JOURNAL OF THE AMERICAN CHEMICAL SOCIETY

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Article

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J. Am. Chem. Soc., **Just Accepted Manuscript** • DOI: 10.1021/jacs.8b06089 • Publication Date (Web): 11 Jul 2018

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Electron Transfer Reactions: KO*t*Bu (but not NaO*t*Bu) Photoreduces Benzophenone, under Activation by Visible Light

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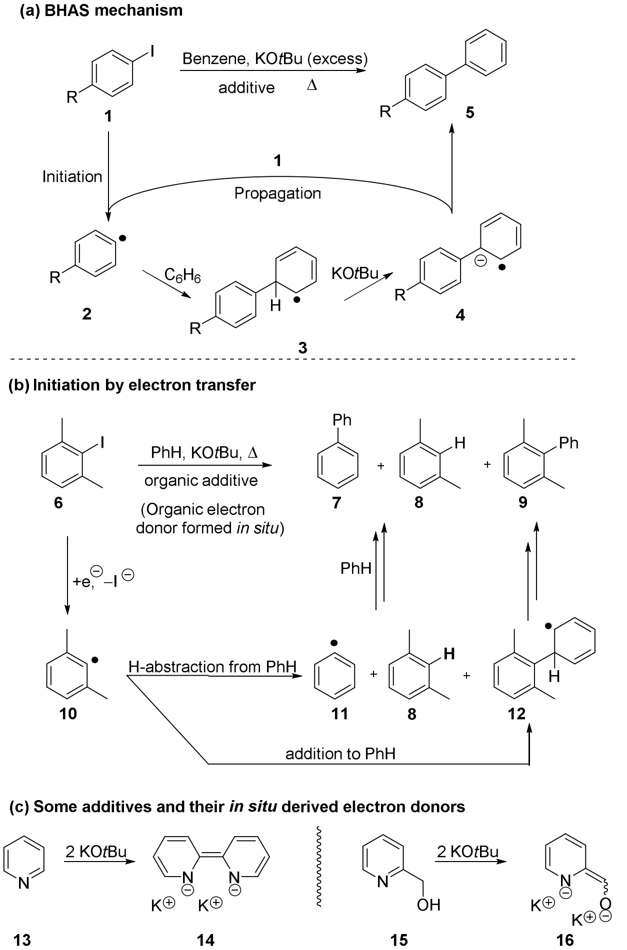
Supporting Information Placeholder

ABSTRACT: Long-standing controversial reports of electron transfer from KO*t*Bu to benzophenone have been investigated and resolved. The mismatch in the oxidation potential of KO*t*Bu (+0.10V *vs*. SCE in DMF) and the first reduction potential of benzophenone (of many values cited in the literature, the least negative value is −1.31 V *vs*. SCE in DMF), preclude direct electron transfer. Experimental and computational results now establish that a complex is formed between the two reagents, with the potassium ion providing the linkage, which markedly shifts the absorption spectrum to provide a tail in the visible light region. Photoactivation at room temperature by irradiation at defined wavelength (365nm or 400nm), or even by winter daylight, leads to the development of the blue color of the potassium salt of benzophenone ketyl, whereas no reaction is observed when the reaction mixture is maintained in darkness. So, no electron transfer occurs in the ground state. However, when photoexcited, electron transfer occurs within a complex formed from benzophenone and KOtBu. TDDFT studies match experimental findings and also define the electronic transition within the complex as n → π*, originating on the butoxide oxygen. Computation and experiment also align in showing that this reaction is selective for KO*t*Bu; no such effect occurs with NaO*t*Bu, providing the first case where such alkali metal ion selectivity is rationalized in detail. Chemical evidence is provided for the photoactivated electron transfer from KO*t*Bu to benzophenone: *tert*-butoxyl radicals are formed and undergo fragmentation to form (acetone and) methyl radicals, some of which are trapped by benzophenone. Likewise, when $KOC(Et)_3$ is used in place of KO*t*Bu, then ethylation of benzophenone is seen. Further evidence of electron transfer was seen when the reaction was conducted in benzene, in the presence of *p*-iodotoluene; this triggered BHAS coupling to form 4-methylbiphenyl in 74% yield.

