ORGANIC LETTERS

2004
Vol. 6, No. 23
4297−4300

Potassium Hydroxide-Mediated Novel Rearrangement of 2-Alkyl-sulfonyl-2-arylsulfonyl-1-phenylethanones to 1-Aryl-2-(arylsulfonylmethanesulfonyl)ethanones

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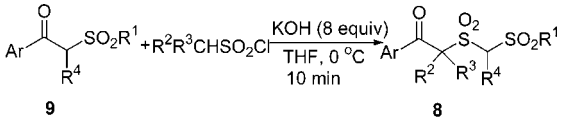
Received September 2, 2004

ABSTRACT



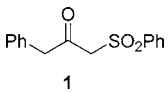
9 **8**

Ar = aryl, R¹ = aryl, R² = H, alkyl,
R³ = H, alkyl, Ph, R⁴ = H

Treatment of a solution of a mixture of 1-aryl-2-arylsulfonylethanones 9 and alkylsulfonyl chlorides (1.5–2.0 equiv) in THF at 0 °C with potassium hydroxide (8 equiv) for 10 min gave a rearrangement product, i.e., 1-aryl-2-(arylsulfonylmethanesulfonyl)ethanones 8, in excellent yields. Regiospecific methyl- and ethylation at the methylene carbon sandwiched between two sulfonyl groups of 8 could be achieved by the reactions of 7i–j with LDA (1 equiv) in THF at room temperature, respectively.

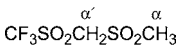
The 1,3-dianions of β-activated sulfones, i.e., β-keto sulfones **1** and mesyltriflones **2**, have received a considerable attention due not only to the reactivity of their 1,3-dianions but also to their potential for use in synthetic sequences requiring alkylation steps.

For example, alkylation of the 1,3-dianion of β-keto sulfone **1** with 1,3-dibromopropane gave C- or O-alkylation product depending on the conditions used.[1a]



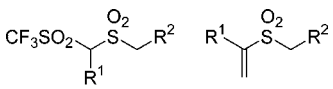
1

On the other hand, the α carbanion of mesyltriflone **2** is known to be much more stable and less reactive than the α′ carbanion, so as to differentiate cleanly the successive alkylations. Furthermore, the polyalkylated mesyltriflone undergoes a Ramberg−Bäcklund reaction with loss of triflinate ion and extraction of SO_2 to form an olefin.[2a,c]



2

On the other hand, treatment of mesyltriflone **3** with K_2CO_3 in THF under nitrogen at room temperature, followed by addition of paraformaldehyde gave vinyl sulfones **4**.[2b] No further reactions of β-activated sulfones appear in the literature.



3 **4**

In connection with a study on the chemistry of a trisulfone **6**, prepared by the *m*-CPBA oxidation of (alkyl) (or aryl)-

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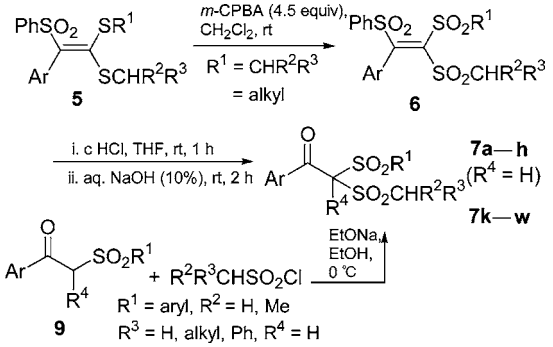
(1) (a) Cooke, F.; Magnus, P. *J. Chem Soc., Chem. Commun.* **1976**, 519−520. (b) Grossert, J. S.; Hoyle, J.; Hooper, D. L. *Tetrahedron* **1984**, *40*, 1135−1140 and references therein.

10.1021/ol0482285 CCC: $27.50
Published on Web 10/16/2004

benzenesulfonylketene (*S*,*S*)-acetals **5** ($R^1 = CHR^2R^3$), it has been found that treatment of compound **6** with concentrated hydrochloric acid, followed by 10% aqueous NaOH at room temperature, gave 1-aryl-2,2-bis(alkylsulfonyl)ethanones **7a**−**h** ($R^1 = CHR^2R^3$; $R^4 = H$) in fair to good yields[3] (Scheme 1).

