Relative β-elimination rates of heteroatoms from alkyl and aminyl radicals

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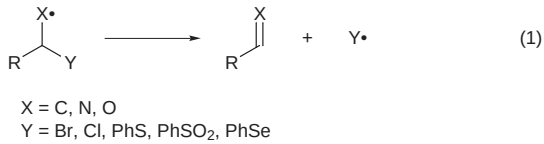
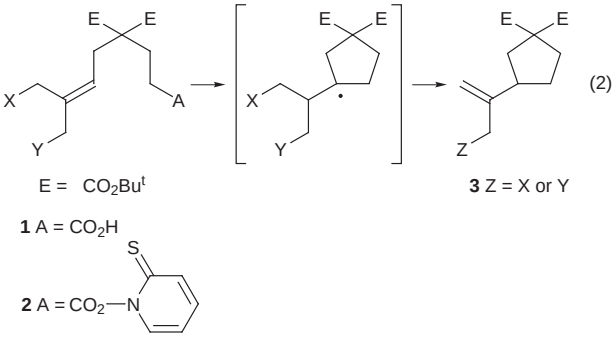
The relative β-elimination rates of heteroatoms from alkyl radicals are in the order of Br≥PhSe > PhS > $PhSO_2$ > Cl, whereas the order of PhSe > $PhSO_2$ > PhS ~ Br is observed for β-eliminations from aminyl radicals, indicating a dependence on the nature of radicals.

The β-elimination reaction of heteroatoms is one of characteristic properties of radical reactions [eqn. (1)][1] and its driving



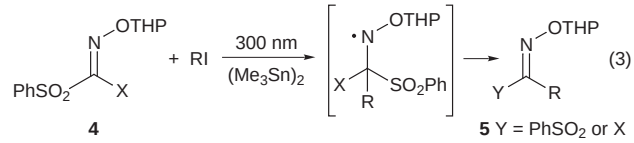
force is known to be relief of ring strain,[2] the evolution of CO_2 and SO_2,[3] or the generation of a π-bond along with the cleavage of a weaker σ-bond. The ease of β-fragmentation depends on (i) the strength of the σ-bond broken (C–Y) and also (ii) the nature of π-bonds formed (C=X).[4] In the former case, it is expected that the weaker the breaking bond is, the faster the β-fragmentation would be. As far as we are aware, there are no reports of the β-elimination of heteroatoms from aminyl radicals. We conceived that it could be possible that the relative β-elimination rates of heteroatoms from alkyl and aminyl radicals would depend on the nature of π-bonds formed and we investigated this intriguing possibility.

Although relative β-elimination rates of heteroatoms from alkyl radicals were reported previously,[6] we briefly examined the β-elimination rates using *N*-hydroxypyridine-2-thione ester **2** [eqn. (2)][7] and experimental results are shown in Table 1.

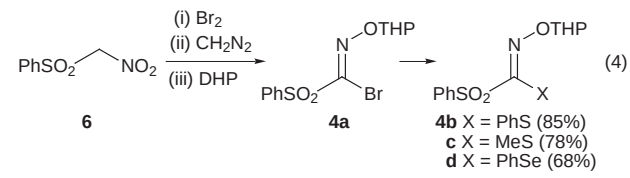


Treatment of acid **1** with *N*-hydroxypyridine-2-thione (1.2 equiv.), DCC (1.2 equiv.) and DMAP (0.1 equiv.) in CH_2Cl_2 at room temperature for 2 h afforded the thiohydroxamate **2**, which decomposed to some extent during isolation. Thus, the reaction was carried out in CH_2Cl_2 at 50 °C without isolation of **2**. To examine the relative β-elimination rates of the bromo and the phenylthio groups, when **2a** was heated at 50 °C for 5 h, the bromide was preferentially eliminated (entry 1). A same result was obtained with **2b** for the competition between the bromide and the phenylsulfonyl groups (entry 2). However, the elimination of the bromide competed more equally with that of the phenylseleno group, although the former was favored over the latter to some extent (entry 5). Furthermore, the phenylsulfonyl group underwent preferential elimination in the presence of the chloride (entry 4) and the elimination of the phenylthio group was much faster than that of the phenylsulfonyl group, although the phenylsulfonyl group underwent elimination to a small extent (3%) (entry 3).[8] When the present reactions were monitored in $CDCl_3$ by ^1H NMR spectroscopy, the allyl species **3** turned out not to be susceptible to radical addition-elimination by the radical species ejected in the elimination step. Thus, the relative rates of β-eliminations of heteroatoms from alkyl radicals are in the order of Br≥PhSe > PhS > $PhSO_2$ > Cl.