Introduction

Alkoxides of alkali metals are widely used in organic chemistry as powerful bases. In the past decade, however, these alkoxides have played a key role in an extremely wide range of reactions that involve, or are proposed to involve, single electron transfer - representative examples are cited here.[1-10] This is paradoxical, because alkoxides are very resistant to oxidation, due to electronegativity of oxygen and the consequent instability of alkoxyl radicals.

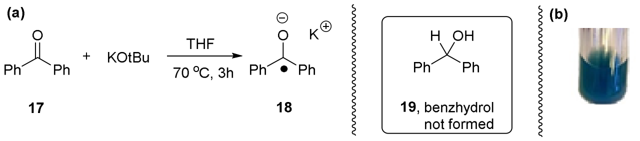


Scheme 1. (a) BHAS mechanism.[2] (b) Initiation by electron transfer.[5b] (c) Examples[5b,10] of additives and their proposed electron donors derived by reaction with KO*t*Bu.

Our interest in these alkoxides, and particularly KO*t*Bu, arose from our studies of the initiation of the Base-Promoted Homolytic Aromatic Substitution (BHAS) class of reactions,[10] (Scheme 1a), where KO*t*Bu[1-10] (sometimes NaO*t*Bu[1c,2c,3a]) promotes the coupling of aryl halides to arenes in the presence of a range of special organic additives. The reactions occur through the conversion of aryl halides **1** to aryl radicals **2** by means of the chain reaction shown.

Some authors proposed that initial radical formation is the result of direct electron transfer from KO*t*Bu or a complex of KO*t*Bu with a ligand to the aryl halide, but our computational and experimental studies indicated[5b,f] that *in situ* chemical reaction between KO*t*Bu and a wide range of additives instead afforded very electron-rich compounds that behaved as powerful organic electron donors (*e.g.* **14**,[5b] **16**[7d,e] in Scheme 1c). These compounds are needed in vanishingly small amounts, as their role is simply to initiate radical formation; once initiated, conversion is amplified through the radical chain reaction shown.

BHAS reaction with substrate **6** (Scheme 1b), has been exploited by us as a very reliable and sensitive indicator of the formation of strong electron donors in solution. Substrate **6** does not react with KO*t*Bu; however, when KO*t*Bu reacts with a suitable additive to form a strong electron donor, electron transfer to **6** occurs, resulting in formation of aryl radical **10**, and an iodide ion. Radical **10** adds to benzene to form radical **12** and ultimately leads to biaryl **9**. But the *ortho*-methyl groups in **10** make the addition to benzene a challenging reaction, allowing a competing hydrogen atom abstraction from benzene to occur, thereby forming radical **11** together with xylene **8**, the latter as a volatile by-product. Radical **11** reacts with the solvent benzene, ultimately forming biphenyl **7**. The formation of **7** and **9** in a defined ratio of *ca*. 3:1 is a hallmark of the BHAS reaction on substrate **6**. Because of its hindered nature, the yields of coupled product from substrate **6** are not high, but the substrate gives a very clear differentiation between the presence of electron donors and their absence and, in this way, the mechanistic information that it provides is very valuable.[5b,5f]

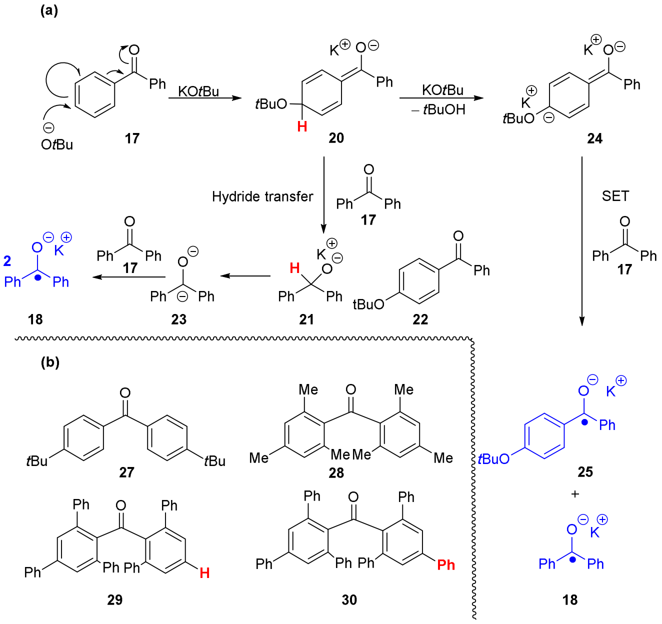


Scheme 2 (a) Ketyl salt formation;[12] no benzhydrol **19** was formed. (b) Photograph shows blue ketyl salt of benzophenone in our repeat of Ashby experiment, but at 70 °C.

