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Trimethyl Borate Induced Thermal Cycloaromatization Of 1-Aryl-1-(prop-2-ynyl)-3,3-bis(alkylthio)-2-propen-1-ols Through Acetylenic Oxy-Cope Rearrangement

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Abstract: The carbinol acetals **2a-h** obtained by 1,2-addition of propargylmagnesium bromide to acyclic α-oxoketene dithioacetals **1a-h** undergo cycloaromatization in the presence of trimethyl borate/methanol to give 2,5-bis(alkylthio)biphenyls **4a-h** through acetylenic oxy-Cope rearrangement and an unprecedented 1,4-alkylthio shift in the resulting allenic intermediate.
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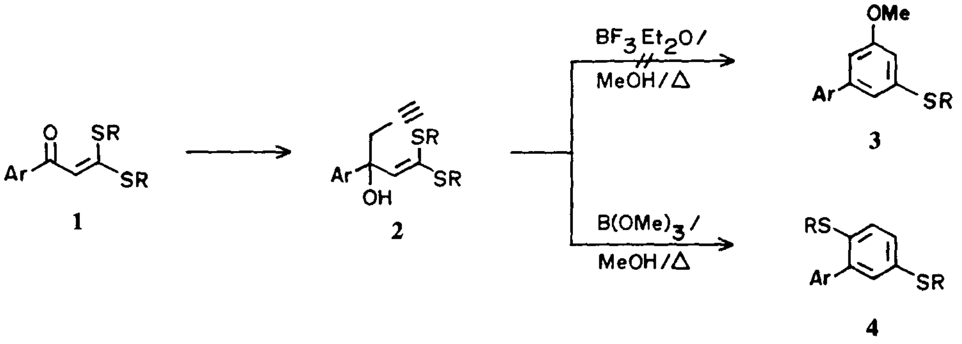
During the course of our cycloaromatization studies involving α-oxoketene dithioacetals as three carbon 1,3-electrophilic components[1], we have reported a facile annulation of thioresorcinol dimethyl ether moiety to α-oxoketene dithioacetals derived from cyclic active methylene ketones[2]. The overall strategy consists of 1,2-addition of propargylmagnesium bromide to α-oxoketene dithioacetals to afford the corresponding carbinol acetals which underwent a facile cationic cyclization in the presence of borontrifluoride etherate and methanol involving the participation of methanol to afford the corresponding benzoannulated products. However, when the carbinol **2a** derived from acyclic oxoketene dithioacetal **1a** was subjected to cyclization under the identical conditions, the expected biphenyl **3a** was not obtained and gave only intractable mixture of products. However, the carbinols **2** underwent smooth cycloaromatization when the reaction mixture was refluxed in methanol in the presence of trimethyl borate. The aromatic products isolated were not the expected derivatives **3** but characterized as the rearranged bis(alkylthio)biphenyls **4** (Scheme 1). We report in this communication, the formation of **4** from **2** and an interesting acetylenic oxy-Cope rearrangement followed by an unprecedented 1,4-alkylthio shift in the resulting allenic intermediate **7**.

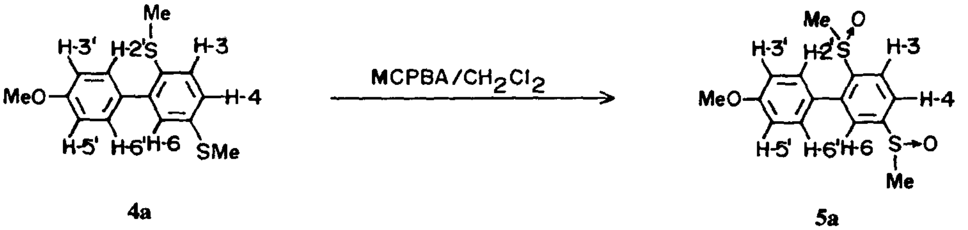
When the oxoketene dithioacetal **1a** was reacted with propargylmagnesium bromide, the carbinol acetal **2a** formed by 1,2-addition of Grignard reagent was isolated in quantitative yield. Attempted cyclization of **2a** in the presence of borontrifluoride etherate/MeOH or other acids (CF_3CO_2H, PTSA/C_6H_6, $TiCl_4$/CH_2Cl_2, $ZnCl_2$ etc.) did not meet with any success and gave only a complex mixture of products. This may be due to less favourable overlap between π end of acetylenic group and the other terminal carbon of the acyclic carbinol **2a** along the correct trajectory. However, when **2a** was refluxed in methanol in the presence of trimethyl borate, product analysis showed formation of a new compound (65%) which was characterized as 2,5-bis(methylthio)-4'-methoxybiphenyl **4a** on the basis of



Entry	1,2,3,4	Ar	R	% Yield 4	m.p.(°C)
1	a	4-MeOC$_6$H$_4$	Me	65	89-90
2	b	C$_6$H$_5$	Me	62	55-56
3	c	4-ClC$_6$H$_4$	Me	68	115-16
4	d	4-BrC$_6$H$_4$	Me	66	132-33
5	e	C$_6$H$_5$	Et	61	Yellow oil
6	f	C$_6$H$_5$	*n*-Pr	63	Yellow oil
7	g	4-MeOC$_6$H$_4$	*i*-Pr	64	95-96
8	h	4-MeOC$_6$H$_4$CH=CH	Me	54	89-90

