 (M$^+$, 2 %); 203 (M$^+$ − 47, 100 %).

Boron Trifluoride Etherate Catalysed Solvolysis of (2); General Procedure:

To a solution of the alcohol **2** (0.01 mol) in methanol (60 ml) boron trifluoride etherate (4 ml) is added and the reaction mixture is refluxed for 6–10 h (Table 2). It is then cooled, poured slowly into water (50 ml), extracted with chloroform (2 × 75 ml), the combined organic layer is washed successively with saturated solution of sodium bicarbonate (50 ml) and water (50 ml), dried with sodium sulfate and evaporated to give crude **9**, which are purified by silica gel chromatography using hexane/benzene (4:1) as eluent (Table 2).

Raney Nickel Desulphurization of 3a–d and 3g; Typical Procedure:

To a stirred solution of **3a** (1 g) in methanol (25 ml), Raney Nickel (8–12 g) is added and the reaction mixture is stirred for 1.5 h at room temperature. It is then filtered through Kieselgur, washed with hot methanol (50 ml), concentrated and diluted with water (25 ml). The product is extracted with chloroform (2 × 50 ml), the chloroform layer is washed with water (25 ml), dried with sodium sulfate and evaporated to give crude **4a**, which is further purified by passing through a small column of silica gel and eluting with hexane.

Similarly the indenes **3b–d** and **3g** are desulphurized to give **4b–d**. The indenes **4a** and **4b** are identified by comparison of their spectral and physical data with that of reported.

4a: m.p. 83 °C (Lit.[3], m.p. 83–84 °C)

4b: m.p. 107–108 °C (Lit.[3], m.p. 109–110 °C).

4c: isolated as a white solid; yield: 29 %; m.p. 146–147 °C.

$C_{23}H_{18}$	calc.	C 93.87	H 6.12
(294.4)	found	94.26	6.37

IR (CHCl$_3$): ν = 1602 cm^{-1}.

^{1}H-NMR (CDCl$_3$): δ = 2.3–2.5 (m, 2 H, CH$_2$); 2.62–2.83 (m, 2 H, CH$_2$); 4.5 (s, 1 H, CH); 7.03–8.0 ppm (m, 13 H$_{\text{arom}}$).

4d: isolated as a white solid; yield 51 %; m.p. 123–124 °C.

$C_{23}H_{18}O$	calc.	C 89.03	H 5.80
(310.4)	found	88.84	6.00

IR (KBr): ν = 1600 cm^{-1}.

^{1}H-NMR (CDCl$_3$): δ = 2.5–2.71 (m, 2 H, OCH$_2$C$\underline{\text{H}}_2$); 4.05–4.41 (m, 2 H, OC$\underline{\text{H}}_2$CH$_2$); 4.50 (s, 1 H, CH); 6.91–8.1 ppm (m, 13 H$_{\text{arom}}$).

G.S. thanks CSIR, New Delhi for a Senior Research Fellowship.

Received: January 7, 1986

---

[1] Part 47 of the series; Part 46; Singh, G., Deb, B., Ila, H., Junjappa, H., submitted to *Synthesis*.

[2] Singh, G., Purkayastha, M. L., Ila, H., Junjappa, H., *J. Chem. Soc. Perkin Trans. 1* **1985**, 1289.

[3] Miller, W.G., Pittman, Jr., C.U. *J. Org. Chem.* **1974**, *39*, 1955.

[4] Tolbert, L.M. *J. Org. Chem.* **1979**, *44*, 4584.

[5] Pittman, Jr., C.U., Miller, W.G. *J. Am. Chem. Soc.* **1973**, *95*, 2947.

[6] Hartke, K., Schilling-Pindur, A. *Justus Liebigs Ann. Chem.* **1984**, 552.

[7] Parham, W.E., Egberg, D.C. *J. Org. Chem.* **1972**, 37, 1545. Parham, W.E., Montgomery, W.C. *J. Org. Chem.* **1974**, *39*, 2048.

[8] Maroni, R., Melloni, G. *Tetrahedron Lett.* **1972**, 2869.