Discussion of electron transfer in reactions KO*t*Bu with benzophenone goes back to Russell *et al.* in 1962,[11a] who showed that radicals were generated when benzophenone and its dihydro derivative, benzhydrol, **19**, were mixed in the presence of KO*t*Bu in DMSO, although the paper did not discuss mechanism. In 1978, Screttas and Cazianis proposed[11b] electron transfer from lithium *s*-butoxide to fluorenones as a result of detection of ketyl radicals. The story was taken up in 1982 by Ashby *et al.*[12] who observed the blue color of the potassium ketyl of benzophenone on reaction of benzophenone with KO*t*Bu (Scheme 2). Ashby attributed the reaction to direct electron transfer from KO*t*Bu to benzophenone. Although not considered then, the reduction potential for benzophenone to its ketyl radical anion (cited values vary from −1.31 V *vs*. SCE in DMF to −2.2 V)[13a-c] and oxidation potential of KO^{t}Bu, (+0.1 V in DMF, *vs*. SCE),[6e] indicate that this is not possible as a direct bimolecular electron transfer. With our background in the *in situ* formation of organic electron donors like **14** and **16**, we therefore explored whether formation of organic electron donors could explain the Ashby reactions.[14]

Results and Discussion

Our first task was to validate the original observations of Ashby qualitatively. Adding sodium metal or potassium metal to a solution of benzophenone (**17**, BZP) (0.5 mmol) in THF (2.5 mL) afforded the blue color of the ketyl at ambient temperature. No color developed when KO*t*Bu (2 equiv) was instead added to benzophenone at room temperature, but heating to 70 °C produced the characteristic blue color after 3h [Scheme 2(b)], supporting Ashby's observation. Given sufficient time, the blue color decays, as reported. Work-up led to isolation of benzophenone, and no benzhydrol **19** was detected, again supporting Ashby's report. Interestingly, and in contrast to KO*t*Bu, NaO*t*Bu (2 equiv) showed no evidence of ketyl formation or other reaction under either set of conditions (see Fig S11 in S.I. file).

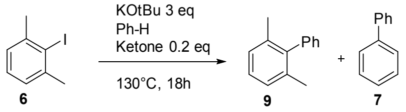


Scheme 3 (a) A proposal for *in situ* formation of electron donors from KOtBu + Ph_2CO. (b) Diarylketones that were synthesized for this study.

We now proposed a number of ways in which organic electron donors[15] might arise in these reactions, one example of which is shown in Scheme 3 (see also S.I.) Attack by KO*t*Bu in the *para*-position of benzophenone **17** would afford anionic intermediate **20**. (Attack in the *ortho*-position should be a comparable alternative, and was considered, see S.I.). Two fates might await **20**: (a) hydride transfer to a molecule of benzophenone **17** would afford **21** and **22** (see ref[5f] for transfer of hydride from an alkoxide under BHAS conditions). As already stated, no benzhydrol **19** is formed in this reaction, so if **21** were formed, it would need to evolve in a different way; deprotonation would afford dianion **23** (see ref.[7d] for formation of dianions with KO*t*Bu under BHAS conditions) which would be a strong electron donor and could reduce benzophenone **17** to form two ketyl radical derivatives **18**. (b) a second possible fate of molecule **20** would involve deprotonation to afford dianion **24**, another candidate for donating an electron to benzophenone **17**. The result of the electron transfer would be two potassium ketyl species, **18** and **25**.