To study the effect of aminyl radicals on the β-eliminations of heteroatoms, we utilized the radical reaction of phenylsulfonyl substituted oxime ethers [eqn. (3)]. Recently, we reported free



radical acylation approaches involving alkyl radical additions to sulfonyl substituted oxime ethers as acylating agents.[9] Phenylsulfonyl bromo oxime ether **4a** was prepared by the known procedure using (phenylsulfonyl)nitromethane **6** by three-step sequence involving bromination, *O*-methylation with CH_2N_2 and the subsequent protection as a THP ether.[10] The bromide group in **4a** was further displaced by sodium thiophenoxide, sodium thiomethoxide and sodium benzeneselenoate in THF to afford **4b** (85%), **4c** (78%) and **4d** (68%) [eqn. (4)]. As shown



in Table 2, when a solution of 4-phenoxybutyl iodide, **4a** and hexamethylditin in benzene was irradiated at 300 nm for 16 h, somewhat surprisingly the bromo oxime ether was obtained in 78% yield (entry 1), indicating that the phenylsulfonyl group

Table 1 β-Eliminations of heteroatoms from carbon-centered radicals[a]

		Substrate **2**[b]		Product **3**	
Entry		X	Y	Z	Yield[c] (%)
1	**a**	Br	PhS	PhS	87
2	**b**	Br	$PhSO_2$	$PhSO_2$	79
3	**c**	PhS	$PhSO_2$	$PhSO_2$	89
				PhS	3
4	**d**	Cl	$PhSO_2$	Cl	80
5	**e**	Br	PhSe	PhSe : Br[d]	76

[a] Reaction time: 5–7 h. [b] *E*/*Z* ratio: **2a** (1.4 : 1), **2b** (5.4 : 1), **2c** (10.8 : 1), **2d** (6.7 : 1), **2e** (3.1 : 1). [c] Isolated yield. [d] Ratio = 76 : 24. The ratio was determined by ^1H NMR spectroscopy.

Table 2 β-Eliminations of heteroatoms from nitrogen-centered radicals

Entry		Substrate **4**[b] X	Substrate **4**[b] Y	Product **5** Z	Yield (%)
1	**a**	$PhSO_2$	Br	Br	78
2	**b**	$PhSO_2$	PhS	PhS	58
3	**c**	$PhSO_2$	MeS	MeS	74
4	**d**	$PhSO_2$	PhSe	$PhSO_2$	65
5	**e**	PhS	Br	messy	

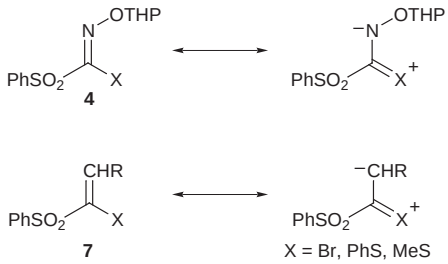


Fig. 1

was preferentially eliminated over the bromide group. This result is in sharp contrast with the above results obtained for alkyl radicals (Table 1). Similar results were also obtained with **4b** and **4c** (entries 2 and 3), showing the preferential elimination of the phenylsulfonyl group over the phenylthio and methylthio groups. However, competition between the phenylsulfonyl and the phenylseleno groups showed that the phenylseleno group was eliminated preferentially (entry 4). Attempts to study the relative β-elimination rate between the phenylthio group and bromide[10,11] were unsuccessful because the intermolecular addition of an alkyl radical onto the phenylsulfenyl bromo oxime ether (entry 5) turned out to be inefficient.

The results obtained in this study are rather interesting and indicate that phenylsulfonyl groups on aminyl radicals undergo facile elimination relative to the bromide, methylthio, and phenylthio groups. We have no clear answer why the relative rates of β-elimination of heteroatoms, particularly the phenylsulfonyl group, from alkyl and aminyl radicals are so different. When the contributing resonance structures of **7** and **4** were compared (Fig. 1), we suggest that resonance in **4** is much more important than resonance in **7**, thereby giving unusually strong carbon–bromine and carbon–sulfur bonds in **4** due to the contribution of significant double bond character. Apparently, resonance contribution from the phenylsulfonyl group is not possible.

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Notes and References

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