Tetrahedron Letters, Vol.32, No.48, pp 7133-7134, 1991
Printed in Great Britain

0040-4039/91 $3.00 + .00
Pergamon Press plc

A Re-examination of the Sonochemical Coupling of Bromoaryls.

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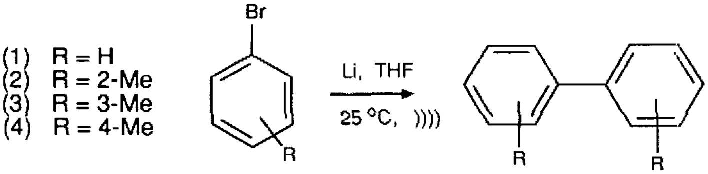
Abstract: The sonochemical coupling of bromotoluenes leads to a mixture of isomeric bitolyls suggesting a radical mechanism, confirmed using radical scavengers which inhibit the reaction.

In recent years, ultrasound has become a very useful tool in synthetic chemistry, sonication leading to increased yield and decreased reaction time in a range of reactions[1-3]. Amongst the most useful are heterogeneous reactions over a metal surface[4-6]. Han and Boudjouk[7] reported the coupling of bromobenzene and bromotoluenes in good yield and this has become a "classic" sonochemical reaction[8]. However, Osborne *et al.*[9] recently studied the reaction in bromopyridines and found that dehalogenation occurred readily and also that mixtures of isomeric bipyridyls were obtained implying that the mechanism was not that of a simple Wurtz type coupling. In order to obtain more information on the reaction mechanism, we have reexamined the reaction in bromobenzene (1) and 2-, 3- and 4-bromotoluene (2-4 respectively).

0.1 mol of (1) - (4) together with 0.76 g (0.11 mol) lithium wire was sonicated under nitrogen gas in 25 cm^3 of freshly distilled THF in a conical flask immersed in a Kerry 'Pulsatron' PUL325 ultrasound bath. The progress of the reaction was followed by GLC[10], suitable amounts of n-decane or n-nonane having been added to the reaction to serve as an internal standard. In contrast to previous workers[7-9], we found that the reaction, measured by the consumption of (1) - (4), was essentially complete in 2 hours.



The major products from the reactions and their yields[11] are shown in Table 1.

Table 1. Product Distributions from Sonochemical Coupling of (1)-(4)

Reactant	Product (% yield)[11]		
(1)	biphenyl (80)		
(2)	2,2'-bitolyl (16)	2,3'-bitolyl (17)	2,4'-bitolyl (5)
(3)	2,3'-bitolyl (6)	3,3'-bitolyl (61)	3,4'-bitolyl (19)
(4)	2,4'-bitolyl (2)	3,4'-bitolyl (25)	4,4'-bitolyl (52)

The remaining product from (1) was benzene while the major side reaction with (2) - (4) was dehalogenation to toluene. The reaction was complete in considerably shorter periods than reported previously with less than 5 % of the starting material remaining after 2 hours. Two other peaks were seen in the GC-MS of product (2) which are yet to be identified. The reactions were also carried out under reflux in the absence of ultrasound and the maximum overall yield of biphenyl isomers was ~ 9 %.

The presence of mixed bitolyls arising from (2) - (4) suggests that, as in the case of the bromopyridines, the reaction is not a simple Wurtz type coupling but suggests a mechanism involving one or more radical intermediates. This is in accordance with the suggestion of Luche[12] that ultrasound primarily influences single electron transfer reactions. In each case, it appears that a substantial amount of each of the three isomeric intermediates were formed.

To confirm the radical mechanism, we repeated the reaction using bromobenzene in the presence of radical inhibitors. Firstly, the reaction was performed as above under air and oxygen gas. The yield of biphenyl was reduced from 80% under nitrogen to 65% in air and 20% under oxygen. The rate constants[13] for the consumption of (1) were 0.0647 s^{-1}, 0.0069 s^{-1} and 0.0033 s^{-1} for the three gases respectively, clearly showing that oxygen has a large inhibiting effect as would be expected if radicals were involved.

Finally, the reactions were carried out in the presence of radical scavengers; 0.01 mol of 3,3,5,5-tetramethylpiperidine-N-oxide, TEMPO, or 2,2'-diphenyl-1-picryl hydrazyl, DPPH, being added to the reaction mixture. Both of these compounds were found to inhibit the coupling reaction with (1) being consumed rapidly but biphenyl not being produced until all the scavenger was consumed.

Hence, we have demonstrated the presence of radical intermediates in the sonochemical coupling of bromoaryls leading to mixed products and hence limiting the synthetic utility of the reaction.

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10. GLC conditions: Nitrogen carrier gas at 40 cm^3 min^{-1} over 3% OV101 on Chromosorb P stationary phase with FID detection. Column oven at 70 °C for 5 min then increased to 150 °C at 16 °C min^{-1}.
11. The yield of mixed bitolyls was isolated using a column of activated silica and 40:60 ethyl acetate:butyl acetate as solvent. The percentage of each bitolyl was calculated from gas chromatography-mass spectroscopy and confirmed by consideration of the methyl peak in the ^{13}C nmr spectrum. Identification of the isomers was by comparison with known samples and by their mass spectra.
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13. The consumption of (1) corresponded to first order kinetics.

(Received in UK 27 September 1991)