To explore this proposal, substituted benzophenones **27**-**30** were prepared (see SI for details). If addition of KO*t*Bu to the aryl rings of these substrates is valid, then at least some of these substrates, substituted in *ortho* and/or *para* positions, are likely to afford significantly diminished amounts of the potassium ketyl on comparison to **17**. In particular, a notable difference should be seen between closely related substrates like **29** (attack at the free *para*-position, followed by deprotonation is possible), and **30**, (where, even if addition of *tert*-butoxide occurs at the substituted *para* position, subsequent deprotonation is not possible, so that an electron donor should not be able to form). We recognized that the simple qualitative color test for ketyl formation could be complicated with some of these substrates due to the extended chromophores of **29** and **30** and also to the likely variation in kinetics, compared to substrate **17**. So we deployed the BHAS reaction with substrate **6** as a sensitive test (Table 1). The experiments with **17** were repeated in triplicate, and the yields were repeatable.

Table 1. BHAS reactions of iodoarene **6**.



Entry	Ketone	**9**[a] (% yield)	**7**[a] (% yield)
1[c]	–	0.2	0.4
2[c]	**17**	1.2	3.5[b]
3	**27**	1.0	3.2
4	**28**	0.7	1.8
5	**29**	0.8	2.4[b]
6	**30**	0.4	1.2[b]

[a] Yield calculated via NMR using 1,3,5-trimethoxybenzene as internal standard. [b] Yield deduced using the ratio 1:3 (**9**:**7**) calculated after isolation of the mixture of the coupled products.[c] Average of 3 runs.

As usual with substrate **6**, the yields of the biphenyl products, **7** and **9**, were not high, but they were at least three times higher than the yields from the non-zero yield in blank reactions.[16] The important point to note is that the BHAS reaction was not at ‘blank’ levels for any of the ketones, indicating that factors other than shown in Scheme 3 were at play. Moreover, we did not succeed in detecting or isolating any products arising from addition of *tert*-butoxide anion to any of the ketones. Coupled with computational studies which indicated unfavorable energy profiles for the proposals in Scheme 3 (see SI), this caused us to think afresh about these reactions.

While performing repeat experiments on the formation of the potassium salt of benzophenone ketyl through reaction with KOtBu on many different days, it was noticed that the time required for the development of the blue color varied by day. During a (rare) sunny day, we noticed that the switch to the blue color was much faster than usual. Performing parallel experiments when sunlight was present with (i) exposed and (ii) foil-covered reactions, showed the result to be strongly dependent on the irradiation.

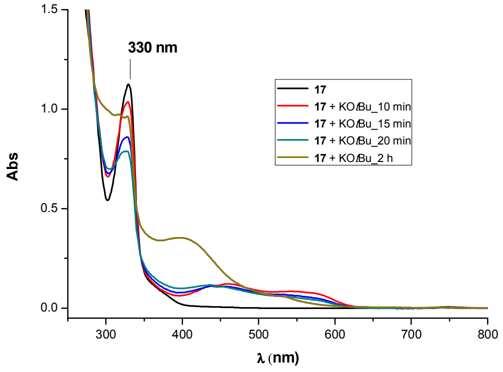


Figure 1. UV measurements of **17** (BZP) + KO*t*Bu with time in THF.

A preliminary study of the UV absorption of **17** and of mixtures of **17** with KO*t*Bu in THF was performed (Figure 1).

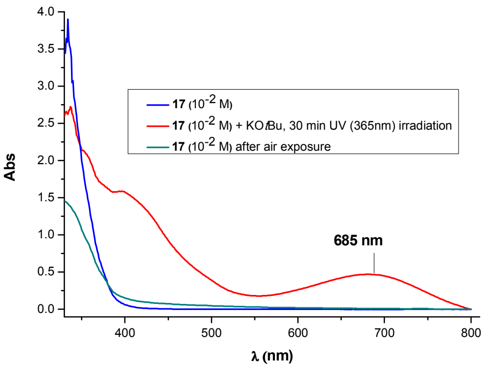


Figure 2. UV measurement of **17** (10^{-2} M in THF) + KO*t*Bu pre- and post-irradiation.

