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Anions from dihydro substituted ethyl benzoates and quinoline. New hydrogen donors for tin-free radical chemistry

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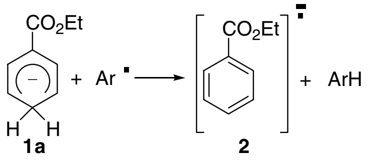
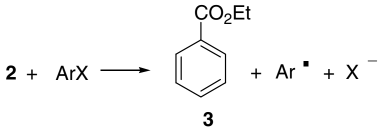
Abstract—The anions of substituted dihydro ethyl benzoates and quinoline are very good hydrogen donors to radicals in liquid ammonia and DMSO. With 4-substituted dihydro ethyl benzoates the rate of hydrogen transfer decreases and excellent yields of products are obtained by 6-*exo* ring closure reaction followed by reduction.

Trialkyltin hydrides, mainly tributyltin hydride, play a central role in radical chemistry.[1] However, tin derivatives are toxic and difficult to eliminate from reactions mixtures. Nowadays there is an increasing interest in the development of new eco-friendly and non-toxic tin hydride substitutes.[2] Among the alternatives available to perform tin-free radical reactions, most of the attention has been focused on silicon hydrides, especially tris-trimethylsilylsilane,[3] and has been recently shown that this reagent behaves as a good hydrogen donor even in water.[4] Other promising reagents, as silylated cyclohexadienes[5] and hypophosphorous acid derivatives,[6] have been studied and used in a wide variety of radical transformations.

With the notable exception of alcoxides,[7] photoinduced ET from suitable anions has been only scarcely investigated as a source of new reactive intermediates for tin-free radical reductions. We have recently demonstrated that the anion of the dihydro ethyl benzoate **1a** is an extremely powerful hydrogen atom donor that can be used for 5-*exo* reductive radical cyclization and hydrodehalogenation reactions in liquid ammonia.[8] This is a chain reaction, and its mechanism is depicted in Eqs. 1 and 2.



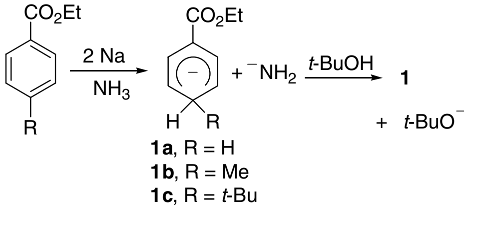
(1)



(2)

The hydrogen transfer step is very fast and is, probably, near diffusion limit rate. The driving force for this reaction (Eq. 1) is the rearomatization of **1a** to give radical anion **2**. This suggests that anion **1a** can be used only in radical reactions that involve very fast rearrangement steps. In this work we wish to present our attempts to diminish the reactivity of this hydrogen donor in order to get other useful reactive intermediates that can be used in the slower 6-*exo* cyclization reaction.

Ethyl benzoate anions **1a**–**c** can be easily prepared in liquid ammonia by reaction of the corresponding ethyl esters with Na metal. The amide ions generated in the formation of **1a**–**c** were neutralized with *t*-BuOH forming *t*-BuO$^-$ ions (Eq. 3):



(3)

Keywords: Reduction; Hydrogen donors; Hydrodehalogenation; 6-*exo* Ring closure.

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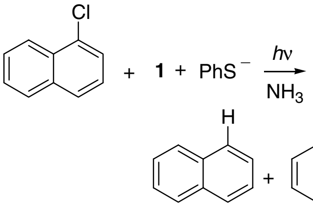
The rate constant for the coupling reaction of 1-naphthyl radical with PhS$^-$ ions in liquid ammonia has been determined electrochemically (2.0×10^{10} M^{-1} s^{-1}).[9] If the amide ions generated in the formation of **1** are neutralized with PhSH, an equimolecular mixture of **1** and PhS$^-$ ions is obtained. When a solution of **1a**, PhS$^-$ ions and 1-chloronaphthalene was irradiated for 15 min, a mixture of naphthalene and the substitution product 1-phenyl-sulfanylnaphthalene[10] (**4**) was obtained (Expt. 1, Table 1). This result indicates that **1a** is ca. 5-fold more reactive than PhS$^-$ ions towards 1-naphthyl radical (Eq. 4):



(4)

With the aim of decreasing the hydrogen donor ability of anion **1a**, anions esters **1b**,**c** were studied. In the competition experiment between **1b** and PhS$^-$ ions towards 1-chloronaphthalene, performed under the same conditions as before, we found that **1b** is ca. 2.2-fold more reactive than PhS$^-$ ions and hence approximately half reactive than **1a** (Expt. 2, Table 1). Probably, the diminished reactivity of **1b** is the statistical result of replacing one of the two active hydrogens of **1a**.

When the 4-*tert*-butyl substituted anion **1c** was employed in the competition experiment, the reduction product naphthalene and substitution product **4** were obtained and then **1c** is ca. 1.4-fold more reactive than PhS$^-$ ions and quarter reactive than **1a** (Expt. 3, Table 1). The steric demand of the bulky *tert*-butyl group in the *para* position accounts for the lower reactivity of anion **1c** compared to **1b**.

