Pergamon

Tetrahedron Letters, Vol. 38, No. 17, pp. 2973-2976, 1997

0040-4039/97 $17.00 + 0.00

PII: S0040-4039(97)00536-4

Ene Reaction of Allenic Sulfones

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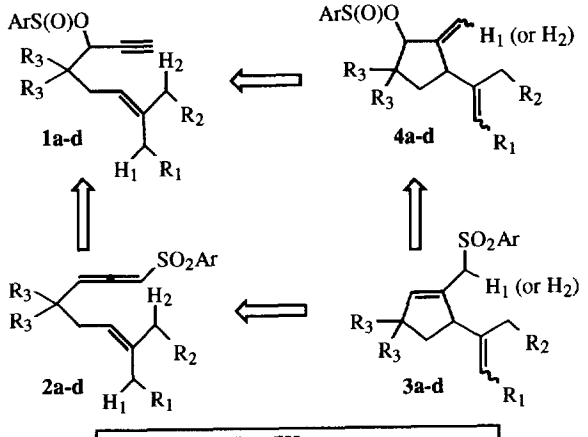
Abstract: *Propargylic* p-*toluenesulfinates* α-*substituted by a* $\Delta^{4,5}$ *unsaturated side-chain rearrange thermally to give 1-tosylmethyl-cyclopentene derivatives with prior isomerisation into the corresponding allenic sulfones.* © 1997 Published by Elsevier Science Ltd.

Though a few Alder-ene reactions[1] in which an electron-deficient allene is acting as enophile are known,[2] there is to date no relevant example with allenic sulfones.[3] Previously, it has been shown that these sulfones react with alkenes, either inter[4a] or intramolecularly,[4b] to give mainly [2+2] cycloadducts in thermal or Lewis-acid-catalysed conditions.

That reluctance of propadienylsulfones to give ene products with olefins appeared surprising, with respect to their well-documented dienophilic properties.[5] Furthermore, an allenic sulfoxide appended to an alkenyl chain has been claimed to undergo an intramolecular Alder-ene (*i.e.* IMAE) reaction.[2b] As part of our continuing effort to use allene sulfones in the synthesis of cyclopentanoids[6] and challenged by the above results, we decided to explore the thermal behaviour of the sulfinate **1a**.

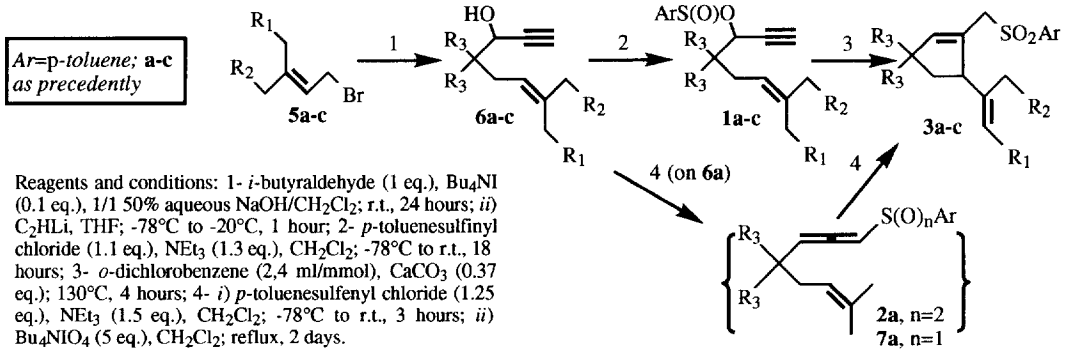


a, R_1=R_2=H; R_3=CH_3
b, R_1=H; R_2=$(CH_3)_2C$=CH-CH_2; R_3=CH_3
c, R_1=$(CH_3)_2C$=CH-CH_2; R_2=H; R_3=CH_3
d, R_1=R_2=R_3=H