Benzophenone does not absorb radiation at > 400 nm (black trace). When KO*t*Bu was added, a tail in the absorption in the range of 400-600 nm was detected; we attribute this to the formation of a transient complex or complexes. With time, the absorption profile changed with the appearance of a new maximum around 400 nm (See Figure 1, trace marked as: ‘**17** + KO*t*Bu_2 h’). This complex is discussed below, based on investigation through computational chemistry. Therefore we irradiated the mixture of KO*t*Bu and **17** in distilled THF with UV (365 nm, see Figure 2) and polychromatic visible light (see S.I.). In both cases, the blue coloration developed. Analysis via UV-vis spectrometry revealed the appearance of a broad band around λ=685 ± 30 nm, diagnostic of the ketyl radical anion of **17**[17] (Figure 2).

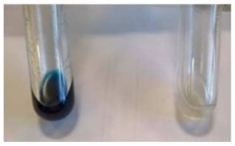


Figure 3. Reaction tubes containing KO*t*Bu and **17** in benzene (a) left: exposed to 400 nm light and (b) right: shielded from light by covering in foil.

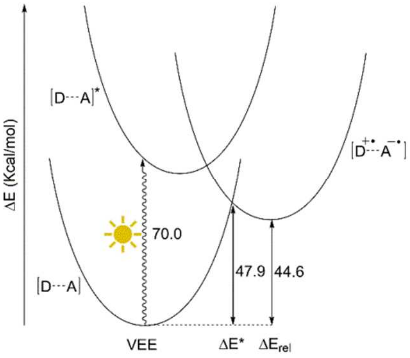


Figure 4. TD-DFT calculated vertical excitation energy (VEE) and DFT calculated single electron transfer energies (calculated using the complexation method)[18] for the complex of benzophenone **A** and KO*t*Bu (monomer) **D**. Geometries optimized using M06-2X/6-31++G(d,p) and subsequent single point energy or TD-DFT calculations carried out using CAM-B3LYP/6-31++G(d,p), all with CPCM solvation parameters for THF.

Given the absorption of the complex just above 400 nm, we also irradiated reaction tubes containing KO*t*Bu and benzophenone **17** in benzene with 400 nm LED light sources. Comparison was again made with a foil-covered reaction, conducted side-by-side and at the same time (see Figure 3). The Figure very clearly shows the effect of the LED light source on the reaction.

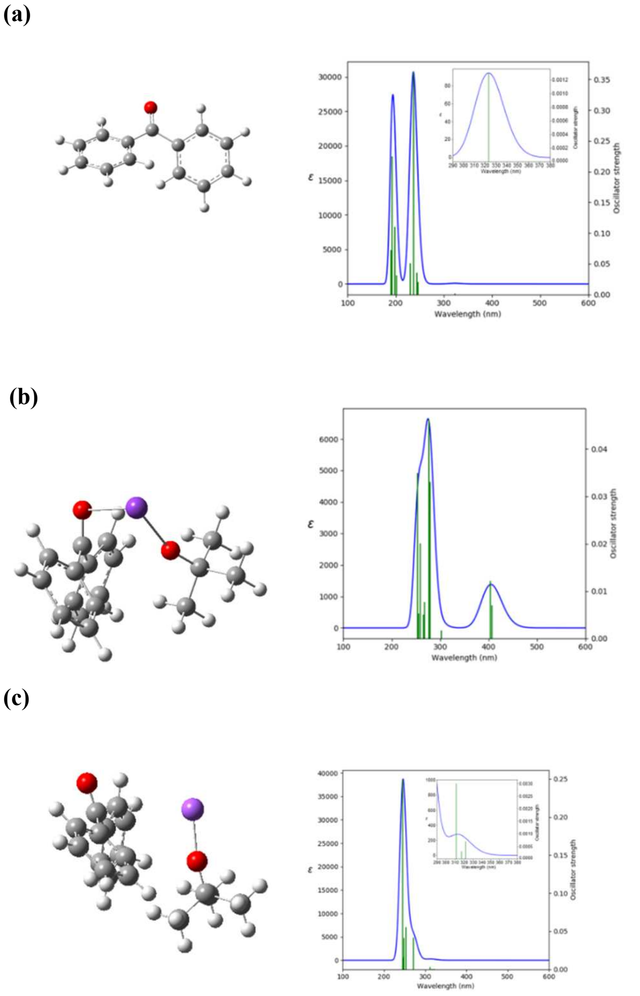
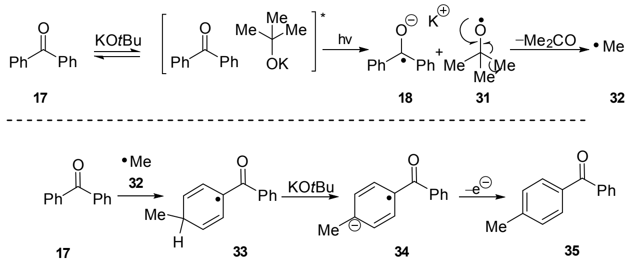


