A Novel Route to Stilbenes *via* Cationic Cycloaromatization[1]

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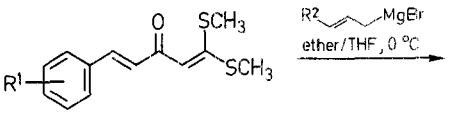
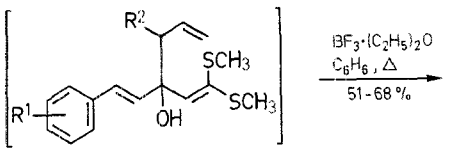
A novel route for substituted stilbenes **3a–j** is developed by cationic cycloaromatization of the corresponding (α-allyl-α-hydroxycinnamyl)-ketene dithioacetal derivatives **2a–j** in the presence of ether-boron trifluoride complex. The hydroxydithioacetals **2a–j** were obtained by 1,2-addition of allyl or crotyl magnesium bromide with the respective styryl β,β-bis(methylthio)vinyl ketones **1a–j**.

A number of approaches for the synthesis of both symmetric and asymmetric stilbenes have been described in the literature.[2,3] Generally, all these approaches involve either transformation of aromatic precursors having built-in stilbene skeleton (Ar–C–C–Ar), coupling of arylmethyl fragments (ArC + ArC or Ar^{1}C) or coupling of aryl fragments with styrene or vinylaromatics (Ar or Ar′ + C=C–Ar). However, the synthesis of stilbene involving direct construction of one or both aromatic ring from acyclic precursors is not known in the literature.[4] We have recently reported a new general method for benzoannelation of active methylene ketones by reacting the corresponding α-oxoketene dithioacetals[5] with allyl magnesium bromide followed by treatment of resulting α-hydroxyketene dithioacetals with ether-boron trifluoride complex.[6,7] We were therefore prompted to study cycloaromatization of cinnamoylketene dithioacetals **1** with a view to developing a novel route to stilbenes; the results of these studies are reported in this communication.

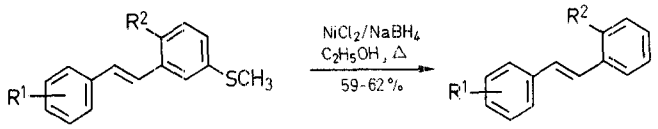
When 1,1-bis(methylthio)-5-phenylpenta-1,4-dien-3-one **(1a)** was reacted with allyl magnesium bromide, 3-allyl-1,1-bis(methylthio)-5-phenylpenta-1,4-dien-3-ol **(2a)** was obtained in quantitative yield. Subsequently, **2a** was directly treated with ether-boron trifluoride complex in benzene, whereby the desired 3-methylthiostilbene **(3a)** was obtained in 67% yield. The structure of **3a** was confirmed by its analytical and spectral data and by its desulphurization (sodium borohydride/nickel(II) chloride)[8] to stilbene **(4a)** (mixed m.p., superimposable IR spectrum). Similarly, the other substituted stilbenes **3b–g** were obtained in 52–68% overall yields. Desulphurization of **3b** and **3c** gave the corresponding 4-methyl- **(4b)** and 4-chloro- **(4c)** stilbenes in good yields. In another experiment, when crotylmagnesium bromide was reacted with **1a–c**, the corresponding 2-methyl-5-methylthiostilbenes **3h–j** were obtained in moderate yields. Dethiomethylation of **3h** yielded the corresponding 2-methylstilbene **(4d)** (superimposable IR and NMR spectra) in 57% yield.



