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Sonochemistry in $S_{RN}1$ Reactions in Liquid Ammonia at Room Temperature

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Abstract: *p*-Iodoanisole and 1-halonaphthalenes (Cl, Br, I) react with Ph_2P^- ions in liquid ammonia by the $S_{RN}1$ mechanism at room temperature stimulated by ultrasound

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 The mechanism of the reaction is a chain process, and the propagation steps are shown in Scheme I [1]

Scheme I depicts a nucleophilic substitution in which radicals and radical anions are intermediates However, this chain process requires an initiation step, such as 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] or by certain inorganic salts.[6]

SCHEME I

Initiation Step.	$RX + e^- \longrightarrow (RX)^{\cdot-}$	1
Propagation Steps	$(RX)^{\cdot-} \longrightarrow R^{\cdot} + X^-$	2
	$R^{\cdot} + Nu^- \longrightarrow (RNu)^{\cdot-}$	3
	$(RNu)^{\cdot-} + RX \longrightarrow RNu + (RX)^{\cdot-}$	4
	$RX + Nu^- \longrightarrow RNu + X^-$	5

We have become interested in other methods to initiate the $S_{RN}1$ reactions Thus we recently found that sodium amalgam [Na(Hg)] reacts with aryl halides in liquid ammonia[7], and also it is a suitable reagent to initiate $S_{RN}1$ reactions of aryl halides and diphenylphosphide (Ph_2P^-) ions[8] and carbanions[9] in liquid ammonia.

There is an increasing interest in the use of sonochemical methods in organic synthesis, clearly shown by the number of reports about this subject.[10a] There is only one report of the use of ultrasound to catalyze $S_{RN}1$ reactions on *aliphatic* halides.[10b]

Liquid ammonia is one of the best solvents for $S_{RN}1$ reactions but since the reactions are carried out at the boiling point of this solvent, and in order to study the influence of ultrasound on aromatic $S_{RN}1$ reactions, we designed a metallic reactor to perform the reactions in liquid ammonia at room temperature and pressure (*ca.* 25°C and 9 Kgr/cm^2). We report here the results of the reactions of haloarenes with Ph_2P^- ions and the influence of ultrasound.

The reaction of *p*-iodoanisole (*p*-IAn) with Ph_2P^- ions in liquid ammonia (-33°C) in 45 min. gives 30% yield of iodide ions, and the substitution product, isolated as the oxide (*p*-An)Ph_2PO, was obtained in 26% yield,[11] together with 5% of anisole (Table I, run 1). In this reaction there is a spontaneous ET, and the product obtained is through an $S_{RN}1$ reaction.[12]

The same results were obtained with the reaction at room temperature in liquid ammonia (Table I, run 2). However, with ultrasound at room temperature there is an important increase in the yield of substitution product. Thus in 45 min there was a 75% of (*p*-An)Ph_2PO after oxidation (Table I, run 5). This reaction was inhibited by *p*-dinitrobenzene (*p*-DNB) (in 45 min the yield of (*p*-An)Ph_2PO was 29%, Table I, run 7). There was no increase in the yield when the reaction time was increased (Table I, run 6)

All these results suggest that with ultrasound there is an increase in the rate of the $S_{RN}1$ reaction

$$p\text{-IAn} + Ph_2P^- \xrightarrow[S_{RN}1]{)))} (p\text{-An})Ph_2P + I^-$$

In the reaction of 1-iodonaphthalene (1-INaph) with Ph_2P^- ions at -33°C there was 20% of I^- ions, but the main product was naphthalene, and only 3% of the substitution product, isolated as the oxide (1-Naph)Ph_2PO was obtained[11] (Table I, run 8) This result suggests that Ph_2P^- ions react mainly with this substrate by a metal-halogen exchange[13] to give naphthalene anion, which is protonated by the ammonia to give naphthalene, and the substitution product is formed in small amounts by an $S_{RN}1$ mechanism.

When the reaction was carried out at room temperature, there was 100% of dehalogenation reaction, with 50% yield of naphthalene and 45% yield of the substitution product. The increase of *ca.* 60°C in the temperature increases both reactions, but when the same reaction was carried out with ultrasound, the yield of the substitution product increases up to 70% (Table I, run 10). The fact that only the ipso substitution product is formed, ruled out an aryne mechanism for this reaction. Indeed, ultrasound catalyzes the ET reaction much faster than the other competing mechanism

In the reaction of 1-BrNaph as substrate with Ph_2P^- ions at room temperature there was only 30% of Br^- ions in 60 min , giving *ca.* 10% of naphthalene and 10% of the substitution product. However, there was a 94% yield of substitution product when the reaction was carried out in the same experimental conditions with ultrasound, with only 6% yield of naphthalene, which suggests that the ET reaction was stimulated much more quickly with ultrasound (Table I, run 11-12). When this reaction was carried out in the presence of *p*-DNB, there was an important decrease of the yield of the substitution product, with an increase of naphthalene (Table I, run 13), which indicates that the substitution is catalyzed by ultrasound.

There is only a small reaction of 1-chloronaphthalene with Ph_2P^- at room temperature in 60 min (7% of the substitution product), but the yield increases to 30% with ultrasound (Table I, runs 14-15).

All these results clearly indicate that it is possible to perform easily the reactions of liquid ammonia at room temperature and that the rate of the ET reactions is increased by ultrasound Studies in other ET reactions are in progress

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TABLE I: Reactions of Haloarenes with Ph_2P^- Ions in Liquid Ammonia Catalyzed by Ultrasound.[a]

Run	ArI	Ph_2P^- mmol	Time (min)	Conditions	I^-	$ArP(O)Ph_2$ (%)	ArH (%)
1	*p*-IAn	1.5	45	-33°C	30	26	5
2	*p*-IAn	1.5	60	rt, ⌒	30	20	10
3	*p*-IAn	1.5	15	rt,)))	17	[b]	[b]
4	*p*-IAn	1.5	30	rt,)))	50	22	7
5	*p*-IAn	1.5	45	rt,)))	87	75	7
6	*p*-IAn	1.5	60	rt,)))	90	70	13
7[c]	*p*-IAn	1.5	45	rt,)))	40	29	3
8	1-INaph	3.0	15	-33°C	20	3	16
9	1-INaph	3.0	15	rt, ⌒	100	45	50
10	1-INaph	3.0	15	rt,)))	100	70	30
11	1-BrNaph	6.0	60	rt, ⌒	30	10	10
12	1-BrNaph	6.0	60	rt,)))	100	94	6
13[c]	1-BrNaph	6.0	60	rt,)))	[b]	20	20
14	1-ClNaph	6.0	60	rt, ⌒	10	7	2
15	1-ClNaph	6.0	60	rt,)))	60	30	4

[a] Reactions carried out in *ca.* 150 mL of liquid ammonia with 1.0 mmol of substrate. *p*-IAn = *p*-iodoanisole, 1-XNaph = 1-halonaphthalenes (Cl, Br, I). rt = room temperature [b] Not quantified [c] *p*-DNB (20 mol%) was added.

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