Figure 5 **(a)** Benzophenone **17** (left) and its computed absorption spectrum[19] (right) with expansion of weak n-π* at 332 nm inset. **(b)** complex of **17** with KO*t*Bu (left) and predicted spectrum showing the n-π* > 400 nm (right) **(c)** complex of **17** with NaO*t*-Bu (left) and predicted spectrum (right).

To understand the visible light promoted formation of the blue benzophenone ketyl radical anion, time-dependent density functional theory (TD-DFT) calculations were conducted. Initially, the first singlet excited state of benzophenone was calculated, which corresponds to an n-π* excitation occurring at 332 nm or 3.73 eV. It was therefore clear that no visible light excitation of benzophenone alone could be taking place. We therefore decided to study the complex between a monomer of KO^{t}Bu and benzophenone, which exhibits singlet excitations at 406 nm (3.05 eV or 70 Kcal/mol) and 404 nm (3.07eV) which correspond to CT from the [HOMO] and [HOMO-1], both residing on KO^{t}Bu, to the LUMO, residing on benzophenone. This suggests that it is indeed possible to photoexcite a complex of KOtBu and benzophenone using visible light. The complex between NaOtBu monomer and benzophenone however, does not exhibit any excitation in the visible region, with excitations occurring at 322 nm (3.85 eV) and 318 nm (3.90 eV) corresponding to CT from the [HOMO] and [HOMO-1], both residing on NaO*t*Bu, to the LUMO, residing on benzophenone. This lack of visible excitation (or indeed excitation around 365 nm) can explain why no ketyl radical anion is observed in reactions with NaO*t*Bu.

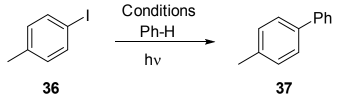
Marcus theory calculations for SET between ground-state KO^{t}Bu and benzophenone (Figure 4) predicts a relative electronic energy of 44.6 kcal/mol (ΔG_{rel} = 42.5 kcal/mol) with a calculated electronic activation energy of 47.9 kcal/mol (ΔG^* = 44.0 kcal/mol). These results indicate that ground state electron transfer between these reactants is not possible. In order to overcome the unfavorable energetics associated with ground state SET, visible light excitation of the reactant complex followed by charge separation would furnish the SET product complex.



Scheme 4. Fragmentation of *tert*-butoxyl radicals leading to formation of methylbenzophenone.

In reactions where electron transfer from *tert*-butoxide anions to benzophenone occurs, evidence ought to be available to support intermediacy of *tert*-butoxyl radicals and of the potassium ketyl of benzophenone. *tert*-Butoxyl radicals undergo fragmentation very rapidly to form acetone and methyl radicals (Scheme 4)[20] In our reactions with benzophenone in THF as solvent, methyl radicals can undergo hydrogen atom abstraction from the solvent, but they can also add to benzophenone to give methylbenzophenone. Whereas the formation of the ketyl occurs with irradiation at 365 nm, or 400 nm or daylight, it occurs most rapidly with excitation at 365 nm. Under these conditions, we looked for benzophenone-related products and detected and characterized the monomethylated analogue of benzophenone by GCMS. To confirm this result, we replaced KO*t*Bu, (*i.e.* KOCMe$_3$) by KOCEt$_3$, and characterized the monoethylated benzophenone GCMS.[21]

Table 2:



Entry	Conditions[a]	Light (λ)	**37** (yield %)
1	**17**, 1 eq KO*t*Bu 2 eq.	365 nm	74
2	KO*t*Bu 2 eq,	365 nm	12

[a]The reactions were firstly put at RT under UV for 15 min and then placed in absence of irradiation at 130°C for 18h.