When Na metal is added to quinoline in liquid ammonia and the amide ions neutralized with *t*-BuOH, a deep brown solution of dihydroquinoline anion (**5**) and *t*-BuO$^-$ ions is obtained. In the competition experiment of 1-chloronaphthalene with **5** and PhS$^-$ ions (Expt. 4, Table 1) we obtained naphthalene as the main product together with **4**. From this result it can be inferred that this anion is ca. 2.8-fold more reactive than PhS$^-$ ions and that its reactivity in the hydrogen transfer step is between that of anion **1a** and **1b**:

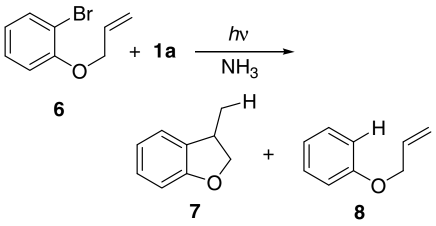
Table 1. Competition experiments of anions **1** and **5** with PhS$^-$ ions towards 1-chloronaphthalene in liquid ammonia[a]

Expt.[a]	Competing anion	Products (% yield)[b]	k_H/k_{Nu}
1	**1a**	Naphthalene (76), **4** (15)	5.1
2	**1b**	Naphthalene (51), **4** (23)	2.2
3	**1c**	Naphthalene (33), **4** (24)	1.4
4[c]	**5**	Naphthalene (72), **4** (26)	2.8

[a] All reactions were performed twice. The concentration of the reducing anion and PhS$^-$ ions were 0.010 M and of 1-chloronaphthalene 0.005 M. All the reactions were irradiated for 15 min using two water-cooled medium pressure Hg lamps.

[b] Determined by CG analysis by the internal standard method with authentic samples as references.

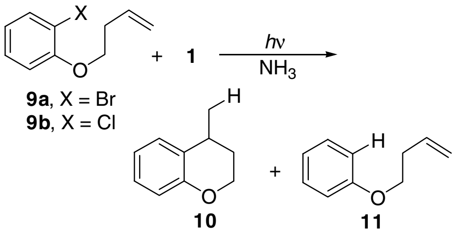
[c] The irradiation time was 30 min.



(5)

We previously reported[8] that anion **1a** reacts with 1-allyloxy-2-bromo-benzene (**6**) to give 3-methyl-dihydro benzofurane (**7**) in 97% and traces of allyloxybenzene (**8**) (Eq. 5).

Anion **1a** reacts with 1-bromo-2-but-3-enyloxybenzene[12] (**9a**)[13] to afford 4-methyl-chroman[14] **10** (53%) together with 41% of open chain product[14] **11** (Eq. 6, Expt. 1, Table 2):

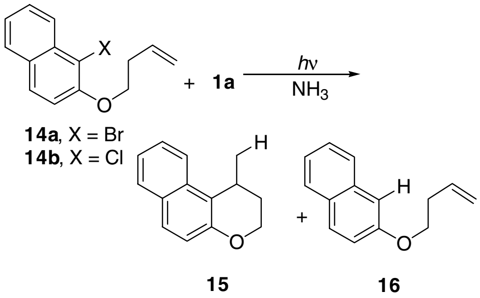


(6)

Probably, the slower 6-*exo* cyclization cannot compete so efficiently with the hydrogen transfer step as the faster 5-*exo* cyclization process,[15] and then a higher yield of the open chain product is obtained.

Anion **1c** reacts with radical probe **9a** to afford cyclized compound **10** in excellent yield and aryl reduced product **11** (Expt. 3, Table 2). As noted before, the rate of hydrogen transfer from **1c** is lower than that from **1a** and hence the ring closure of intermediate aryl radical **12** to afford the rearranged radical **12-r** can compete efficiently with the direct hydrogen transfer to yield **11** (Scheme 1). Ultimately radical anion **13** propagates the chain reaction.

In the same fashion, anion **1a** reacts with substrate **14a** (Eq. 7) to give a mixture of cyclized (**15**) and open chain (**16**) products (89% and 11%, respectively, Expt. 2 in Table 2):



(7)

Table 2. Photostimulated reductive radical cyclization and hydrodehalogenation reactions of aryl halides with different reagents and under different reaction conditions[a,11]

Expt.	Substrate	Reagent	X^- (%)[b]	Product (% yield)[c]
1	**9a**	**1a**	100	**10** (53), **11** (41)
2	**14a**	**1a**	100	**15** (89), **16** (11)
3	**9a**	**1c**	98	**10** (84), **11** (9)
4[d]	**9b**	**1c**	54	**10** (41), **11** (3)
5	**14a**	**1c**	85	**15** (71), **16** (1)
6[d]	**14b**	**1c**	99	**15** (89), **16** (9)
7	**9a**	**5**	85	**10** (55), **11** (15)
8[e]	1-Chloronaphthalene	**5**	77	Naphthalene (65)
9[e]	9-Bromophenanthrene	**5**	86	Phenanthrene (88)
10[e,f]	1-Chloronaphthalene	**5**	79	Naphthalene (68)
11[e,g]	1-Chloronaphthalene	**5**	78	Naphthalene (61)
12[e,g,h]	1-Chloronaphthalene	**5**	77	Naphthalene (65)
13[e]	1-Chloronaphthalene	[i]	8	Naphthalene (0)

[a] All reactions were performed in liquid ammonia and irradiated for 2 h using two water-cooled medium pressure Hg lamps. The concentration of the substrates were 0.0033 M and of the reducing anion 0.0067 M.

