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Photoreduction of Benzophenones by Amines in Room-Temperature Ionic Liquids

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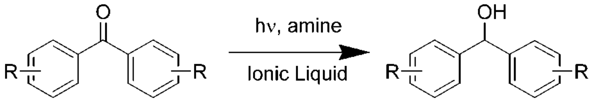
ABSTRACT



The amine-mediated photoreduction of benzophenones in room temperature ionic liquids was investigated. Unlike the analogous reaction in organic solvents, the photoreduction produces mainly the corresponding benzhydrol in most cases. Because the reaction consumes only 1 equiv of amine and the solvent can be easily recycled, the photoreduction allows a very clean method for the conversion of benzophenones to benzhydrols.

Room-temperature ionic liquids (RTILs) are salts that freeze below 25 °C.[1] Although such salts have been known for almost a century, they have recently gained popularity as “green” alternatives to conventional solvents. Because RTILs are generally immiscible with water and many organic solvents, products and byproducts can be removed via extraction, which allows for immediate reuse of the solvent. This property, coupled with extremely low vapor pressure, makes a RTIL much less environmentally intrusive than conventional solvents. A variety of reactions are compatible with ionic liquids, including Diels−Alder cycloadditions,[2] alkene halogenations,[3] and Stille couplings.[4] Investigations of reactions in RTILs continue to be an area of increasing activity.

In addition to the “green” properties of RTILs, the ionic nature of the solvent can affect the course of reactions. RTILs are highly conductive, although there is some controversy concerning the polarity of these solvents.[1,5] Most reactions carried out in RTILs have solvent effects consistent with a polar nature for these solvents. One investigation revealed that the Heck reaction could be selectively directed through an ionic pathway at the expense of a neutral pathway. In toluene, this reaction displayed an approximately 1:1 preference for the two pathways, whereas in the RTIL, the selectivity was >99 to 1.[6]

Pagni has described photoinduced electron transfer (PET) in RTILs.[7] This report, among others, found that the conducting nature of the solvent provided an excellent medium for the generation of radical ions.[7,8]

These findings suggest that photoreduction in RTILs may provide interesting mechanistic phenomena; this prompted our consideration of amine-mediated ketone photoreduction, which is usually initiated by a PET reaction.[9] A simplified mechanism for this reaction is shown in Scheme 1. Charge transfer following excitation gives a solvent separated radical−ion pair, which diffuses to a contact radical−ion pair. Proton transfer produces ketyl radical **2** and α-amino radical **3**, which reduces a second ketone. Coupling of the resulting ketyl radicals, through a neutral pathway, gives pinacol as the usual product.

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Scheme 1. Mechanism of Amine-Mediated Photoreduction

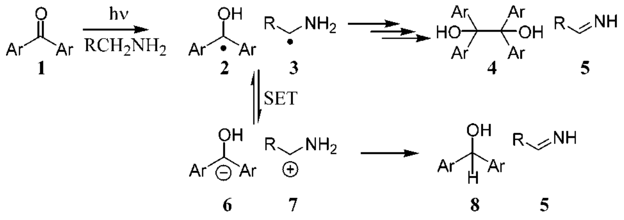


Table 1. Benzhydrol (BH):Benzpinacol (BP) Ratios in the Photoreduction of Various Benzophenones in RTILs

entry	cmpd	solvent	amine	BH[a]	BP[a]
1	**9**	benzene[b]	*s*BA	0	100
2	**9**	*s*BA(TFA)[d]	*s*BA	0[c]	100
3	**9**	*i*PA(NO$_3$)[e]	*i*PA	0[c]	100
4	**9**	EMI(OTf)	*s*BA	100	0[c]
5	**9**	BMI(BF$_4$)	*s*BA	100(90)	0[c]
6	**9**	BMI(BF$_4$)	CHA[f]	100	0[c]
7	**9**	BMI(BF$_4$)[g]	*s*BA	100	0[c]
8	**9**	BMI(BF$_4$)[h]	*s*BA	100	0[c]
9	**10**	BMI(BF$_4$)	*s*BA	100(97)	0[c]
10	**10**	BMI(BF$_4$)	TEA[i]	100	0[c]
11	**11**	BMI(BF$_4$)	*s*BA	45(22)	55
12	**11**	EMI(OTf)	*s*BA	30	70
13	**12**	BMI(BF$_4$)	*s*BA	80	20
14	**13**	BMI(BF$_4$)	*s*BA	100	0[c]
15	**14**	BMI(BF$_4$)	*s*BA	100	0[c]