1a-j



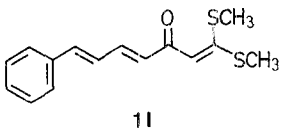
2a-j



3a-j **4a-d**

Product	R^1	R^2	Product	R^1	R^2
1-3a	H	H	**1-3h**	H	CH_3
b	*p*-CH_3	H	**i**	*p*-CH_3	CH_3
c	*p*-Cl	H	**j**	*p*-Cl	CH_3
d	*m*-CH_3O	H	**4a**	H	H
e	*o*-Cl	H	**b**	*p*-CH_3	H
f	2,6-Cl_2	H	**c**	*p*-Cl	H
g	3,4-Cl_2	H	**d**	H	CH_3

The present procedure was, however, not successful for the synthesis of 4-methoxystilbene. The corresponding hydroxydithioacetal **2k** (R^1 = *p*-CH_3O, R^2 = H) yielded intractable tar, when reacted with ether-boron trifluoride complex under varying conditions. Similarly, (5-phenyl-2,4-pentadienoyl)ketene dithioacetal **1l** reacted smoothly with allyl magnesium bromide; however, the resulting hydroxydithioacetal failed to undergo cycloaromatization to give the desired 1,4-diphenylbutadiene under differing conditions.



1l

In summary, the present method provides a novel entry to stilbenes through cycloaromatization of acyclic precursors derived from easily available starting materials.

Table. 3-Methylthiostilbenes **3a–j** Prepared

Product	Yield (%)	m.p. (°C)	Molecular Formula[a]	MS (70 eV)[b] m/e (M^+)	IR (KBr/film)[c] $\nu_{C=C}$ (cm^{-1})	^{1}H-NMR (CCl_4)[d] δ (ppm)
3a	68	61	$C_{15}H_{14}S$ (226.3)	226	1592	2.40 (s, 3H, SCH_3); 6.90 (s, $2H_{olefin}$); 7.01–7.65 (m, $9H_{arom}$)
3b	62	74–76	$C_{16}H_{16}S$ (240.4)	240	1590	2.31 (s, 3H, CH_3); 2.49 (s, 3H, CH_3); 6.90 (s, $2H_{olefin}$); 6.91–7.39 (m, $8H_{arom}$)
3c	68	79	$C_{15}H_{13}ClS$ (260.8)	260, 262	1595	2.48 (s, 3H, CH_3); 6.92 (s, $2H_{olefin}$); 7.0–7.43 (m, $8H_{arom}$)
3d	57	[e]	$C_{16}H_{16}OS$ (256.4)	256	1595	2.41 (s, 3H, CH_3); 3.63 (s, 3H, CH_3); 6.90 (s, $2H_{olefin}$); 6.92–7.38 (m, $8H_{arom}$)
3e	61	[e]	$C_{15}H_{13}ClS$ (260.8)	260, 262	1595	2.41 (s, 3H, SCH_3); 6.85 (d, 1H, $J = 16$ Hz, H_{olefin}); 6.95–7.90 (m, $9H_{arom+olefin}$)
3f	52	[e]	$C_{15}H_{12}Cl_2S$ (295.2)	294, 296	1585	2.39 (s, 3H, CH_3); 6.64–7.43 (m, $9H_{arom+olefin}$)
3g	53	[e]	$C_{15}H_{12}Cl_2S$ (295.2)	294, 296	1582	2.49 (s, 3H, CH_3); 6.89 (s, $2H_{olefin}$); 6.95–7.61 (m, $7H_{arom}$)
3h	52	[e]	$C_{16}H_{16}S$ (240.4)	240	1590	2.30 (s, 3H, CH_3); 2.41 (s, 3H, CH_3); 6.9–7.51 (m, $10H_{arom+olefin}$)
3i	51	[e]	$C_{17}H_{18}S$ (254.4)	254	1595	2.30 (s, 6H, 4-CH_3 and 2′-CH_3); 2.41 (s, 3H, CH_3); 6.7–7.35 (m, $9H_{arom+olefin}$)
3j	51	[e]	$C_{16}H_{15}ClS$ (274.8)	274, 276	1595	2.29 (s, 3H, CH_3); 2.40 (s, 3H, CH_3); 6.86–7.45 (m, $9H_{arom+olefin}$)

[a] Satisfactory microanalyses obtained: C ±0.32, H ±0.21.
[b] Recorded on a Jeol JMS - D-300 spectrometer.
[c] Recorded on a Perkin-Elmer 297 spectrophotometer.
[d] Recorded on a Varian EM-390 spectrometer.
[e] Viscous semisolids.

