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SmI_2 Catalyzed $S_{RN}1$ Reactions of Haloarenes with Acetophenone Enolate Ions in DMSO

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Abstract: *Iodobenzene, 2-halopyridines (Cl, Br), 2-chloroquinoline and 1-halonaphthalenes (Cl, Br) react with acetophenone enolate ion in DMSO by the $S_{RN}1$ mechanism catalyzed by SmI_2.*

The aromatic radical nucleophilic substitution, or $S_{RN}1$, has been shown to be an excellent means of affecting the nucleophilic substitution of unactivated aromatic compounds possessing suitable leaving groups with many types of nucleophiles. The mechanism of the reaction is a chain process, and the propagation steps are shown in Scheme I,[1] in which radicals and radical anions are intermediates. However, this chain process requires an initiation step (eq. 1). In a few systems, spontaneous electron transfer (ET) from the nucleophile to the substrate has been observed.[2] When ET does not occur spontaneously, it can be induced by light,[3] by solvated electrons in liquid ammonia,[4] by cathodically generated electrons,[5] by certain inorganic salts,[6] sodium amalgam,[7] or under sonication.[8]

SCHEME I

Initiation Step:

$$RX + e^- \longrightarrow (RX)^{-\cdot} \qquad 1$$

Propagation Steps.

$$(RX)^{-\cdot} \longrightarrow R^{\cdot} + X^- \qquad 2$$

$$R^{\cdot} + Nu^- \longrightarrow (RNu)^{-\cdot} \qquad 3$$

$$(RNu)^{-\cdot} + RX \longrightarrow RNu + (RX)^{-\cdot} \qquad 4$$

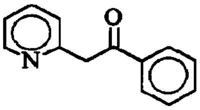
Although certain carbanions have been found to be efficient nucleophiles in $S_{RN}1$ reactions with aryl halides,[1] stabilized carbanions such as the enolate ions of acetophenone[9a] or the anions of α-β unsaturated ketones[9] were found to be unreactive toward halobenzenes under photostimulation in liquid ammonia. A similar behavior was determined for the reaction of acetophenone anion with 1-chloronaphthalene.[10] The photostimulated reaction of iodobenzene and 1-iodonaphthalene with acetophenone enolate ion in DMSO gave good yields of the substitution product.[11]

SmI_2 has been used as one electron reductor of many organic halides,[12] and we thought that it could be used to initiate the $S_{RN}1$ reaction of aryl halides.

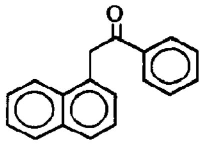
Acetophenone enolate ion was prepared in DMSO, and after the addition of chloro- or bromobenzene, a solution of SmI_2 in THF was dropped to the solution, but no substitution products were found (Expts. 1-2). However, when iodobenzene was the substrate, a 47 % yield of the substitution product α-phenylacetophenone[7b] was formed in only 15 minutes of reaction (Expt. 3) (eq. 5)

$$PhI \;+\; {}^{-}CH_2COPh \xrightarrow[\text{DMSO}]{SmI_2/THF} PhCH_2COPh \qquad 5$$

With 2-chloropyridine and with a 1:1 ratio between substrate and SmI_2 the yield of substitution product α-(2-pyridyl)acetophenone **1** was 28%, whereas with a 1:2 ratio, the product **1** was obtained in 48% yield. (Expts. 4-5).



1



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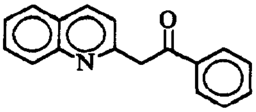

3

The reaction with 1-chloronaphthalene as substrate gave a 47% yield of α-(1-naphthyl)acetophenone[7b] **2** in 4 min of reaction with substrate: SmI_2 ratio of 1:0.5.[13] When the SmI_2 concentration is increased, there is a rise of the yield of substitution product, then with 1:1.8 ratio, the yield of **2** was 93% (Expts. 6-8).

Lower amount of SmI_2 were needed in the reaction of 1-bromonaphthalene as substrate. Thus, with a 1:0.4 ratio of substrate: SmI_2, the yield of substitution product **2** was 77% (Expt. 9), and with a 1:0.5 ratio, a 93% yield of substitution product was found in 15 min. of reaction (Expt. 10), and with a ratio close to 1:1.3, the yield was 97% of the substitution product **2** (Expt. 11).

The reaction of 2-chloroquinoline with SmI_2 (with a substrate: SmI_2 ratio of 1:0.26) in 15 min. gave the substitution product **3** with 94% yield (Expt. 12).

It has been proposed that the reaction of organic halides with SmI_2 gives free radicals, or organosamarium intermediates.[12] Although the actual mechanism of these reactions is still under study, the fact that the amount of substitution product obtained in the reaction of 1-bromonaphthalene and 2-chloroquinoline in relation to the SmI_2 used indicates that there is a chain process in this system. In the other examples studied, with more positive reduction potentials of the substrates, an excess of SmI_2 has to be used to obtain good yields of substitution products. With chloro- or bromobenzenes there were no coupling products.

The reaction of aryl halides with nucleophiles catalyzed by SmI_2 is a promising system, due to the simplicity of the procedure and in a relative fast reaction, neither reduction of the aromatic moiety, nor the carbonyl group were observed. We will study further these reactions with other nucleophiles and other aromatic as well as alkyl halides[14] in order to know the scope of this novel catalyzed reaction, and their synthetic applications.