To look for further evidence of electron transfer, we examined the BHAS reaction in benzene with *p*-iodotoluene **36**, a substrate that is much less hindered than substrate **6**, and so the yield should be higher than for substrate **6**. As radical generation is simply part of the initiation process, we irradiated at 365 nm for 15 min and then turned off the irradiation and heated for 18h at 130°C. This afforded 4-methylbiphenyl (74%, Table 2); a blank experiment in which benzophenone was omitted gave 4-methylbiphenyl in 12% by comparison.

Conclusions. The historical observation by Ashby *et al.*[12] of formation of the potassium ketyl of benzophenone from reaction of benzophenone with KO*t*Bu was hitherto unexplained. The redox potentials of the two molecules are seriously mismatched, so that an outer sphere electron transfer can be discounted. Our studies show that mixing KO*t*Bu with benzophenone gives rise to a metastable complex with absorption just above 400 nm that can be excited in daylight or under activation with LED illumination at 400 nm or with UV illumination at 365 nm, resulting in electron transfer from the alkoxide to benzophenone **17**. The reaction seems very specific to KO*t*Bu; changing to NaO*t*Bu gave no reaction.[22] The important point to note is that while Ashby's observation of electron transfer is validated here, his conclusion that this reaction is a ground state reaction is wrong. KO*t*Bu can only transfer an electron to benzophenone upon photoactivation that is facilitated by a special complex formed between KOtBu and benzophenone.

Benzophenone plays a central role in pure and applied organic photochemistry.[23] Although benzophenone absorbs strictly in the UV, this paper reveals that formation of discrete complexes can lead to absorption in the visible region of the spectrum. This may be part of a much more general phenomenon allowing access to benzophenone photochemistry with visible light. In connection with that, two recent reports[24] highlighted 'excitations of benzophenone' with visible light sources, although no characterization of the absorbing species was carried out. Perhaps complexation also leads to species that absorb visible light. Potassium *tert*-butoxide is an unusual partner for electron transfer reactions. A recent paper highlighted KO*t*Bu as an electron donor to a highly oxidising iridium complex[25] and backed this with Stern-Volmer studies to show the involvement of the KO*t*Bu, but our paper now discloses the first characterized case of electron transfer to an organic substrate. It may be that further recently reported cases of the activity of KO*t*Bu as an electron donor actually constitute complexes that don't occur in the ground state but are photoactivated by sunlight.[6e] Placing this in context, the exploitation of organic molecular complexes absorbing visible light has been highlighted recently by Melchiorre and others as a growth area,[26,7e,8i] and adds to other recent developments[27] in chemical reactivity triggered by visible light.

Acknowledgements. We thank the University of Strathclyde and AstraZeneca for support; the Generalitat Valenciana (Spain) for funding a postdoctoral fellowship (to F.P.). High resolution mass spectrometry was carried out at the EPSRC National Mass Spectrometry Centre, Swansea University. Computational results were obtained using the EPSRC funded ARCHIE-WeSt High Performance Computer (www.archie-west.ac.uk). EPSRC grant no. EP/K000586/1. We thank Drs. Glynn Williams and Lee Edwards (GSK) for calibrating our LED device, and Dr. Xu Chao for helpful discussions.

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¥ These authors contributed equally to the research.

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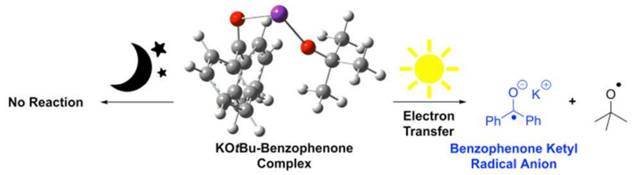
TOC Graphic


No Reaction
KO*t*Bu-Benzophenone
Complex
Electron
Transfer
O
K
Ph
Ph
+
O
Benzophenone Ketyl
Radical Anion