Scheme 1



On the other hand, unsymmetrically substituted 2-alkylsulfonyl-1-aryl-2-(arylsulfonyl)ethanones **7k**−**w** (R^1= aryl; R^2 = H, Me; R^3 = H, alkyl, Ph; R^4 = H) were prepared by reactions of arylsulfonylbenzoylmethane[4] **9** with alkylsulfonyl chloride in the presence of sodium ethoxide in EtOH (Scheme 1).[5]

Yields of **7** are summarized in Table 1. The structures of compounds **7** may be characterized by the presence of a methine hydrogen activated by three electron-withdrawing groups, i.e., two sulfonyl groups and one carbonyl group. This type of compound possessing two sulfonyl groups and a carbonyl group has seldom been reported.[5] This has aroused curiosity concerning the alkylation of a carbanion generated from **7** in view of the chemistry of the precedent β-activated sulfones.

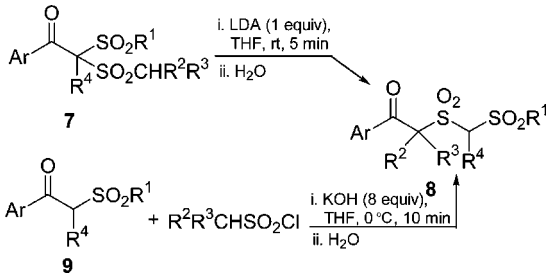
Surprisingly, addition of LDA (2.0 M solution in *n*-heptane/THF/ethylbenzene, 2 equiv) to **7a** (R^1 = Me; R^2 = R^3 = R^4 = H; Ar = Ph) in THF at room temperature under a nitrogen atmosphere led to a new product in less than 5 min. The product was readily separated by chromatography (silica gel, 70−230 mesh, EtOAc) and identified to be 2-methanesulfonylmethylsulfonyl-1-phenylethanone (**8a**) (Scheme 2). There is only one analogous compound reported, namely, α′-cyclopropylketo-methyl-α-methylmesyltriflone.[2c]

Table 1. Yields of 1-Aryl-2,2-bis(alkylsulfonyl)ethanones **7a**−**j**, 2-Alkylsulfonyl-1-aryl-2-arylsulfonylethanones **7k**−**w**, and 2-Alkylsulfonylmethanesulfonyl-1-arylethanones **8**

						yield,[a] %	
Ar	R^1	R^2	R^3	R^4	compd	**7**	**8**[d]
Ph	Me	H	H	H	**a**	83	90
Ph	Et	H	Me	H	**b**	73	84
Ph	*n*-Pr	H	Et	H	**c**	72	83
Ph	*i*-Pr	Me	Me	H	**d**	72	70
Ph	*n*-Bu	H	*n*-Pr	H	**e**	68	78
3-MeC_6H_4	Me	H	H	H	**f**	77	86
4-BrC_6H_4	Et	H	Me	H	**g**	78	56
1-Naphthyl	Et	H	Me	H	**h**	73	79
Ph	Me	H	H	Me	**i**	84[b]	67
Ph	Me	H	H	Et	**j**	78[b]	57
Ph	Ph	H	H	H	**k**	70[c]	63(91)
Ph	Ph	H	Me	H	**l**	42[c]	60(93)
Ph	Ph	Me	Me	H	**m**	40[c]	65(92)
Ph	Ph	H	*n*-Pr	H	**n**	50[c]	45(90)
Ph	Ph	H	Ph	H	**o**	53[c]	58(88)
Ph	4-MeC_6H_4	H	H	H	**p**	39[c]	58(91)
Ph	4-MeC_6H_4	H	Me	H	**q**	57[c]	73(88)
Ph	4-MeC_6H_4	H	*n*-Pr	H	**r**	52[c]	70(89)
Ph	4-MeC_6H_4	H	Ph	H	**s**	50[c]	63(88)
Ph	4-$MeOC_6H_4$	H	H	H	**t**	45[c]	63(90)
Ph	4-$MeOC_6H_4$	H	Me	H	**u**	53[c]	68(89)
Ph	4-$MeOC_6H_4$	Me	Me	H	**v**	52[c]	62(87)
Ph	4-$MeOC_6H_4$	H	Ph	H	**w**	48[c]	61(88)
Ph	Et	H	*n*-Pr	H	**x**		(77)
Ph	*n*-Bu	H	Me	H	**y**		(80)

[a] Isolated yields. [b] Compounds **7i**−**j** were prepared according to the literature.[6] [c] Yields from **9** of Scheme 1 or otherwise from **6**. [d] Number in parentheses represents yield from **9** of Scheme 2.

