

ULTRASOUND - PROMOTED COUPLING OF HETEROARYL HALIDES IN THE PRESENCE OF LITHIUM WIRE. NOVEL FORMATION OF ISOMERIC BIPYRIDINES IN A WURTZ - TYPE REACTION

Alan G. Osborne*, Kathryn J. Glass and Miriam L. Staley
Department of Chemistry, City University, LONDON EC1V 0HB, U.K.

Summary Ultrasonic irradiation of 2-bromopyridine in THF solution in the presence of lithium wire gives 2,2'-bipyridine, 2,4'-bipyridine and 4,4'-bipyridine, a novel formation of isomers in a Wurtz-type reaction. Similar reaction with 3-bromopyridine mainly results in debromination.

The application of ultrasound to facilitate organic reactions has recently attracted considerable interest.^{1,2} Biphenyl (4) may be obtained from bromobenzene (1) in 70% yield through a Wurtz-type sonochemical coupling reaction with lithium wire in THF solution.^{3,4} Lindley, Lorimer and Mason⁵ have reported that ultrasonic irradiation of activated aryl halides, e.g. 2-iodonitrobenzene, produced a 50-fold increase in reactivity compared to the classical Ullmann reaction.

However, as far as the present authors are aware,⁶ applications of the above reactions for the syntheses of bipyridines have not been reported. In connection with our NMR spectral studies of biheteroaryls,^{7,8} we now report some preliminary results using 2-bromopyridine (2) and 3-bromopyridine (3) as starting materials.

The procedure of Lash and Berry⁴ was used; after sonication (Decon FS300 bath, 10 hours) the reaction mixture was diluted with ether, filtered, and the residue, after removal of solvent, examined by ¹³C NMR spectroscopy. The results are shown in the Table.

With 3 minimal formation of the dimer resulted, the main reaction being debromination, such reductions have already been shown to be facilitated by ultrasound.⁹

In complete contrast, a totally unexpected reaction resulted with 2 in that a mixture of isomeric bipyridines was obtained. In the Wurtz and Ullmann reactions the dimer formed is normally bonded only at those positions previously occupied by the halogen substituent.¹⁰ Although there have been isolated instances¹⁰ where isomeric products have resulted, these have only been formed in minimal quantities (< 1%). The present work therefore represents the first example of the formation of significant quantities of isomeric biheteroaryls in this synthesis, the reaction direction being altered in response to ultrasound. The formation of the "crossed" product, 2,4'-bipyridine (¹³C NMR spectrum assigned by comparison⁷ with 2,2'-bipyridine and 4,4'-bipyridine and consideration of D_C / D_N effects⁸) would appear to be consistent with the operation of a radical mechanism at the metal surface.

TABLE
 Ultrasonic induced coupling of bromopyridines

<u>Starting material</u>	<u>Reaction product (% composition)</u> ^{a, b}
1	1 ^c (29), 4 (71)
2	2,2'-BiPy (65), 4,4'-BiPy (30), 2,4'-BiPy (5) ^d
3	3 ^c (75), Py (14), 3,3'-BiPy (12)

a : BiPy - bipyridine, Py - pyridine

b : determined by ¹³C NMR spectroscopy in CDCl₃ solution,⁷
 components confirmed by "spiking" with authentic material

c : unreacted starting material

d : 2,4'-bipyridine - ¹³C NMR spectrum (15 MHz, CDCl₃ solution,
 δ p.p.m.) : 154.82 (C-2), 150.72 (C-2'), 150.34 (C-6),
 146.60 (C-4'), 137.28 (C-4), 124.02 (C-5), 121.26 (C-3'),
 121.01 (C-3).

The reaction pathways with the bromopyridines are clearly very different from the simple bromobenzenes. Studies of further reactions, involving the use of activating substituents and the introduction of blocking groups, are in progress. In the quinoline series, early results indicate that the reaction with 3-bromoquinoline parallels that for 3-bromopyridine.

REFERENCES

1. T. J. Mason, *Ultrasonics*, **24**, 245 (1986)
2. J. Lindley and T. J. Mason, *Chem. Soc. Rev.*, **16**, 275 (1987)
3. B. H. Han and P. Boudjouk, *Tetrahedron Letters*, 2757 (1981)
4. T. D. Lash and D. Berry, *J. Chem. Educ.*, **62**, 85 (1985)
5. J. Lindley, J. P. Lorimer and T. J. Mason, *Ultrasonics*, **24**, 292 (1986)
6. Yu. Goldberg, R. Sturkovich and E. Lukevics, *Heterocycles*, **29**, 597 (1989)
7. A. G. Osborne, *Monatsh. Chem.*, **119**, 1385 (1988)
8. A. G. Osborne, R. Green, I. H. Sadler and D. Reed, *Magn. Reson. Chem.*, **27**, 4 (1989)
9. B. H. Han and P. Boudjouk, *Tetrahedron Letters*, 1643 (1982)
10. P. E. Fanta, *Chem. Rev.*, **64**, 613 (1964)

(Received in UK 18 May 1989)