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NUCLEOPHILIC SUBSTITUTION AT NITROGEN-CENTERED RADICALS: REACTIONS OF DIPHENYLPHOSPHIDE IONS WITH *N,N*-DIBUTYL-*p*-TOLUENESULFONAMIDE BY THE $S_{RN}1$ MECHANISM

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The photostimulated reaction of *N,N*-dibutyl-*p*-toluenesulfonamide with diphenylphosphide ions in liquid ammonia leads to the corresponding phosphinic amides after oxidation Inhibition experiments with *p*-dinitrobenzene and 2,2,6,6-tetramethyl-1-piperidinyloxy free radical (TEMPO) and the fact that the reaction is retarded in the dark suggest that it proceeds by the $S_{RN}1$ mechanism.

1. INTRODUCTION

The synthetic applications of radical reactions have been extensively studied in recent years, especially those concerning carbon-centered radicals.[1,2] Less attention has been paid to the mechanism and synthetic aspects of the reactions of heterocentered radicals.[2–10]

With regard to nitrogen centered radicals, some progress has been made in recent years, including new sources of aminium cation[5] and aminyl,[6–8] amidyl[9] and iminyl radicals[10] and the determination of the regiochemistry and rate constants for nitrogen radical reactions.

Radical nucleophilic substitution by the $S_{RN}1$ mechanism at a carbon atom (aliphatic or non-activated aromatic) is a well known process[11] and the synthetic potential of this mechanism has been widely explored.[12] However, no studies involving heterocentered radicals have so far been reported.

The photodetosylation of sulfonamides initiated by electron transfer (ET) from excited *β*-naphthoxide anions has been described.[8] The radical anion of the sulfonamide fragments and leads to the corresponding aminyl radical, which is reduced to the amine in the presence of sodium borohydride.

Therefore, sulfonamides appear to be suitable substrates for an $S_{RN}1$ mechanism as a novel source of aminyl radicals, and we report here the photostimulated reactions of sulfonamides with diphenylphosphide ions (**2**) in liquid ammonia.

EXPERIMENTAL AND RESULTS

N,N-Dibutyl-*p*-toluenesulfonamide (**1**), synthesized from *N,N*-dibutylamine and *p*-toluenesulfonyl chloride,[13] reacts with **2** within 7 min under photostimulation to give the substitution product *N,N*-dibutyl-*P,P*-diphenylphosphinous amide (**3**). This compound was isolated in moderate yields (49%) as the oxide (**4**) by column chromatography with diethyl ether as eluent. ^{1}H NMR (CDCl$_3$), δ 0·78 (6H, t, $J = 7{\cdot}2$ Hz), 1·16 (4H, m), 1·51 (4H, m), 2·93 (4H, m), 7·46 (4H, m), 7·84 (6H, m); ^{13}C NMR (CDCl$_3$), δ 13·67 (CH$_3$), 20·04 (CH$_2$), 30·70 (CH$_2$, $J_{C-P} = 3{\cdot}62$ Hz), 45·35 (CH$_2$, $J_{C-P} = 2{\cdot}89$ Hz), 128·304 ($^3J_{C-P} = 12{\cdot}5$ Hz), 131·479 ($^4J_{C-P} = 2{\cdot}65$ Hz), 132·296 ($^2J_{C-P} = 9{\cdot}23$ Hz), 132·339 ($^1J_{C-P} = 128{\cdot}65$ Hz); IR (KBr) (cm^{-1}1), 2959, 2933, 2874, 1471, 1438, 1378, 1201, 1122, 726, 707 Lit.[14] (Table 1, Expt 1) [equation (1)].

$$\underset{\mathbf{1}}{(\mathrm{Bu})_2\mathrm{NTs}} + \underset{\mathbf{2}}{\mathrm{Ph_2P^-}} \xrightarrow{h\nu}$$

$$\underset{\mathbf{3}}{(\mathrm{Bu})_2\mathrm{NPPh_2}} \xrightarrow{[\mathrm{O}]} \underset{\mathbf{4}}{(\mathrm{Bu})_2\mathrm{NP(O)Ph_2}} \qquad (1)$$

$$\mathrm{Bu} = n\text{-}\mathrm{C_4H_9}; \qquad \mathrm{Ts} = p\text{-}\mathrm{CH_3C_6H_4SO_2}$$

This reaction is sluggish in the dark (6% of **4**) and is inhibited in the presence of *p*-dinitrobenzene. The photostimulated reactions are inhibited by the presence of *p*-dinitrobenzene or 2,2,6,6-tetramethyl-1-piperidinyloxy free radical (TEMPO) (11% and 33% yield of **4**, respectively), well known inhibitors of $S_{RN}1$

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reactions[11] (Table 1, Expts 2–4). These results suggest that the reaction proceeds by the $S_{RN}1$ mechanism, outlined in Scheme 1, in which the initiation step is the photostimulated ET from **2** to the substrate **1** to yield the corresponding radical anion $\mathbf{1}^{-\bullet}$ [equation (2)]. The radical anion thus formed fragments in the next step to give the aminyl radical **5** and the *p*-toluenesulfinate anion [equation (3)]. Fragmentation of the C-S bond was not observed, since the are is no evidence for the formation of diphenyl-*p*-tolylphosphine. The aminyl radical **5** can give the radical anion of the substitution product $\mathbf{3}^{-\bullet}$ by coupling with **2** [equation (4)], and the reduced product *N*,*N*-dibutylamine (**6**) by hydrogen atom abstraction from the diethyl ether used to dissolve the substrate before addition (similar hydrogen abstraction by nitrogen radicals from tetrahydrofuran has been reported previously)[15] [equation (6)] or the disproportionation products **6** and *N*-butylidenebutylamine (**7**) [equation (7)]. Finally, the radical anion of the substitution product transfers the odd electron to the substrate to give **3** and the radical anion of the substrate, which continues the chain reaction [equation (5)].