Scheme 2



Similar treatment of **7b**−**w**, which under the same conditions yields the corresponding rearrangement products **8b**−**w**. Yields of **8a**−**w** are summarized in Table 1.

While preparing **7k**−**w**, which possesses one alkylsulfonyl group and one arylsulfonyl group, and which requires sodium ethoxide and absolute ethanol at 0 °C, according to the reported procedure, we desired to find simpler and milder reaction conditions. Accordingly, 1-phenyl-2-phenylsulfonylethanone **9k** (Ar = R^1 = Ph; R^4 = H) was treated with

(2) (a) Hendrickson, J. B.; Boundreaux, G. J.; Palumbo, P. S. *Tetrahedron Lett.* **1984**, *25*, 4617−4618. (b) Hendrickson, J. B.; Palumbo, P. S. *Tetrahedron Lett.* **1985**, *26*, 2849−2852. (c) Hendrickson, J. B.; Boundreaux, G. J.; Palumbo, P. S. *J. Am. Chem. Soc.* **1986**, *108*, 2358−2366.

(3) **Typical Procedure.** To a solution of 1-benzenesulfonyl-2,2-bis(methanesulfonyl)-1-phenylethene (**6a**) (700 mg, 1.75 mmol) in THF (30 mL) was added concentrated HCl (0.5 mL). The mixture was stirred at room temperature for 1 h, followed by addition of aqueous NaOH (10%, 10 mL) with stirring for 2 h. Removal of the solvent in vacuo gave a residue, which was extracted (CH_2Cl_2, 100 mL × 2), and dried over $MgSO_4$. Removal of the solvent, followed by chromatography (silica gel, 70−230 mesh, 2 × 10 cm, *n*-hexane and EtOAc = 1:1) gave 2,2-bis(methanesulfonyl)-1-phenylethanone (**7a**) (400 mg, 83%): mp 186−187 °C (CH_2Cl_2−*n*-hexane); ^{1}H NMR (300 MHz, $CDCl_3$) δ 3.34 (s, 6H), 6.14 (s, 1H), 7.40−8.05 (m, 5H); IR (KBr) 3024, 1677, 1395, 1308 cm^{-1}. Anal. Calcd for $C_{10}H_{12}O_5S_2$: C, 43.46; H, 4.38; S, 23.21. Found: C, 43.37; H, 4.41; S, 23.25.

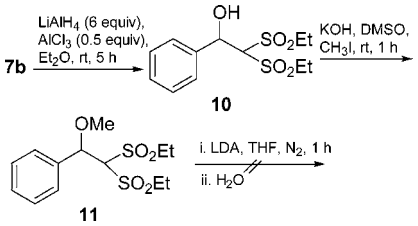
(4) Hamed, E. A.; El-saadi, M. S. M.; El-Hegazy, F. M. *Synth. Commun.* **1995**, *25*, 3471−3478.

(5) Neplyuev, V. M.; Kukhar', V. P.; Sinenko, T. A.; Pel'kis, P. S. *Zh. Org. Khim.* **1976**, *12*, 1746−1749.

methanesulfonyl chloride in the presence of KOH (8.0 equiv) in THF for 10 min at room temperature (Scheme 2). The progress of the reaction was monitored by TLC (silica gel, EtOAc/*n*-hexane = 2:3). TLC of the reaction mixture showed several spots, which were separated by column chromatography (silica gel, 70−230 mesh, 2 × 10 cm, EtOAc) to give **8k** in 20% yield together with unidentifiable unknowns. Surprisingly, the same reaction conducted at 0 °C under the same conditions gave **8k** in 91% yield.[7] No compound **7k** was detected.