Propargylic sulfinates are known to rearrange thermally into the corresponding allene sulfones[7] and it could be expected that heating the sulfinate **1a** would result in the formation of the sulfone **2a**. In the event, **2a** could give

the sulfone **3a** by IMAE reaction. Molecular models suggested that the vinylsulfonyl moiety in **2a** was suitably located, relatively to the remote unsaturation, to participate in such an electrocyclic process. Obviously, a thermal electrocyclisation of the sulfinate **1a** in which the ethynyl group would act as enophile, followed by transposition of the tosyl group in the resulting sulfinate **4a** would lead to the same product (*i.e.* **3a**). Ene reaction of related acetylenic compounds are known to occur at very high temperature however[8] and, accordingly, it could be expected that the former way, involving the transient formation of an allene sulfone, would be preferred. This proved to be the case effectively.

The sulfinate **1a** was prepared, as shown, by alkylation of isobutyraldehyde with prenyl bromide, **5a**, followed by condensation of the homologated aldehyde with lithium acetylide and treatment of the resultant propargylic alcohol **6a** with *p*-toluenesulfinyl chloride. Heating a 0.4M solution of **1a** in *o*-dichlorobenzene at 130°C[9] for four hours resulted in the complete disappearance of the starting material and formation of a new product, to which the structure **3a** was unambiguously attributed (elemental analysis, NMR).[10]



Reagents and conditions: 1- *i*-butyraldehyde (1 eq.), Bu_4NI (0.1 eq.), 1/1 50% aqueous NaOH/CH_2Cl_2; r.t., 24 hours; *ii*) C_2HLi, THF; -78°C to -20°C, 1 hour; 2- *p*-toluenesulfinyl chloride (1.1 eq.), NEt_3 (1.3 eq.), CH_2Cl_2; -78°C to r.t., 18 hours; 3- *o*-dichlorobenzene (2,4 ml/mmol), $CaCO_3$ (0.37 eq.); 130°C, 4 hours; 4- *i*) *p*-toluenesulfenyl chloride (1.25 eq.), NEt_3 (1.5 eq.), CH_2Cl_2; -78°C to r.t., 3 hours; *ii*) Bu_4NIO_4 (5 eq.), CH_2Cl_2; reflux, 2 days.

Independently, the propargylic alcohol **6a** was treated by *p*-toluenesulfenyl chloride and the resulting sulfoxide **7a** was oxidised by tetrabutylammonium periodate in refluxing methylene chloride[11] to give, after a few hours, a mixture of the cyclopentenyl sulfone **3a** with the allene sulfone **2a**. Further heating resulted in the exclusive formation of **3a**. Since an allylic sulfinate related to **4a** proved stable (*vide infra*) in the thermal conditions (*i.e.* *o*-dichlorobenzene, 130°C) where the **1a**-**3a** conversion took place, it can be concluded with some confidence that the thermal isomerisation of sulfinate **1a** into the sulfone **3a** proceeds by propargylic transposition of the tosyl group, followed by IMAE reaction of the resulting allene sulfone **2a**.

The sulfinates **1b-c** were subsequently prepared, starting from geranyl and neryl bromide, respectively, and submitted to thermal conditions as above in order to determine which hydrogen atom -*i.e.* H_1 or H_2 (*vide supra*)- would be preferentially displaced. In both cases (Table 1), a mixture of IMAE products were formed, the isomer resulting from migration of the *trans* allylic proton (*i.e.* H_2) being the main product however.