Reaction of 5-Aryl-1,1-bis(methylthio)penta-1,4-dien-3-ones 1 With Allyl Magnesium Bromide; General Procedure:
To a well stirred and cooled (0 °C) suspension of allyl magnesium bromide [0.016 mol prepared from allyl bromide (1.92 g, 0.016 mol) and magnesium turnings (1.2 g, 0.52 mol) in dry ether (40 ml)], a solution of **1** (0.008 mol) in dry tetrahydrofuran (30 ml) is added and the reaction mixture is further stirred at 0 °C for 1 hr. The reaction mixture is then poured into a saturated ammonium chloride solution (300 ml), extracted with ether (3 × 30 ml), dried with sodium sulfate and evaporated *in vacuo* to give crude *3-allyl-5-aryl-1,1-bis(methylthio)penta-1,4-dien-3-ols* **2a–g** as yellow oils in nearly quantitative yields. Compounds **2a–g** are unstable and therefore used as such for subsequent reactions without further purification.

Reaction of 1a–c With Crotyl Magnesium Bromide; General Procedure:
To magnesium (1.2 g, 0.52 mol) and a pinch of iodine in dry tetrahydrofuran (40 ml), two drops of crotyl bromide is added to initiate the reaction and a solution of crotyl bromide (2.20 g, 0.016 mol) and dithioacetal **1** (0.008 mol) in tetrahydrofuran (30 ml) is added dropwise (30 min) at room temperature. After stirring the reaction mixture for 10– h at room temperature, it is worked up as described above to give the crude *1-Aryl-3-hydroxy-4-methyl-3-[β,β-bis(methylthio)vinyl]hexa-1,5-dien-3-ols* **2h–j**, which are used as such for further cyclization.

Cycloaromatization of 2a–j; Synthesis of Stilbenes 3a–j; General Procedure:
To a solution of crude hydroxydithioacetal **2** (0.008 mol), obtained as above, in dry benzene (60 ml), ether-boron trifluoride complex (10 ml) is added. The reaction mixture is refluxed for 45 minutes, poured into water (300 ml). The resultant mixture is neutralized with saturated sodium hydrogen carbonate solution (100 ml) and extracted with chloroform (4 × 30 ml). The organic extract is dried with sodium sulfate and evaporated to give crude 3-methylthiostilbenes **3a–j**, which are purified by column chromatography over silica gel (hexane as eluent) (Table).

Dethiomethylation of Stilbenes 3a–c and 3h; General Procedure:
To a solution of methylthiostilbene (**3**, 0.002 mol) in ethanol (200 ml), is added nickel(II) chloride hexahydrate (14.20 g, 0.06 mol) followed by sodium borohydride (6.70 g, 0.18 mol) in small portions with stirring and cooling (30 min). After refluxing for six hr, the reaction mixture is filtered, and the residue is washed with hot acetone (10 × 50 ml). The filtrate is evaporated, and the viscous residue dissolved in chloroform (100 ml) and washed with water (100 ml) to remove trace nickel chloride. The chloroform layer is dried with sodium sulfate and evaporated to give crude desulphurized stilbenes **4a–d**, which were further purified by passing through a silica gel column (hexane as eluent).

Stilbene **4a**; yield: 59%; m.p. 123–124 °C (lit m.p. 124 °C[9a], superimposable IR and NMR spectra).
4-Methylstilbene **4b**; yield: 61%; m.p. 119–20 °C (lit m.p. 120 °C[9b], superimposable IR and NMR spectra).
4-Chlorostilbene **4c**; yield: 62%; m.p. 127–8 °C (lit. m.p. 129 °C[9c], superimposable IR and NMR spectra).
2-Methylstilbene **4d**; yield: 60%; m.p. 31–32 °C (lit m.p. 31–32 °C[10], superimposable IR and NMR spectra).

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