In addition, treatment of **7i** (Ar = Ph; $R^1 = R^4 = Me$; $R^2 = R^3 = H$), prepared by the *m*-CPBA oxidation of 2,2-bis(methanesulfonyl)-1-phenylpropanone, with LDA under the foregoing conditions gave **8i** (Ar = Ph; $R^1 = R^4 = Me$; $R^2 = R^3 = H$) in 67% yield. The result indicates that the existence of an α-proton to the carbonyl group is not essential for rearrangement leading to **8**. However, the existence of a *β*-carbonyl group to two sulfonyl groups is essential in view of the recovery (77%) of 2,2-bis(ethanesulfonyl)-1-methoxylethylbenzene (**11**), prepared from 2,2-bis(ethanesulfonyl)-1-phenylethanol (**10**) and iodomethane (Scheme 3).

Scheme 3

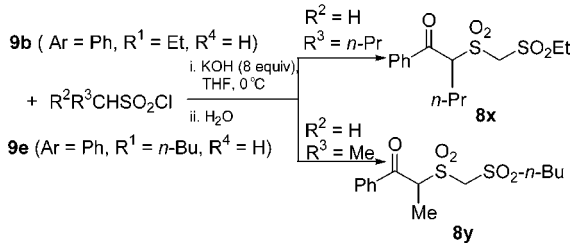


Alternatively, when 2-methanesulfonyl-1-phenylethanone (**9a**) was treated with benzenesulfonyl chloride under the same conditions, the yield of **8k** (7%) decreased drastically concomitant with the formation of unknowns together with recovery of unreacted starting *β*-keto sulfone **9a** (87%).

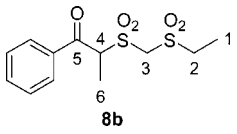
Interestingly, treatment of *β*-keto sulfone **9b** (Ar = Ph; R^1 = Et; R^4 = H) and **9e** (Ar = Ph; R^1 = *n*-Bu; R^4 = H) with butane- and ethanesulfonyl chlorides under the same conditions gave **8x** and **8y** as sole products in 77 and 80% yields, respectively. No the structural isomers **8y** and **8x** were found from the former and latter reactions, respectively (Scheme 4).

The structures of **8** were determined on the basis of the spectroscopic (^{1}H and ^{13}C NMR, IR) and analytical data. In

Scheme 4



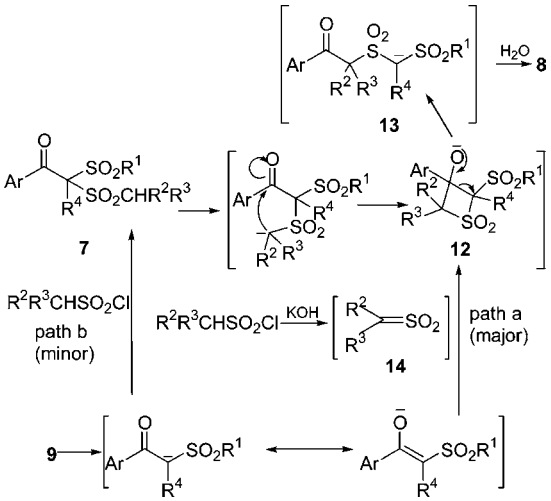
particular, the HMBC (500 MHz, $CDCl_3$) spectrum of **8b** exhibited a correlation between the carbonyl carbon (C-5, 193.1 ppm) and H-4 (5.54 ppm) and H-6 (1.78 ppm) protons. The result clearly indicates that the methyl group was introduced to the α-position (C-4) to the carbonyl group instead of the carbon atom (C-3) between two sulfonyl groups.



8b

The mechanism for the formation of **8** from **7** may be rationalized by an intramolecular nucleophilic attack of a carbanion generated by deprotonation from the CHR^2R^3 group (when R^1 = aryl) onto the carbonyl carbon to give thiethane 1,1-dioxide intermediate **12**, followed by cleavage of the C−C bond concomitant with the generation of the carbonyl group. This leads to carbanion intermediate **13**, which undergoes protonation to give **8** (Scheme 5). In the

Scheme 5



case of R^4 = H, dicarbanions, i.e., on the α-carbon to the carbonyl group and on the α-carbon to the sulfonyl group in the CHR^2R^3 moiety, would be formed because the proton on the carbon of the former would be expected to be a more acidic proton compared to that on the carbon of the latter.