$$\underset{\mathbf{1}}{(\mathrm{Bu})_2\mathrm{NTs}} + \underset{\mathbf{2}}{\mathrm{Ph_2P^-}} \xrightarrow[\mathrm{ET}]{h\nu} \underset{\mathbf{1}^{-\bullet}}{[(\mathrm{Bu})_2\mathrm{NTs}]^{-\bullet}} + \mathrm{Ph_2P^\bullet} \tag{2}$$

$$\underset{\mathbf{1}^{-\bullet}}{[(\mathrm{Bu})_2\mathrm{NTs}]^{-\bullet}} \longrightarrow \underset{\mathbf{5}}{(\mathrm{Bu})_2\mathrm{N}^\bullet} + p\text{-}\mathrm{CH_3C_6H_4SO_2^-} \tag{3}$$

$$\underset{\mathbf{5}}{(\mathrm{Bu})_2\mathrm{N}^\bullet} + \underset{\mathbf{2}}{\mathrm{Ph_2P^-}} \longrightarrow \underset{\mathbf{3}^{-\bullet}}{[(\mathrm{Bu})_2\mathrm{NPPh_2}]^{-\bullet}} \tag{4}$$

$$\underset{\mathbf{3}^{-\bullet}}{[(\mathrm{Bu})_2\mathrm{NPPh_2}]^{-\bullet}} + \underset{\mathbf{1}}{(\mathrm{Bu})_2\mathrm{NTs}} \longrightarrow \underset{\mathbf{3}}{(\mathrm{Bu})_2\mathrm{NPPh_2}} + \underset{\mathbf{1}^{-\bullet}}{[(\mathrm{Bu})_2\mathrm{NTs}]^{-\bullet}} \tag{5}$$

$$\underset{\mathbf{5}}{(\mathrm{Bu})_2\mathrm{N}^\bullet} \xrightarrow{\mathrm{SH}} \underset{\mathbf{6}}{(\mathrm{Bu})_2\mathrm{NH}} \tag{6}$$

$$2\,\underset{\mathbf{5}}{(\mathrm{Bu})_2\mathrm{N}^\bullet} \longrightarrow \underset{\mathbf{6}}{(\mathrm{Bu})_2\mathrm{NH}} + \underset{\mathbf{7}}{\mathrm{BuN{=}CHCH_2CH_2CH_3}} \tag{7}$$

(Scheme 1)

The fact that the mass balance for the reaction is between 63 and 85% can be ascribed to the formation of **6** and the imine **7** from disproportionation, and/or only to **6** from reduction, which could not be trapped when the reaction residue was extracted with diethyl ether and water, after evaporation of the liquid ammonia. When the extraction was performed only with diethyl ether, the amine **6** was recovered and the mass balance was 100% (Table 1, Expt 7), showing that reaction (7) does not take place.

Table 1. Photostimulated reaction of *N*,*N*-dibutyl-*p*-toluenesulfonamide (**1**) with $\mathrm{Ph_2P^-}$ ions (**2**) in liquid ammonia[a]

			Products, yield (%)[b]	
Expt	**2** (mmol)	Unreacted **1**, yield (%)[b]	$\mathrm{Bu_2NH}$	$\mathrm{Bu_2NP(O)Ph_2}$
1	1·01	4	4	49
2[c]	1·01	79	—[d]	6
3[e]	1·00	64	—[d]	11
4[f]	1·02	—[d]	—[d]	33
5	1·51	3	18	60
6	2·00	8	—[d]	73
7[g]	2·51	<2	20	79
8[c,e]	2·51	95	—	—

[a] Reactions carried out in *ca* 300 ml of liquid ammonia with 1·00 mmol of **1** (dissolved in *ca* 2 ml of diethyl ether) during 7 min of irradiation with four 250 W lamps.
[b] Determined by GC using the internal standard method.
[c] Dark reaction.
[d] Detected but not quantified (<5%).
[e] 20 mol% of *p*-dinitrobenzene was added.
[f] 24 mol% of TEMPO was added.
[g] The reaction mixture was extracted with diethyl ether without adding water, and quantified by GC.

The yield of the substitution product **4** can be increased with increase in the concentration of nucleophile **2**, reaching 79% with 2·5 mmol of **2** (Table 1, Expts 5–7). There is no reaction in the dark and in the presence of *p*-dinitrobenzene (Table 1, Expt 8). Hence sulfonamides are appropriate substrates for an $S_{RN}1$ mechanism.

This first example of radical nucleophilic substitution by diphenylphosphide ion (**2**), at a nitrogen atom enlarges the scope of this mechanism to aminyl radicals. Further studies involving other sulfonamides (aliphatic and aromatic) and carbanions as nucleophiles are in progress.

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