[a] Ratios were determined by ^{1}H NMR and do not represent yields. Isolated yields are noted in parentheses. [b] From ref 11. [c] Not detectable in the ^{1}H NMR spectrum of the crude product. [d] *sec*-Butylammonium trifluoroacetate. [e] *iso*-Propylammonium nitrate. [f] Cyclohexylamine. [g] Solvent recycled once. [h] Solvent recycled twice. [i] Triethylamine.

However, photoreduction of 4-benzoylbenzoic acid in aqueous amine gives the benzhydrol, suggesting an ionic pathway in the photoreduction.[10] Later studies showed that this is general; when benzophenones bearing electron-withdrawing groups are photoreduced, products (**8** and **5**) consistent with the formation of ions (**6** and **7**) are produced as the primary products.[11]

One possible explanation for the formation of **8** is an equilibrium, between radical pair **2/3** and ion pair **6/7**, that is shifted toward the ions in polar solvents (radical pair/ion pair equilibria have been shown to be both solvent and substituent dependent).[12] Thus, the formation of benzhydrols could be a result of a shift in the radical/ion equilibrium toward the ion pair. This shift is manifested by a single-electron transfer from easily oxidized **3**[13] to radical **2**, producing a benzyl anion, **6**, which is stabilized by either resonance or solvation.

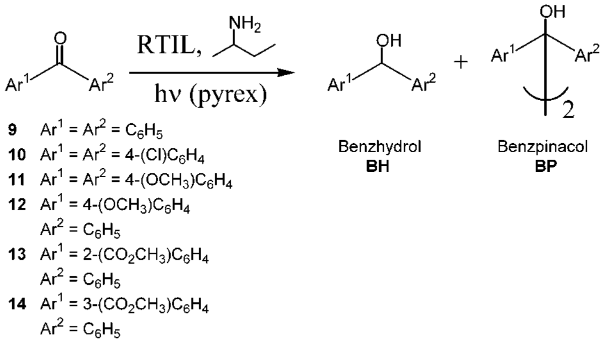
We chose to explore whether a conductive medium, such as an RTIL, could shift the equilibrium from the radical pair to an ion pair in the photoreduction of aryl ketones bearing no electron-withdrawing groups. We report our preliminary findings below.

We initially investigated the use of primary ammonium liquid salts as the medium and the corresponding free amine as the electron donor for the photoreduction. We prepared two new ionic liquids, *sec*-butylammonium trifluoroacetate and *iso*-propylammonium nitrate.[14] Photoreduction of benzophenone in these solvents with excess free amine, however, produced only benzpinacol (Table 1, entries 2 and 3). We were encouraged that the photoreduction proceeded smoothly and without apparent decomposition of the solvent.

We shifted focus to the common RTILs, 1-butyl-3-methylimidazolium tetrafluoroborate (BMI(BF$_4$)) and 1-ethyl-3-methylimidazolium triflate (EMI(OTf)).[1,14] The preparation and manipulation of these RTILs were straightforward.[14] We found that both solvents are stable to irradiation through Pyrex for over 24 h. In addition, no reaction occurred when the RTIL was irradiated in the presence of either amine or ketone alone. Photoreduction of benzophenone in BMI(BF$_4$) and EMI(OTf) gave benzhydrol, cleanly, as the only detectable product (entries 4 and 5). Benzhydrol was the only product detectable by NMR of the crude reaction mixture and was isolated in excellent yield. We were able to measure the benzhydrol:benzpinacol ratios in the following reactions by examination of the distinctive ^{1}H NMR peaks.[15] We also determined that disproportionation of the corresponding benzpinacols did not occur to an appreciable extent under the reaction conditions and did not account for the production of the benzhydrols.

As expected, benzophenones bearing electron-withdrawing groups ortho or para to the ketone photoreduced to give the corresponding benzhydrol (entries 9, 10, and 14).[11] In contrast to photoreduction in acetonitrile, an electron-withdrawing group meta to the ketone produced the benzhydrol exclusively when photoreduced with amines (entry 15) in BMI(BF$_4$).[16] We also found that a tertiary amine was capable of photoreducing a benzophenone to a benzhydrol (entry 10).