[b] Determined potentiometrically.

[c] Product yields were determined by CG analysis using authentic samples as references.

[d] The irradiation time was 3 h and 0.0067 of acetone enolate anion was used as entrainment reagent.

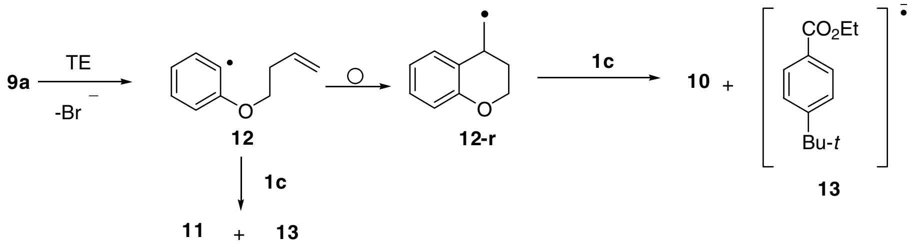
[e] The solvent was DMSO and the concentration of the substrates was 0.05 M and of **5** 0.10 M. The irradiation time was 1 h.

[f] With 15% of DTBN.

[g] Dark condition.

[h] The reaction time was 15 min.

[i] Reaction with quinoline and *t*-BuOK in 0.10 M.



Scheme 1.

The higher selectivity observed for the reaction of **14a** agrees with the expected higher reactivity in the cyclization step of the 1-naphthyl radical compared with phenyl radical.[16]

It is known that acetone enolate anion does not react with primary alkyl radical but initiates effectively $S_{RN}1$ reactions (*Entrainment Reagent*).[17,18] On the other hand, it has been demonstrated that anion **1a** does not initiate efficiently the reduction of 1-allyloxy-2-chlorobenzene in liquid ammonia.[8] The amide ions obtained in the formation of anion **1c** were neutralized with acetone, and mixture of **1c** and $^-CH_2COCH_3$ anions were tested in the reductive cyclization reaction of chloride substrate **9b**. The reduction process took place with good yield and high selectivity (Expt. 4, Table 2). Likewise, very good results were obtained in the reactions of naphthyl derivatives **14a**,**b** (Expts. 5 and 6, Table 2).

Dihydroquinoline anion **5** reacts with substrate **9a** in liquid ammonia to yield cyclized compounds **10** (55%) and **11** (15%, Expt. 7 in Table 2). The distribution of cyclized to open chain products agrees with hydrogen donor ability determined in the competition experiment. Although liquid ammonia is a useful solvent for a wide variety of $S_{RN}1$ and related reactions,[18] DMSO is easier to handle than liquid ammonia.

With the aim of exploring the scope of the reduction reactions, dihydroquinoline was prepared by Birch reduction of quinoline[19] and tested in photostimulated hydrodehalogenation reactions of aryl halides in DMSO.

Upon treatment of dihydroquinoline with *t*-BuOK in DMSO, a dark solution of anion **5** is obtained. Anion **5** reacts with 1-chloronaphthalene and with 9-bromophenanthrene under photostimulation (1 h) to afford hydrodehalogenation products in high yield (Expts. 8 and 9, Table 2).

The photostimulated reaction of 1-chloronaphthalene with **5** in DMSO (1 h) is only slightly inhibited in the presence of 15% DTBN, which is a good radical trap. A similar result was obtained when the reaction was performed in the dark for 1 h or 15 min (entries 10–12 in Table 2). On the other hand, only traces of naphthalene were obtained in the photoinduced reaction of

1-chloronaphthalene with quinoline and *t*-BuOK. These results suggest a spontaneous ET from **5** to the aryl halide to initiate the reaction, and a very effective propagation cycle, probably due to good electron acceptor ability of the substrate and good electron donor ability of quinoline radical anion. The basicity of anion **5** precluded its use in the cyclization reactions in DMSO. However, small amounts of cyclized compounds were obtained in these reactions.[20]

In summary, in this work we describe new hydrogen donors derived from 4-substituted ethyl benzoate ester that can be used for reductive 6-*exo* cyclization in liquid ammonia. The ester with a *tert*-butyl group in the *para* position is a quarter reactive than the unsubstituted compound, which allows its use in slower 6-*exo* cyclization reactions with excellent yields. On the other hand, the anion of dihydroquinoline **5** behaves as powerful hydrogen donor that gives good results in the cyclization reaction in liquid ammonia, and also can be used for hydrodehalogenation reactions of aryl halides in DMSO.

Acknowledgements

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Supplementary data

Supplementary data associated with this article can be found, in the online version, at doi:10.1016/j.tetlet.2006.02.139.

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