(6) Morel, G.; Marchand, E.; Foucaud, A. *Synth.* **1980**, 918−921.

(7) **Typical Procedure.** To a stirred heterogeneous solution of potassium hydroxide (517 mg, 9.22 mmol) in THF (20 mL) was added 2-benzenesulfonyl-1-phenylethanone (**9a**) (300 mg, 1.15 mmol). The mixture was additionally stirred for 10 min at 0 °C, followed by a dropwise addition of methanesulfonyl chloride (198 mg, 2.30 mmol). The yellow solution turned immediately colorless. Insoluble potassium hydroxide was filtered, followed by removal of the solvent in vacuo. Water (60 mL) was added to the residue, which was extracted with dichloromethane (20 mL × 3). Removal of the solvent gave **8k** (355 mg, 91%): mp 132−134 °C (CH_2Cl_2−*n*-hexane); ^{1}H NMR (300 MHz, $CDCl_3$) *δ* 5.06 (s, 2H), 5.10 (s, 2H), 7.53−8.01 (m, 10H); ^{13}C NMR (75 MHz, $CDCl_3$) *δ* 59.9, 71.8, 128.8, 128.9, 129.2, 129.5, 134.9, 135.0, 135.3, 138.3, 188.9; IR (neat) 1681, 1590, 1332, 1218, 1147, 1087 cm^{-1}. Anal. Caled for $C_{15}H_{14}O_5S_2$: C, 53.24; H, 4.17; S, 18.95. Found: C, 53.22; H 4.17; S, 18.90.

However, the direct formation of **8** from **9** is envisaged to be achieved via the formation of sulfene **14** (Scheme 5), which is known to be formed by the reactions of sulfonyl halides with at least one α-hydrogen and tertiary bases.[8] Similarly, the intermediate **14**, generated from alkylsulfonyl chlorides and KOH, is believed to be trapped by the C=C double bonds of the enolate ions of **9** (path a) to give the intermediate **12**, which ends up as **8**. The formation of **8x** and **8y** from each reaction (Scheme 4) clearly indicates the involvement of sulfene **14** as an intermediate. Nevertheless, the pathway leading to **8** via **7** (path b), generated from the enolate ion of **9** and alkylsulfonyl chlorides cannot be completely ruled out since **8k** was obtained in 7% yield, albeit a low yield, by the reaction of **9a** with benzenesulfonyl chloride.

In summary, 1-aryl-2,2-bis(alkylsulfonyl)ethanones **7a**−**h**, prepared by the reactions of 1-aryl-1-benzenesulfonyl-2,2-bis(alkylsulfonyl)ethenes **6** in THF with concentrated HCl at room temperature, underwent a rearrangement reaction in the presence of KOH (8 equiv) at 0 °C in 10 min, yielding 1-aryl-2-(arylsulfonylmethylsulfonyl)ethanones **8a**−**h**. On the other hand, treatment of (aroyl)arylsulfonylmethanes **9** with alkylsulfonyl chlorides under the same conditions directly produced the same type of rearrangement products **8k**−**w** in excellent yields. Consequently, regiospecific introduction of one or two alkyl(s) or an aryl group at the α-position to the carbonyl group of **8** could be achieved depending on the structures of the alkylsulfonyl groups. By employing **7i**−**j** (Ar = Ph; R^1 = Me; R^2 = R^3 = H; R^4 = Me, Et), regiospecific methylation and ethylation at the carbon atom sandwiched between two sulfonyl groups of **8** could be achieved, respectively.

(8) (a) Block, E.; Aslam, M. *Tetrahedron Lett*. **1982**, *23*, 4203−4206. (b) Schank, K. In *The Chemistry of Sulphones and Sulphoxides*; Patai, S., Rappoport, Z., Stirling, C. J. M., Eds.; John Wiley & Sons, Ltd.: Chichester, 1988; Chapter 7, pp 165−231.

Acknowledgment. This work was supported by the Brain Korea 21 program.

Supporting Information Available: Copies of ^{1}H and ^{13}C NMR spectra IR and elemental analyses of **7b**−**w**, **8a**−**j**, and **8e**−**y**. This material is available free of charge via the Internet at http://pubs.acs.org.

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