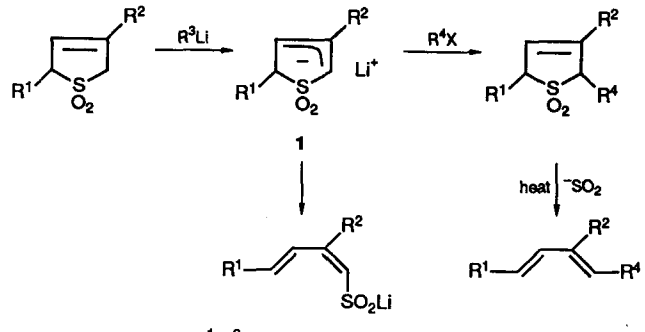
Cross-coupling of Organomanganese Derivatives of 3-Sulfolenes with Allyl and Propargyl Bromides. A Simple Synthesis of Functionalised Dienes

Aleksander N. Kasatkin,* Yulia A. Prokopenko, Arthur M. Khabibov and Genrikh A. Tolstikov

Institute of Organic Chemistry, Ural Branch of the Russian Academy of Sciences, 450054 Ufa, Russian Federation. Fax: +7 347 234 2914

Reactions of organomanganese derivatives of 3-sulfolene and 2-methyl-3-sulfolene with allyl- and propargyl bromides result in high yields of related 2-substituted or 2,5-disubstituted 3-sulfolenes; thermolysis of the cross-coupled products gives 1,3,6-trienes or 1,3-dien-6-ynes.

The synthesis of 3-sulfolenes is undoubtedly of interest owing to their ability to be transformed into related 1,3-dienes.[1] Following the results reported in the literature,[2–6] alkylation of the lithium reagents **1** prepared *in situ* is the most effective procedure for insertion of α-substituents into the sulfolenes. Due to the extremely low stability of the carbanions **1**, which show a tendency to decyclisation in dienylsulfinic acid salts, it was necessary to conduct the reactions at −105 °C[2–4] or with a base effecting a mixture of the starting sulfolene with an electrophile.[5–7] Me_3SiCl, Bu^n_3SnCl, alkyl, allyl or benzyl halides containing no functional groups were used as substrates (Scheme 1).



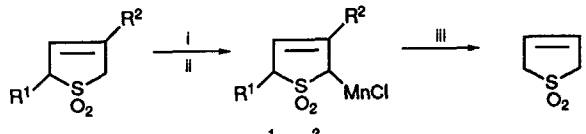
R^1,R^2 = H, alkyl
R^3 = Bu^n, $(Me_3Si)_2N$
R^4 = Me_3Si, Bu^n_3Sn, alkyl, allyl, $PhCH_2$
X = Cl, Br, I

Scheme 1

We observed that the range of allyl halides appropriate for the reaction may be usefully expanded if the reagents **1** are replaced by related manganese(II) derivatives.

Complexes **2a–c** were prepared *in situ via* treatment of 3-sulfolene, 2-methyl- and 3-methyl-3-sulfolenes firstly with Bu^nLi and then with Li_2MnCl_4 (Scheme 2). Compared with the lithium reagents, the complexes showed much higher stability. Thus, (3-sulfolen-2-yl)lithium decomposes completely even at −78 °C, whereas the manganese complex **2a** yields 70% of the starting sulfolene after heating to 20 °C with subsequent hydrolysis.

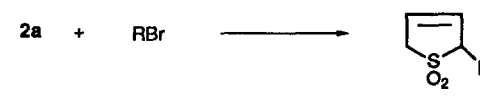
Reactions of (3-sulfolen-2-yl)manganese chloride **2a** with allyl and but-2-enyl bromides were performed under heating from −78 to +20 °C, which led to 2-substituted sulfolenes **3a** or **3b**, respectively (Scheme 3). In the latter case, the cross-coupling



2a $R^1 = R^2 = H$
2b R^1 = Me, R^2 = H
2c R^1 = H, R^2 = Me

Scheme 2 *Reagents and conditions*: i, Bu^nLi, THF–HMPTA, −105 °C, 15 min; ii, Li_2MnCl_4, −105 to −78 °C, 30 min; iii, −78 to +20 °C, 3 h, then H_3O^+

involved only the primary carbon atom of the substrate. Reaction of (*E*)-1,4-dibromobut-2-ene resulted mainly in the monosulfolenation product **3c**. Selective monosubstitution was also observed in reactions of allylic 1,4-dibromides with allylmanganese halides.[8] The methoxycarbonyl group is entirely retained after reaction of the complex **2a** with methyl 4-bromocrotonate, which leads to an α,β-unsaturated ester **3d** containing a sulfolenyl fragment. Note that $BrCH_2CH{=}CH{-}CO_2Me$ treated with organomanganese compounds as $R^1CH{=}C(R^2)CH_2MnCl$ (R^1, R^2 = H, alkyl) yielded cyclopropanecarboxylates.[9,10] Reactions of the complex **2a** with prop-2-ynyl and hept-2-ynyl bromides gave the 2-propargyl sulfolenes **3e** and **3f**, respectively, with no trace of the related allenes.