Table 1: **1** $\xrightarrow[130°C]{\text{o-dichlorobenzene}}$ **3**

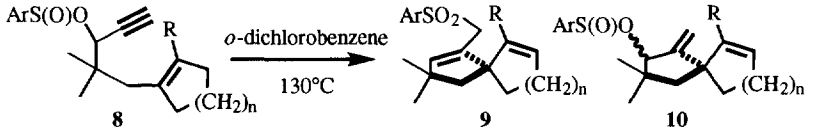
Substrate	Products (ratio)	Yield
1a, R_1=R_2=H; R_3=CH_3	**3a**	90%
1b, R_1=H; R_2=$(CH_3)_2C$=CH-CH_2; R_3=CH_3	**3b/3c*** (1/3)	75%
1c, R_1=$(CH_3)_2C$=CH-CH_2; R_2=H; R_3=CH_3	**3b/3c*** (9/1)	78%
1d, R_1=R_2=R_3=H	**3d**	80%

*E/Z *ratio not determined*

Additionally, we tested the simpler substrate **1d**. As can be seen (last entry of table 1), the gem-dimethyl effect which can be advocated for explaining the success of the IMAE cyclisation of the sulfone **2a** was not essential: **1d** gave efficiently the expected sulfone **3d** (80%); a result which extends greatly the synthetic utility of such ene processes.

The possibility to convert thermally the propargylic sulfinate **1a** into the cyclopentene derivative **3a** being thus firmly established, we used a deeper modification of the substitution pattern of the 6-heptene-1-yne framework of **1a** in order to get some insight on the potential of these reactions in the preparation of spiro compounds. Accordingly, the cycloalkenyl substrates **8a-c** were prepared and submitted likewise to cyclisation conditions.[12]

Table 2:



8 **9** **10**

Substrate	Products (Yield, %)	
8a, R=H; n=1	**9a** (0)	**10a** (78)
8b, R=CH_3; n=1	**9b** (46)	**10b** (6)
8c, R=CH_3; n=2	**9c** (74)	**10c** (0)

In each instance (Table 2), spiro-bicycloalkenes were formed. Contrary to which was observed precedently (compare with entries 2 and 3 of table 1), the *trans* allylic protons were *exclusively* affected in the present cases. Moreover, only compounds in which the cycloalkene residue was substituted by a methyl group (*i.e.* **8b** and **8c**) gave an allylic sulfone. With the sulfinate **8a**, in which such a methyl group is missing, the only observed product was the allylic sulfinate **10a**, formed presumably by an ene process involving the carbon carbon triple bond of **8a** as enophile.

The sulfinate **10a** proved stable upon prolonged heating at 130°C. This result, coupled with that obtained with **1a** (*vide supra*), substantiates the view that sulfones **3a-d**, on one hand, **9b-c**, on the other hand, are formed from the sulfinates **1a-d** and **8b-c**, respectively, by a pathway involving the conversion of the starting sulfinate into the corresponding allene sulfone, followed by a relatively fast IMAE cyclisation of that propadienylsulfone. The observed dichotomy in reactivity of sulfinates **1** and **8** (only allylic protons *anti* to the allenic substituant are affected in the IMAE reaction of sulfones **8b** and **8c**) awaits explanation. A free-radical mechanism has been suggested elsewhere to account for the greater reactivity of the ring allylic hydrogen atoms, as compared to that of the methyl group, in the intermolecular ene reaction of 1-methyl-cyclohexene with current enophiles.[13] Whether or not the present cyclisations involve a biradical species remains to be established. Another point waiting for explanation is the ease with which the propargylic sulfinate **8a** undergoes an ene reaction.

In conclusion, propargylic sulfinates **1** and **8** have been shown to rearrange thermally to give IMAE products **3** and **9**, respectively. In one case (*i.e.* **1a**), it has been clearly demonstrated that such a rearrangement proceeds by prior isomerisation of the starting sulfinate into an allene sulfone, which then undergoes an IMAE process. When the starting propargylic sulfinate is substituted by a cycloalkenyl residue (*e.g.* **8c**), this rearrangement appears to be of great promise, paving the way for a general method of synthesis of spiro compounds. An illustration of this potential has been presented (Bintz-Giudicelli, C.; Weymann, O.; Uguen, D.; De Cian, A.; Fischer, J. *Tetrahedron Letters*, **1997**, *38*, 2841-2844).

Acknowledgements: Best thanks are due to the Fondation Roussel-Uclaf for a grant (to C. B.-G.).

