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Radical Rearrangements of α-Iodoalkyl Phenyl Sulfones Involving 1,5 Hydrogen Atom Transfer Reactions

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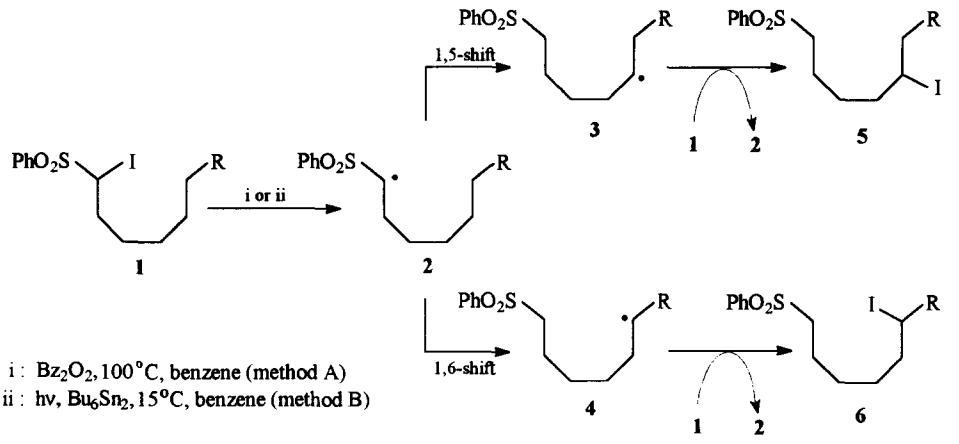
Abstract: α-Iodoalkyl phenyl sulfones undergo radical rearrangement to 5-iodo-1-phenylsulfonyl derivatives when heated with benzoyl peroxide or when irradiated with a sunlamp in the presence of hexabutylditin. Products of these rearrangements, upon treatment with bases, can be easily and stereoselectively converted into *trans* phenylsulfonyl derivatives of cyclopentane.

Intramolecular 1,5 hydrogen transfer reactions are among the most common processes in free radical chemistry. Although both heteroatom and carbon centered radicals may be involved in these transformations, until recently the preparative application of such reactions was limited mainly to the heteroatom cases.[1] In particular, intramolecular self-halogenation reactions of hypohalites (Barton type reaction) and N-halo amines (Hofmann-Löffler-Freytag reaction) gained considerable attention as a synthetic tool.[2] To our best knowledge none of the analogous self-halogenation reactions involving carbon centered radicals has been commonly used in organic synthesis. In this communication we report one such reaction which in our opinion might be preparatively useful.

During our study on free radical reactions of α-iodoalkyl phenyl sulfones[3] we found that such compounds, containing sufficiently long alkyl chain (C_5 or longer), provide 5-iodo-1-phenylsulfonyl derivatives, together with the small amount of their 6-iodo-1-phenylsulfonyl isomers, when heated at 100° C in the presence of benzoyl peroxide (method A),[4] or when irradiated with a sunlamp in the presence of hexabutylditin (method B).[5] A few examples of such rearrangement reactions along with the postulated mechanism are presented in Scheme 1. As shown, the 1,5 and 1,6 hydrogen atom shifts to α-sulfonyl radical centers are the key steps of these chain processes. The predominant 1,5 hydrogen migrations lead to the major reaction products whereas the minor compounds come from the less favored 1,6 hydrogen migrations. Formation of the 1,6 migration products in our reactions was not surprising; 1,6 hydrogen migrations typically accompany 1,5 hydrogen shifts.[1a]

High efficiency of the rearrangement reactions, coupled with the easy access to the wide variety of α-iodoalkyl phenyl sulfones[6] makes the method presented preparatively attractive. Reactions initiated by thermal decomposition of benzoyl peroxide seem to be particularly suited to large scale preparation. This

approach affords satisfactory yields and may be conveniently applied without any special equipment. The alternative photochemical route seems to be less efficient, although in this case somewhat higher regioselectivity was observed.



i : Bz_2O_2, 100°C, benzene (method A)
ii : hv, Bu_6Sn_2, 15°C, benzene (method B)

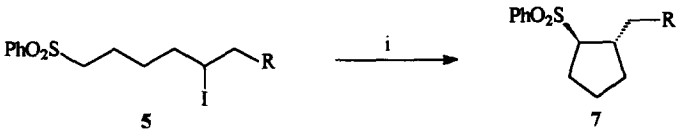
a : R = H
b : R = CH_3
c : R = C_6H_{13}

Substrate	Method	Products (5 + 6)	
		Yield (%)	5 / 6 ratio
1a	A	83	>96/4 [a]
	B	50	>96/4 [a]
1b	A	89	82/18 [b]
	B	50	86/14 [b]
1c	A	80	80/20 [c]
	B	60	-

a) Isomer **6** was not detected in ^{1}H NMR; b) Determined by ^{1}H NMR; c) Assessed by ^{13}C NMR, in ^{1}H NMR spectrum all diagnostic signals were overlaped.

Scheme 1

The presence of the versatile iodo and phenylsulfonyl groups in the products makes them very attractive intermediates in organic synthesis. For instance, on the basis of the well established chemistry of sulfonyl carbanions,[7] one could expect that compounds **5** would undergo intramolecular nucleophilic substitution upon treatment with bases providing cyclic phenylsulfonyl derivatives. In fact, when **5a**, **5b** and **5c** were subjected to the reaction with sodium bis(trimethylsilyl)amide in toluene solution the cyclic products **7a**, **7b** and **7c** were obtained in good yield (Scheme 2).[8] We were delighted to find that the cyclizations were highly stereoselective and only single stereoisomers were detected in the reaction mixtures. The *trans* stereochemistry of **7a** was clearly indicated by the chemical shift of the methyl group in ^{1}H NMR spectrum.[9] The CH_3 signal appeared at 0.95 ppm which was in good agreement with the position of the methyl group (0.98 ppm) reported for the same compound prepared in different way.[10] For comparison, the methyl group in the *cis* isomer resonates at 1.30 ppm.[10] We assumed that the reactions with **5b** and **5c** should take the same course and by analogy the *trans* stereochemistry was assigned also to compounds **7b** and **7c**.