Scheme 1

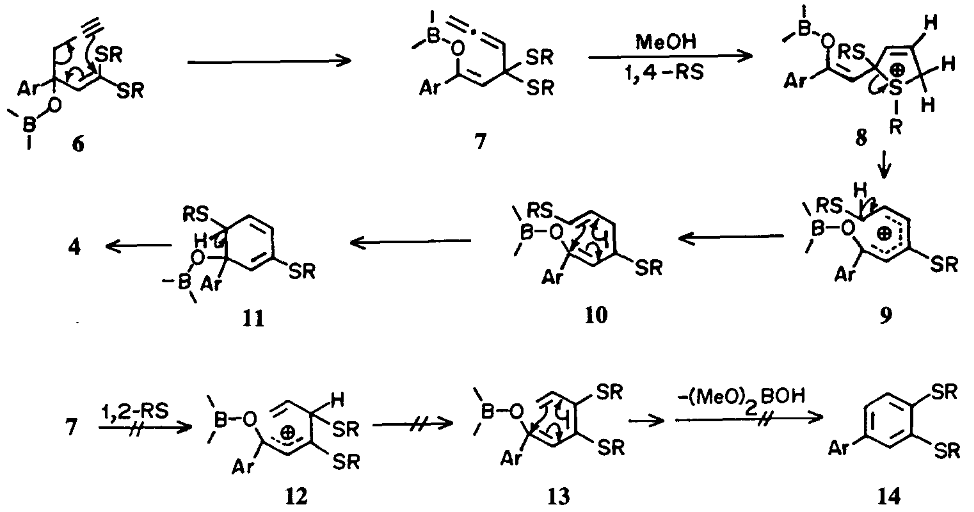
spectral and analytical data[3]. The regiochemistry of the two methylthio groups in **4a** was confirmed by differential NOE experiment[3] as well as by its oxidation (MCPBA) to the corresponding sulfoxide **5a** (Scheme 2)[4]. The other carbinol acetals **2b-g** similarly afforded the substituted bis(alkylthio)biphenyls **4b-g** in 61-68% overall yields[5]. The corresponding carbinol **2h** from the cinnamoyl ketene dithioacetal **1h** similarly yielded the bis(methylthio)stilbene **4h** in 54% yield (Table)[5].



Scheme 2

The probable mechanism for the formation of **4a-h** from **2a-h** is depicted in the Scheme 3. It is initiated by the acetylenic oxy-Cope rearrangement of the borate complex **6** for which there are good analogies[6]. The resulting allenic intermediate **7** could then undergo sequentially:(i) 1,4-alkylthio shift through sulfonium ion intermediate **8** to give pentadienyl cation **9** (ii) deprotonation of **9** to hexatriene intermediate **10** (iii) electrocyclization of **10** to cyclohexadiene **11** (iv) aromatization of **11** to biphenyls

4 by elimination of $(MeO)_2B$-OH. Interestingly, no trace of the isomeric (3,4-alkylthio)biphenyls **14a-h** could be detected from any of the reaction mixtures. Apparently, a 1,4-alkylthio shift in the allenic intermediate **7** leading to more stable pentadienyl carbocation **9** is preferred pathway over 1,2-alkylthio shift (through episulfonium ion intermediate) to give less stable allylic carbocation **12** (Scheme 3). Also, the ease with which the carbinol **2g** bearing bis(*i*-propylthio) groups undergoes rearrangement and cyclization to **4g** further supports preference for 1,4-alkylthio shift since an 1,2-alkylthio shift in **2g** would yield sterically crowded triene intermediate **13** (R=*i*-Pr) for electrocyclization[7].



Scheme 3

The reaction represents a novel cycloaromatization route to substituted biphenyls involving trimethyl borate assisted oxy-Cope rearrangement of propargylvinyl carbinol[8] in the initial step. Only a few reports of oxy-Cope rearrangement of open-chain system containing triple bond are described in the literature[6a]. The synthetic utility of this rearrangement is considerably limited due to undesirable cleavage reaction as well as thermal cyclization of the intermediate allenol to either vinylcyclopropane or cyclopentene derivatives[9]. In the present case, the borate derivative of allenol **7** prevents undesirable side reactions and facilitates cycloaromatization of triene **10**. Another noteworthy feature of the rearrangement is an interesting 1,4-alkylthio shift in the allene intermediate **7** for which to our knowledge, there is no precedence in the literature. As stated earlier, the driving force for this 1,4-alkylthio shift appears to be the formation of stable pentadienyl carbocation **9**. Further work to explore the synthetic scope of this boroxy-Cope rearrangement[10] as well as detail mechanistic study of 1,4-alkylthio shift in the allene **7** is in progress.

