

Photosensitized (Electron-Transfer) Deconjugation of 1-Arylcyclohexenes

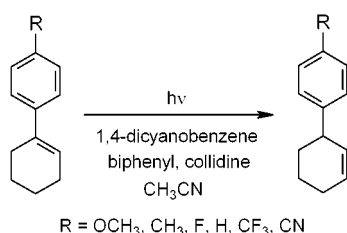
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ABSTRACT



A series of 1-arylcyclohexenes have been deconjugated to the corresponding 3-arylcyclohexenes via a photosensitized electron-transfer reaction. The introduction of substituents on the aryl group has provided insight into the underlying mechanism and has defined the scope and limitations of the reaction.

Earlier studies from our laboratory demonstrate that it is possible to deconjugate 1-phenyl- and 1,1-diphenylalkenes by means of a photochemically induced electron-transfer reaction.^{1,2} The method exhibits promising synthetic potential, resulting in high yields of the 3-phenyl- and 3,3-diphenylalkenes from the readily accessible conjugated tautomers. For example, a mixture of 1,4-dicyanobenzene (**1**), biphenyl (**2**), collidine (2,4,6-trimethylpyridine, **3**) and 2-methyl-1-phenylpropene (**4a**) in acetonitrile, irradiated by means of a 1 kW medium-pressure mercury lamp, yielded 2-methyl-3-phenylpropene (**4b**) in 90% yield.²

A photoinduced electron-transfer mechanism from the electron donor (alkene) to the electron acceptor (cyanoarene) excited singlet state was proposed (Scheme 1). This mechanism includes several key steps:

(a) The cyanoarene absorbs light, resulting in its excitation to the first excited singlet state. This is followed by electron transfer from the alkene to the cyanoarene excited state. The yield of radical ions can be enhanced by the addition of a co-donor such as biphenyl (**2**).³ This process relies on the

redox potentials of the electron-transfer couple and the singlet excited-state energy of the light absorber, as defined by the Weller equation⁴ (steps 1–3).

(b) The alkene radical cation deprotonates. This step depends on the acidity of the radical cation and can be promoted by the addition of a nonnucleophilic base, such as collidine (**3**) (step 4).

(c) The resulting allylic radical is reduced to the corresponding anion via electron transfer from the acceptor radical anion. At this stage, the reduction potentials of the allylic radical and of the cyanoarene play an important role (step 5).

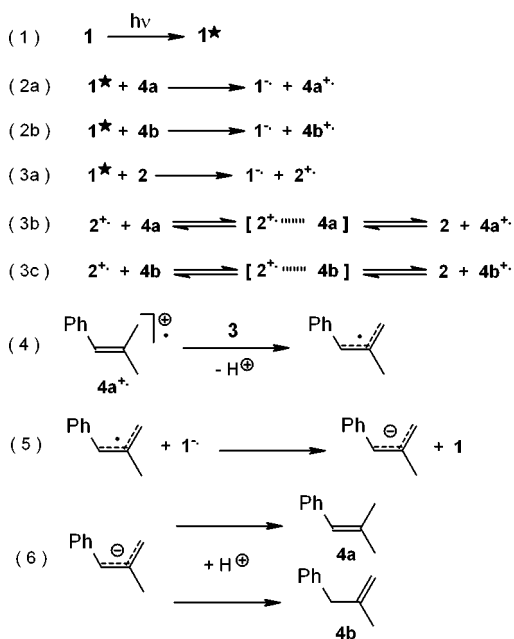
(d) The allylic anion is reprotonated at either terminus to regenerate the starting material **4a** or yield the deconjugated tautomer **4b** (step 6).

The aims of the present study are two-fold: we are interested in defining the scope and limitations of this deconjugation reaction for synthetic purposes, and we also want to elucidate the mechanism proposed in our earlier work. The introduction of substituents on the phenyl ring of the alkene can serve as a useful probe for the various steps in the mechanism, which are expected to respond differently

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(3) (a) Gould, I. R.; Ege, D.; Moser, J. E.; Farid, S. *J. Am. Chem. Soc.* **1990**, *112*, 4290. (b) Lewis, F. D.; Bedell, A. M.; Dykstra, R. E.; Elbert, J. E.; Gould, I. R.; Farid, S. *J. Am. Chem. Soc.* **1990**, *112*, 8055.

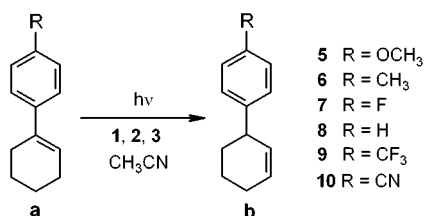
(4) Rehm, D.; Weller, A. *Isr. J. Chem.* **1970**, *8*, 59.