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9- No reaction occurred at lower temperature. For a detailed account of the experimental conditions used for preparing propargylic sulfinates, see ref. 6b. A well-deaerated (freeze and thaw protocol) 0.4M solution of sulfinate in *o*-dichlorobenzene was heated at 130°C under argon with added $CaCO_3$ (0.35 eq.) for 4 hours. Usual work-up involved: *i*) cooling, then filtration of the reaction mixture on Celite; *ii*) distillation of the solvents under a good vacuum (τ=0.05; T(bath)=40-50 °C); *iii*) filtration of the residue on silica gel (CH_2Cl_2).

10- Selected data: **3a**: m.p. 64 °C; elemental analysis: C 71.06 (calc. 71.01), H 8.13 (calc. 7.94); ^{1}H NMR: 0.94 (s, 3H), 1.02 (s, 3H), 1.44-1.59 (m, 1H), 1.53 (s, 3H), 1.78-1.89 (m, 1H), 2.44 (s, 3H), 3.31 (t, J=7.2 Hz, 1H), 3.71 (d, J=3.2 Hz, 2H), 4.6 (s, 1H), 4.79 (s, 1H), 5.42 (s, 1H), 7.32 (d, J=8.2 Hz, 2H), 7.72 (d, J=8.2 Hz); ^{13}C NMR: 19.4, 21.7, 28.7, 44.5, 44.8, 54.3, 56, 113, 128.7, 129.5, 135.7, 144.6, 145.9, 146.8; **3d**: m.p. 50-51 °C; elemental analysis: C 69,61 (calc. 69,53), H 7.33 (calc. 7.29); ^{1}H NMR: 1.53 (s, 3H), 1.78-1.89 (m, 1H), 2.44 (s, 3H), 3.31 (t, J=7.2 Hz, 1H), 3.71 (d, J=3.2Hz, 2H), 4.6 (s, 1H), 4.79 (s, 1H), 5.42 (s, 1H), 7.32 (d, J=8.2 Hz, 2H), 7.72 (d, J=8.2 Hz); ^{13}C NMR: 18.9, 21.6, 29, 31.9, 54.5, 56.2, 112.2, 128.3, 129.5, 136.1, 136.3, 144.5, 145.9; **9b**: ^{1}H NMR: 1.03 (s, 3H), 1.04 (s, 3H), 1.32 (d, J=1.5, 3H), 1.38-1.75 (m, 4H); 2-2.2 (m, 2H), 2.43 (s, 3H), 3.55 (AB system, J_{AB}=15 Hz (Δν=34 Hz), 2H), 5.39 (d, J=1.5 Hz, 1H), 5.77 (s, 1H), 7.35 (d, J=8.3 Hz, 2H), 7.74 (d, J=8.3 Hz); ^{13}C NMR: 12.7, 21.7, 29.5, 29.7, 30.6, 37.8, 44.1, 49.8, 54.2, 88.8, 127.2, 128.9, 129.6, 131.6, 136.2, 143.2, 144.6; **9c**: ^{1}H NMR: 1.02 (s, 3H), 1.03 (s, 3H), 1.1-1.7 (m, 6H), 1.31 (d, J=1.7 Hz, 3H), 1.8-1.9 (m, 2H), 2.42 (s, 3H), 3.55 (AB system, J_{AB}=15 Hz (Δν=44 Hz), 2H), 5.45 (s, 1H), 5.82 (s, 1H), 7.31 (d, J=8 Hz, 2H), 7.75 (d, J=8 Hz, 2H); ^{13}C NMR: 19.5, 19.7, 21.6, 25.4, 29.8, 30.8, 34.9, 44.1, 49.7, 54.6, 125.6, 128.9, 129.5, 132.2, 136.3, 143.5. The ^{1}H and ^{13}C NMR spectra described herein have been recorded at 200 and 50 MHz, respectively, in $CDCl_3$.

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(*Received in France* 2 *February* 1997; *accepted* 15 *March* 1997)