Scheme 2. Photoreduction in RTILs



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(14) For experimental procedures, please see Supporting Information.

(15) Samples of the corresponding benzyhydrols and benzpinacols were obtained by reduction of the ketone using NaBH$_4$ and photoreduction using 2-propanol, respectively. See Supporting Information.

In this case, 1 equiv of triethylamine hydrochloride was included as a proton source. Photoreduction of a benzophenone bearing a single electron-donating group para to the ketone (4-methoxybenzophenone) led to the production of some pinacol (entry 13). Introduction of a second methoxy group shifted the reaction so that the pinacol was the major product (entries 11 and 12).

In keeping with the "green" chemistry goal of using RTILs in synthesis, photoreductions of benzophenone were carried out in the same solvent three times (entries 7 and 8). In each case, the solvent appeared to be unchanged upon visual inspection after the reaction and product isolation. Furthermore, the ^{1}H NMR spectrum for the solvent was unchanged after each reaction. The reactions were complete in the same amount of time, and yields and product ratios were unchanged.

Because the photoreduction of dimethoxybenzophenone produced a mixture of benzhydrol and benzpinacol, this substrate provided a handle for the assessment of the effect of changing reaction conditions on product selectivity. One obvious varible that has an effect on the product ratio was the RTIL itself. In BMI(BF_4), dimethoxybenzophenone photoreduced to give a 45:55 mixture of benzhydrol: benzpinacol, while the ratio dropped to 30:70 in EMI(OTf). Therefore, we studied the photoreduction of dimethoxybenzophenone in eight RTILs (Table 2).

Table 2. Benzhydrol (BH):Benzpinacol (BP) Ratios in the Photoreduction of **11** in Various RTILs

entry	RTIL	BH[a]	BP[a]
1	BMI (OTf)	30	70
2	EMI (OTf)	30	70
3	EMI (BF_4)	35	65
4	BMI (OTs)	40	60
5	BMI (BF_4)	45	55
6	EMI (NO_3)	50	50
7	BMI (PF_6)	55	45
8	BMI (NO_3)	75	25

[a] Ratios were determined by ^{1}H NMR and do not represent yields.

While we have so far been unable to find any correlation between product ratios with known physical properties of the solvent, there was obviously a significant effect in changing the nature of the ions. In general, for a given anion, the BMI cation provided the higher yield of benzhydrol (e.g., Table 2, entries 3 and 5). Table 2 also showed that the yield of benzhydrol versus anion increased in the order OTf < BF_4 < OTs < PF_6 < NO_3.

The reactions described above were carried out using a ketone concentration of 25 mM and an amine concentration of 1 M. We found that the product distribution was not significantly affected by the concentration of ketone, ratios remaining the same over the concentration range 5−100 mM. The effect of amine concentration on the reaction was also small. However, we found that using at least 40 equiv of amine gave optimal results with a slight increase in benzpinacol production at lower amine concentrations.

We speculated that the high viscosity of the RTILs might favor the formation of benzhydrol by inhibiting diffusion of the ketyl radicals. To investigate this possibility, we photoreduced benzophenone in BMI (BF_4) at 0, 25, and 50 °C. No benzpinacol was produced in any of the reactions.

In conclusion, we have found that photoreduction of benzophenones by amines is an efficient reaction in room temperature ionic liquids. The unique properties of these interesting solvents alter the reaction pathway so that large amounts of the corresponding benzhydrol, and not the benzpinacol, are formed. While the substituent effects on the course of the photoreduction appear to be consistent with the mechanism proposed in Scheme 1, it is unclear why only benzpinacol is obtained in non-imidazolium-based RTILs. The observed requirement that an imidazolium cation is required for production of benzhydrol may indicate that this species is actively involved in the mechanism. A recent pulse radiolysis study of 1-butyl-3-methylimidazolium salts indicates that these cations are efficient electron acceptors.[17] The role of the imidazolium cation is central to our ongoing investigation of photochemistry in ionic liquids.

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Supporting Information Available: Experimental procedures and analytical methods. This material is available free of charge via the Internet at http://pubs.acs.org.

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[16] See ref 11. Photoreduction in acetonitrile produced a 7:3 mixture of the corresponding benzhydrol/benzpinacol.

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