Pergamon

Tetrahedron Letters, Vol. 36, No. 6, pp. 913-914, 1995
Elsevier Science Ltd
Printed in Great Britain
0040-4039/95 $9.50+0.00

0040-4039(94)02370-0

Radical Isomerization via Intramolecular Ipso Substitution of N-Arylamides: Aryl Translocation from Nitrogen to Carbon.

Eun Lee*, Ho Sung Whang, and Cheol Keun Chung

Department of Chemistry, College of Natural Sciences, Seoul National University, Seoul 151-742, Korea

Abstract : N-Aryl-N-(3-bromopropyl)amides are converted to N-(3-arylpropyl)amides under standard radical generating conditions via intramolecular ipso attack of the alkyl radicals which generates spiro cyclohexadienyl radical intermediates.

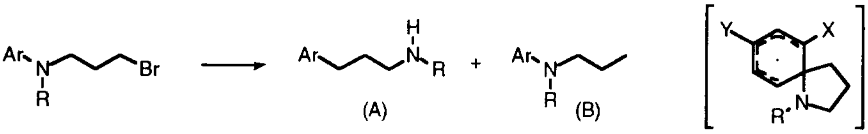
Rearrangements of aromatic systems triggered by intramolecular ipso attack of free radicals are now well documented.[1] A few examples have been reported, in which aryl migration occurs from nitrogen to carbon. Intramolecular radical substitution during the reduction of 2-halogenobenzanilides is known to proceed via azaspiro cyclohexadienyl radical intermediates.[2] Different types of azaspiro cyclohexadienyl radical intermediates are proposed in quinoline annulation reactions.[3]

Recently, we reported radical rearrangement reactions in which 3-arylpropanol products are formed from aryl 3-bromopropyl ethers under the standard radical generating conditions in the presence of tributylstannane and AIBN.[4] The efficiency of rearrangement depended strongly on the substitution pattern of the aromatic ring. We now wish to report here that N-aryl-N-(3-bromopropyl)amides also rearrange and N-(3-arylpropyl)amides are obtained via the same type of radical rearrangement reactions.

The substrate N-aryl-N-(3-bromopropyl)amides were synthesized by alkylation of the corresponding N-arylamides with 1,3-dibromopropane in DMF in the presence of sodium hydride. The substrates were reacted with tributylstannane under standard high dilution conditions: 1.2 eq. Bu_3SnH and 0.2 eq. AIBN in benzene were added to a substrate solution (0.03 M) in benzene under reflux via syringe pump for 7 hours (total reflux time 8 hours). The results are summarized in Table 1.

In the cases of N-aryl-N-(3-bromopropyl)carbamates, aryl ortho or para methoxy substitution led to more efficient rearrangement (Entries 1 and 3) than meta substitution (Entry 2). Rearrangement yield from the toluenesulfonamide substrate increased slightly (Entry 4). Methanesulfonamide derivatives were superior substrates as they reacted more efficiently and cleanly (Entries 5 and 6). Aryl para substitution by electron-withdrawing methoxycarbonyl group and aryl ortho and para dimethoxy substitution resulted in reasonably good rearrangement yield (Entries 7 and 8). The best yield of the rearrangement product was obtained when both electron-donating and -withdrawing substituents were present strategically at aryl ortho and para positions (Entry 9).

It is clear from the results of these experiments that the efficiency of the rearrangements resulting in the aryl migration from nitrogen to carbon depends strongly on the stability of the intermediate spiro



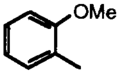
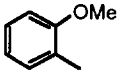
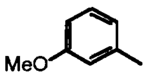
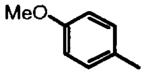
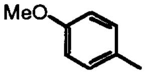
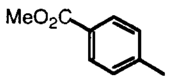
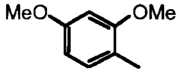
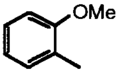
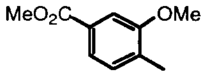
Entry	Ar	Isolated Yield (%)		Entry	Ar	Isolated Yield (%)	
		(A)	(B)			(A)	(B)
	R=CO_2Me				R=SO_2Me		
1		30	36	5		38	40
2		5	80	6		26	57
3		25	45	7		29	51
	R=SO_2Tol			8		38	48
4		35	43				
				9		72	5

Table 1

cyclohexadienyl radicals. Radical ipso attack is most efficient if the intermediate is "captodatively" stabilized,[5] which then undergoes kinetically favored homolytic cleavage of C-N bond for rearomatization

Acknowledgements : Authors thank the Ministry of Education, Republic of Korea, (BSRI-93-314), the Organic Chemistry Research Center (KOSEF), and S.N.U.-Daewoo Research Fund for financial support.

REFERENCES

1. See the survey of literature in the reference 4.
2. a) Grimshaw, J.; Hamilton, R.; Trocha-Grimshaw, J. *J. Chem. Soc. Perkin I* **1982**, 229.
   b) Grimshaw, J.; Haslett, R. J. *J. Chem. Soc. Perkin I* **1980**, 657.
3. a) Leardini, R.; Nanni, D.; Pedulli, G. F.; Tundo, A.; Zanardi, G. *J. Chem. Soc. Perkin I* **1986**, 1591.
   b) Curran, D. P.; Liu, H. *J. Am. Chem. Soc.* **1991**, *113*, 2127.
4. Lee, E.; Lee, C.; Tae, J. S.; Whang, H. S.; Li, K. S. *Tetrahedron Lett.* **1993**, *34*, 2343.
5. The same type of stabilization was invoked in the rearrangement of aryl 3-bromopropyl ethers.

(*Received in Japan* 26 *July* 1994; *revised* 25 *October* 1994; *accepted* 30 *November* 1994)