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2. Gupta, A.K.; Ila, H.; Junjappa, H. *Tetrahedron Lett*. **1987**, *28*, 1459.
3. **4a**: ^{1}H NMR (400 MHz, CCl_4) δ 2.49 (s, 3H, SCH_3), 2.53 (s, 3H, SCH_3), 3.85 (s, 3H, OCH_3), 6.97 (d, 2H, J=8.2Hz, H-3',H-5'), 7.26 (d, 1H, J=7.96Hz, H-3), 7.33 (dd, 1H, J=7.96, 1.87Hz, H-4), 7.38 (d, 1H, J=1.87Hz, H-6), 7.50 (d, 2H, J=8.2Hz, H-2',H-6'); m/z 276 (M^+, 100%). Regiochemistry of two methylthio groups in **4a** was further supported by differential NOE experiment which showed intensity increase of all three protons (H-3, H-4, H-6) signals on irradiation of two methylthio groups signal showing that all the three protons are ortho to two SMe groups unlike in **14a**.
4. **5a**: Colorless crystals (84%); m.p. 147-148 °C; IR ν_{max} (KBr) 1602, 1575, 1510, 1060 (ν_{S-O}) cm^{-1}. The ^{1}H NMR spectrum (400 MHz, CCl_4) of **5a** displayed considerable downfield shift of all the three protons (H-3, H-4, H-6) ortho to sulfoxide moieties; δ 2.91 (s, 3H, $SOCH_3$), 2.93 (s, 3H, $SOCH_3$), 3.87 (s, 3H, OCH_3), 7.02 (d, 2H, J=8.5Hz, H-3',H-5'), 7.65 (d, 2H, J=8.5Hz, H-2',H-6'), 7.91 (dd, 1H, J=8.11, 1.72Hz, H-4), 8.09 (d, 1H, J=8.11Hz, H-3), 8.25 (d, 1H, J=1.72Hz, H-6); ^{13}C NMR (17.0 MHz, $CDCl_3$) δ 43.00, 43.12 ($SOCH_3$), 54.96 (OCH_3), 114.18, 120.60, 123.74, 127.97, 129.70(ArCH), 130.37, 140.00, 143.26, 144.89, 159.93 (quaternary C); m/z 308(M^+, 100%).
5. Structures of all products **4b-h** were confirmed with the help of spectral and analytical data. **4b**: Colorless needles (62%); m.p. 55-56 °C; IR ν_{max} (KBr) 1595, 1575, 1540 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.51 (s, 3H, SCH_3), 2.53 (s, 3H, SCH_3), 7.28 (d, 1H, J=7.9Hz, H-3), 7.35 (dt, J=7.3, 1.4Hz, H-4'), 7.38 (dd, 1H, J=7.9, 1.96Hz, H-4), 7.43 (d, 1H, J=1.96Hz, H-6), 7.44 (d, 2H, J=7.3Hz, H-3',H-5'), 7.57 (d, 2H, J=7.3Hz, H-2',H-6'); ^{13}C NMR (62.97 MHz, $CDCl_3$) δ 16.54, 16.61 (SCH_3), 124.82, 126.25, 126.85, 127.33, 127.66, 128.72 (ArCH), 137.25, 138.36, 139.28, 140.45 (quaternary C); m/z 246 (M^+, 100%).
   4g: colorless needles (64%); m.p. 95-96 °C; IR ν_{max} (KBr) 1604, 1518, 1458, 1440 cm^{-1}; ^{1}H NMR (250 MHz, $CDCl_3$); δ 1.35 (d, 6H, J=6.71Hz, CH_3), 1.36 (d, 6H, J=6.71Hz, CH_3), 3.48-3.54 (m, 2H, SCH<), 3.84 (s, 3H, OCH_3), 6.98 (d, 2H, J=8.85Hz, H-3',H-5'), 7.32 (dd, 1H, J=7.93, 1.83Hz, H-4), 7.38 (d, 1H, J=7.93Hz, H-3), 7.50 (d, 2H, J=8.85Hz, H-2',H-6'), 7.52 (d, 1H, J=1.83Hz, H-6); ^{13}C NMR (22.6MHz, $CDCl_3$) δ 22.98 (CH_3), 37.14 (CH), 55.36 (OCH_3), 114.29, 124.74, 127.88, 135.84, 139.18(ArCH), 128.93, 131.14, 132.71, 137.93, 159.28 (quaternary C); m/z 332 (M^+, 100%).
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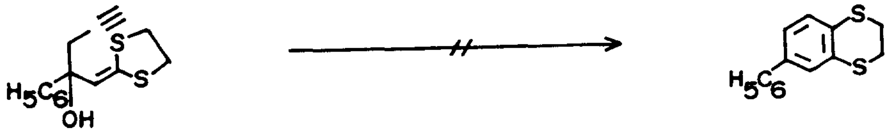
7. Attempted cyclization of carbinol **2i** under indentical conditions ($B(OMe)_3$/MeOH/△) did not give any trace of biphenyl **15** involving 1,2-alkylthio shift.



2i **15**

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