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TABLE 1: Reactions of Haloarenes with Acetophenone Enolate Ions Catalyzed by SmI_2.[a]

Expt.	ArX (mmole)	SmI_2, mmole	ArX:SmI_2 ratio	Reaction Time, min.	$ArCH_2COPh$, %
1	PhCl (0.49)	0.50	1:1	10	0
2	PhBr (0.48)	1.0	1:2.1	10	0
3	PhI (0.54)	1.0	1:1.8	15	47
4	2-ClPyr (0.53)	1.0	1:2	30	10
5	2-BrPyr (0.53)	0.3	1:0.6	15	77
6	1-ClNaph (0.54)	0.29	1:0.5	4	47
7	1-ClNaph (0.54)	0.32	1:0.6	1	53
8	1-ClNaph (0.54)	0.96	1:1	6	93
9	1-BrNaph (0.52)	0.21	1:0.4	4	77
10	1-BrNaph (0.52)	0.25	1:0.5	15	93
11	1-BrNaph (0.52)	0.66	1:1.3	15	97
12	2-ClQuin (0.51)	0.13	1:0.26	15	94

[a] Reactions carried out in *ca.* 25 mL of DMSO with 0.50 mmol of acetophenone enolate ions. 2-XPyr. = 2-halopyridines (Cl, Br); 1-XNaph = 1-halonaphthalenes (Cl, Br), 2-ClQuin = 2-chloroquinoline.

References and Notes

1. For reviews, see: (a) Norris, R. K.; *The Chemistry of Functional Groups*; Patai, S., Rappoport, Z., Eds., Wiley: Chichester, UK, **1983**; Supplement D, Chapter 16. (b) Rossi, R. A.; de Rossi, R. H.; *Aromatic Substitution by the $S_{RN}1$ Mechanism*; ACS Monograph 178; American Chemical Society: Washington, DC, **1983**. (c) Norris, R. K., *Comprehensive Organic Synthesis*, Trost, B. M., Ed., **1991**, Vol. 4, Pergamon, 451.

2. (a) Kim, J. K, Bunnett, J. F., *J. Am Chem. Soc.*, **1970**, *92*, 7463. (b) Scamehorn, R. G.; Bunnett, J. F., *J. Org. Chem.*, **1977**, *42*, 1449 (c) Scamehorn, R. G., Hardacre, J. M., Lukanich, J. M.; *J. Org. Chem.*, **1984**, *49*, 4881.

3. (a) Rossi, R. A., Bunnett, J. F., *J. Org. Chem.*, **1973**, *38*, 1407. (b) Hoz, S., Bunnett, J. F., *J. Am. Chem. Soc.*, **1977**, *99*, 4690. (c) Fox, M. A., Younathan, J., Fryxell, G. E., *J. Org. Chem.*, **1983**, *48*, 3109.

4. (a) Kim, J. K; Bunnett, J. F.; *J. Am. Chem. Soc.* **1970**, *92*, 7464. (b) Rossi, R. A.; Bunnett, J. F.; *J. Am. Chem. Soc.* **1974**, *96*, 112.

5 (a) Savéant, J. M., *Acc. Chem. Res.* **1980**, *13*, 323 (b) Savéant, J. M., *Adv. Phys. Org. Chem.* **1990**, *26*, 1, and references cited therein.

6 (a) Galli, C., Bunnett, J. F.; *J. Am. Chem. Soc.* **1984**, *49*, 3041. (b) Galli, C.; Gentile, P.; *J. Chem. Soc., Perkin Trans. 2*, **1993**, 1135. (c) Leeuwen, M. v., Mckillop, A., *J. Chem. Soc., Perkin Trans. 1*, **1993**, 2433.

7. (a) Austin, E., Alonso, R. A., Rossi, R. A., *J. Org. Chem.* **1991**, *56*, 4486. (b) Austin, E., Ferrayoli, C. G., Alonso, R. A., Rossi, R. A., *Tetrahedron*, **1993**, *49*, 4495

8. Manzo, P. G., Palacios, S. M., Alonso, R. A., *Tetrahedron Lett.*, **1994**, *35*, 677.

9. (a) Bunnett, J. F., Sundberg, J. E., *J. Org. Chem.* **1976**, *41*, 1702. (b) Alonso, R. A.; Austin, E.; Rossi, R. A. *J. Org. Chem.* **1988**, *53*, 6065.

10. Rossi, R. A., de Rossi, R. H.; López, A.F., *J. Am. Chem. Soc.* **1976**, *98*, 1252.

11. Borosky, G. L., Pierini, A. B., Rossi, R. A., *J. Org. Chem.* **1992**, *57*, 247.

12. Curran, D. P., Fevig, T. L.; Jasperse, C. P., Totleeben, M. J.; *Synlett*, **1992**, 943, and references cited therein.

13 The reactions were carried out in a 100-mL three-neck round-bottomed flask equipped with a nitrogen inlet and magnetic stirrer. To 25 mL of dry and degassed DMSO under nitrogen was added 6.0 mmol of potassium *t*-butoxide, 5.0 mmol of acetophenone, and 0.52 mmol of 1-bromonaphthalene. To this solution was added 0.25 mmol of SmI_2 (2.50 mL of 0.1M solution in THF). The SmI_2 solution was stored under nitrogen in a foil wrapped flask and transferred by syringe to preclude contact with air. After 15 minutes, the reaction was quenched by adding ammonium nitrate in excess and 100 mL of water,and extracted with ether. The ether extract was washed twice with water, dried and quantified by GLC. 9, 10-Dibromoanthracene was used as internal standard. The reaction product was compared with an autentic sample[7b] and it was identified as α-(1-naphtyl)acetophenone

14. Preliminary results indicate that 7-iodonorcarane reacts with acetophenone enolate ions to give the substitution product catalyzed by SmI_2.

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