5 7

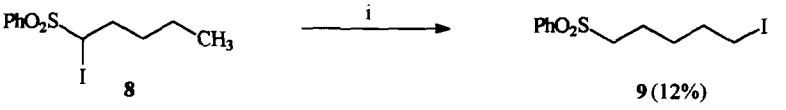
i : $[(CH_3)_3Si]_2NNa$, toluene

a : R = H
b : R = CH_3
c : R = C_6H_{13}

Substrate	Product	Yield (%)
5a	**7a**	72
5b	**7b**	74
5c	**7c**	75

Scheme 2

Since both 1,6 and 1,5 hydrogen shift processes, are of the same nature, as illustrated in Scheme 1, the formation of the undesired 1,6 hydrogen migration products during the rearrangement reactions seems to be difficult to overcome. In particular instances, however, when for some reasons the competitive 1,6 hydrogen migrations are significantly impeded, the 1,5 hydrogen migrations can be the only reactions. Rearrangement of iodosulfone **1a** that led to the single product **5a** (Scheme 1) was such an example. In this case the 1,6 hydrogen migration could proceed only by the abstraction of hydrogen atom from the methyl group, which must be a disfavored process due to the high CH_2-H bond dissociation energy.[11] The low reactivity of the methyl groups in radical transformations is exemplified by the isomerisation of iodosulfone **8** which provides only a small amount of the rearrangement product **9** (Scheme 3), despite the fact that in this reaction the preferred 1,5 hydrogen shift is involved.

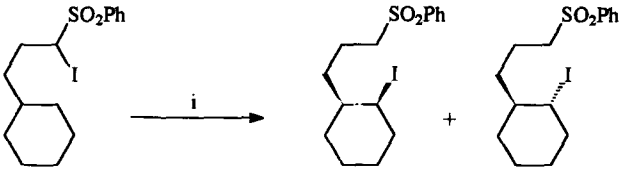


8 **9** (12%)

i : Bz_2O_2, 100° C, benzene

Scheme 3

We were looking for additional examples of reactions which could provide exclusively 1,5 hydrogen shift products. Rearrangement of iodosulfone **10** was such a case (Scheme 4). Apparently, in this reaction the 1,6 hydrogen transfer would proceed through a bridged transition state, which makes the process noncompetitive to the 1,5 hydrogen shift reaction due to steric reasons.



10 **11** (37%) **12** (36%)

i : Bz_2O_2, 100°C, benzene

Scheme 4

In conclusion, the method presented enables an easy and efficient preparation of compounds containing a 5-iodo-1-phenylsulfonyl moiety from readily accessible α-iodoalkyl phenyl sulfones. We believe that products of our reaction might be attractive intermediates in organic synthesis. In particular, these compounds are very convenient precursors of cyclopentane derivatives.

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3. a) Masnyk, M. *Tetrahedron Lett.* **1991**, 32, 3259-3262. b) Jankowski, P.; Masnyk, M.; Wicha, J. *Synlett* **1995**, 866-868.
4. In a typical procedure a mixture of iodosulfone (2 mmol), benzoyl peroxide (0.2 mmol) and benzene (1.5 ml) was heated in a sealed tube for 5 h and then chromatographed on silica gel.
5. In a typical procedure a mixture of iodosulfone (0.2 mmol), benzene (0.6 ml) and hexabutylditin (0.02 mmol) was placed in a pyrex tube and irradiated with a 280 W sunlamp for 3h at 15°C in a reactor cooled with water.
6. Iodoalkyl phenyl sulfones can be prepared by the phase transfer catalytic alkylation of iodomethyl phenyl sulfone with alkyl bromides (tetrabutylammonium bromide/50% aq NaOH/benzene). In particular, iodosulfones **1a**, **1b**, **1c**, **8** and **10** were prepared by alkylation of iodomethyl phenyl sulfone with 1-bromopentane, 1-bromohexane, 1-bromoundecane, 1-bromobutane and 2-cyclohexylethyl bromide respectively. For preparation of iodomethyl phenyl sulfone and other examples of alkylation see: Jończyk, A.; Pytlewski, T. *Synthesis* **1978**, 883-886.
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8. In a typical procedure sodium bis(trimethylsilyl)amide (0.6 mmol) was added to a solution of 5-iodo-1-phenylsulfonyl derivative (0.3 mmol) in toluene (3.0 ml) and the mixture was stirred for 3h at room temperature. Then the mixture was washed with water, dried over $MgSO_4$ and chromatographed on silica gel.
9. **7a**: ^{1}H NMR (200 MHz, $CDCl_3$): δ = 7.95-7.84 (m, 2H), 7.68-7.47 (m, 3H), 3.03 (dt, J = 9.2, 6.6 Hz, 1H), 2.47 (m, 1H), 2.18-1.55 (m, 5H), 1.24 (m, 1H), 0.95 (d, J = 6.9 Hz, 3H). - ^{13}C NMR (50 MHz, $CDCl_3$): δ = 138.90, 133.36, 129.06, 128.45, 70.68, 35.63, 35.40, 28.23, 24.77, 20.63.
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