3a R = $CH_2{=}CHCH_2$ (62%) **3a-f**
3b R = $MeCH{=}CHCH_2$ (65%)
3c R = $BrCH_2CH{=}CHCH_2$ (59%)
3d R = $MeO_2CCH{=}CHCH_2$ (82%)
3e R = $HC{\equiv}CCH_2$ (43%)
3f R = $Bu^nC{\equiv}CCH_2$ (67%)

Scheme 3 *Reagents and conditions*: THF–HMPTA, −78 to +20 °C, 3 h, ratio **2a**: substrate = 1.5–2:1

According to the ^1H and ^{13}C NMR spectral data, the product **3d** is of *trans*-configuration, while the product **3b** shows the same ratio of stereoisomers (*E*/*Z* = 86:14) as but-2-enyl bromide. Quite a different case is observed with (*E*)-1,4-dibromobut-2-ene. This change the double bond geometry under the reaction conditions, leading to the monobromide **3c** as a mixture of *cis*- and *trans*-isomers (*E*/*Z* = 30:70).

Reactions of $BrCH_2CH{=}CHCH_2Br$, $BrCH_2CH{=}CH{-}CO_2Me$ and $Bu^nC{\equiv}CCH_2Br$ with (5-methyl-3-sulfolen-2-yl)manganese chloride **2b** proceed similarly to those of the complex **2a**, resulting in 2,5-disubstituted sulfolenes **3g–i** (Scheme 4). A satisfactory yield of the acetylene **3i** may be obtained with no less than 3 equiv. of the manganese derivative (2 equiv. of **2b** yields only 36% of **3i**). The sulfolenes thus prepared exhibit a *trans*-2,5-configuration, as evidenced from a comparison of the ^{13}C NMR spectra of **3g** and **3i** with those of the corresponding *cis*-isomers; the latter were prepared *via* isomerisation of **3g** and **3i** in the presence of 10 mol % NaOH in methanol.

In contrast to the complexes **2a** and **2b**, (3-methyl-3-sulfolen-2-yl)manganese chloride **2c**, with its reaction centre shielded by

3g R = $BrCH_2CH{=}CHCH_2$ (42%) **3g-i**
3h R = $MeO_2CCH{=}CHCH_2$ (60%)
3i R = $Bu^nC{\equiv}CCH_2$ (64%)

Scheme 4 *Reagents and conditions*: THF–HMPTA, −78 to +20 °C, 3 h, ratio **2b**: substrate = 2:1 or 3:1

a methyl moiety, does not react with allyl and propargyl bromides under the conditions stated here.

A typical experimental procedure for the synthesis of the substituted sulfolenes **3a–i** is as follows. A solution of Bu^nLi in hexane (2.5 mol dm^{-3}; 2 ml, 5 mmol) was added to a solution of 3-sulfolene (0.6 g, 5.08 mmol) in a mixture of THF (20 ml) and HMPTA (1.6 ml) with cooling to −105°C. The mixture was then stirred for 15 min at −105°C, after which a solution of Li_2MnCl_4 in THF (1.5 mol dm^{-3}; 11 ml, 5.5 mmol), cooled to −78°C, was poured into the prepared solution of (3-sulfolen-2-yl)lithium. The mixture was stirred for 30 min as the temperature increased from −105°C to −78°C, and methyl 4-bromocrotonate (0.447 g, 2.5 mmol) was added. The reaction mixture was heated to 20°C for 3 h, hydrolysed with HCl (2 mol dm^{-3}; 5 ml), and extracted with ethyl acetate (3 × 10 ml). The organic layer was washed with saturated aqueous NaCl (3 × 10 ml), dried over $MgSO_4$ and concentrated. Methyl 4-(3-sulfolen-2-yl)but-2-enoate **3d** (0.443 g, 82%) was isolated by column chromatography (silica gel, hexane–EtOAc, 2:1 to 1:1) as a colourless oil.†

When the monosubstituted sulfolenes **3c**, **3d**, **3f** in HMPTA and the disubstituted sulfolene **3i** in ethanol in the presence of K_2CO_3 were heated,[5] the trienes **4a** and **4b** and dienynes **4c** and **4d** (all *trans* isomers) were formed (Scheme 5). The configuration of **4a–d** was estimated from coupling constants of the olefinic protons in the ^1H NMR spectra (14–16 Hz) and also from the chemical shifts of the carbons of allylic CH_2- and CH_3-groups in the ^{13}C NMR spectra.

Therefore, reactions of organomanganese derivatives of 3-sulfolenes with allyl and propargyl bromides, followed by thermolysis of the resultant products, represent a convenient and stereoselective synthetic pathway to various unsaturated species containing 1,3-diene fragments.

† Spectral data for **3d**: ^1H NMR ($CDCl_3$) 2.14–3.00 (m, 2H, CH_2), 3.45–4.10 (m, 3H, CH_2 + CH), 3.75 (s, 3H, CH_3O), 6.00 (d, 1H, CH=, J 15.0 Hz), 6.07–6.20 (m, 2H, CH=) and 6.98 (dt, 1H, CH=, J_1 15.0 Hz, J_2 7.0 Hz); ^{13}C NMR ($CDCl_3$) 31.4 (t), 51.63 (q), 55.62 (t), 62.73 (d), 124.09 (d), 124.55 (d), 128.99 (d), 142.44 (d) and 166.20 (s).

4a $R^1 = H$, $R^2 = BrCH_2CH{=}CH$ (60%)
4b $R^1 = H$, $R^2 = MeO_2CCH{=}CH$ (51%)
4c $R^1 = H$, $R^2 = Bu^nC{\equiv}C$ (59%)
4d $R^1 = Me$, $R^2 = Bu^nC{\equiv}C$ (64%)

Scheme 5 *Reagents and conditions*: HMPTA, 125°C, 2 h or EtOH, 2 equiv. K_2CO_3, 125°C, 2.5 h

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