Scheme 1



to the substituents. For this purpose we investigated the photochemical deconjugation of six 1-arylcyclohexenes, **5a**–**10a**, bearing different substituents ranging from methoxy to cyano, in the 4-position of the aryl group (Scheme 2).

Scheme 2



Experimental details and product yields are shown in Table 1. Products **5b**–**10b** were isolated on silica gel by flash chromatography and/or preparative, centrifugally accelerated, radial, thin-layer chromatography using a Chromatotron and were fully characterized by spectroscopic methods.⁵ Typically, the co-donor **2** and the base **3** were quantitatively recovered. The acceptor **1** was generally partially consumed

(5) **9b**: oil; ¹H NMR (250.13 MHz, CDCl₃, TMS) δ 1.45–1.75 (m, 3H), 1.98–2.19 (m, 3H), 3.40–3.50 (m, 1H), 5.66–5.70 (m, 1H), 5.90–5.98 (m, 1H), 7.30–7.60 (m, 4H, AA'BB'); ¹³C NMR (62.9 MHz, CDCl₃) δ 21.0 (t), 24.9 (t), 32.4 (t), 41.7 (d), 124.4 (s, q, ¹J_{C-F} = 272 Hz), 125.2 (d, q, ³J_{C-F} = 4 Hz), 128.0 (d), 128.6 (s, q, ²J_{C-F} = 33 Hz), 129.1 (d), 129.2 (d), 150.7 (s); IR (film, NaCl) ν (cm⁻¹) 836 (m), 1018 (w), 1069 (s), 1124 (s), 1164 (m), 1326 (s), 1418 (w), 1619 (w), 2835 (w), 2865 (w), 2934 (m), 3026 (w); MS (EI) *m/z* 226 (M⁺, 24%), 211 (19), 129 (100); M⁺, 226.0991, C₁₃H₁₃F₃ requires M, 266.0969. **10b**: oil; ¹H NMR (250.13 MHz, CDCl₃, TMS) δ 1.44–1.53 (m, 3H), 2.07–2.13 (m, 3H), 3.43–3.50 (m, 1H), 5.63–5.67 (m, 1H), 5.92–6.00 (m, 1H), 7.30–7.60 (m, 4H, AA'BB'); ¹³C NMR (62.9 MHz, CDCl₃) δ 20.8 (t), 24.8 (t), 32.2 (t), 41.9 (d), 109.7 (s), 119.1 (s), 128.4 (d), 128.5 (d), 129.6 (d), 132.1 (d), 152.2 (s); IR (film,

Table 1. Photochemical (Electron-Transfer) Deconjugation of 1-Arylcyclohexenes **5a**–**10a**^a

entry	starting alkene (% consumption) ^b	irradiation time (h)	product alkene (% yield) ^b
1	5a (86)	2.5	5b (26), 5c (40)
2	6a (87)	2.5	6b (44)
3	7a (88)	2.5	7b (61)
4	8a (91)	2.5	8b (72)
5	8a (89) ^c	2.5	8b (48)
6	8a (57) ^d	2.5	8b (17)
7	9a (85)	5.0	9b (54)
8	10a (80)	5.0	10b (16)

^a Reaction mixture composition: alkene **5a**–**10a** (0.05 M), **1** (0.02 M), **2** (0.05 M), **3** (0.05 M) in acetonitrile. Reaction conditions: 1 kW medium-pressure mercury lamp, 10 °C, Pyrex filter. ^b Consumption and yield percentages were determined by calibrated GC-FID using 10 mL reaction volumes in 1 cm i.d. Pyrex tubes. Products were isolated from large scale reactions under identical conditions. ^c No biphenyl (**2**) in this reaction. ^d No biphenyl (**2**) or collidine (**3**) in this reaction.

by a competing side reaction that involves reaction with the alkenes. This alternative mode of reactivity becomes the dominant pathway in the absence of base.⁶ It is commonly observed in the photochemistry of aliphatic alkenes and cyanoarenes in nonnucleophilic, polar media.⁷ This competing reaction was largely responsible for the nonquantitative product yields.

1,4-Dicyanobenzene (**1**) exhibits two absorption maxima, at 281 nm ($\epsilon = 1650 \text{ dm}^3 \text{ mol}^{-1} \text{ cm}^{-1}$) and 290 nm ($\epsilon = 1650$). The other reaction constituents generally do not absorb appreciably beyond the 280 nm absorption cutoff of Pyrex, thus rendering **1** the major light absorber. There are some exceptions: alkenes **9a** and **10a** do absorb competitively, which might be partly responsible for their slower reactivity. Electronic excitation of **1** enhances its oxidizing properties such that the first excited state will undergo electron transfer with any substrate having an oxidation potential less than 2.4 V.⁸ As shown in Table 2, photoinduced electron transfer is predicted to be diffusion-controlled with almost all the conjugated alkenes as well as with some of the deconjugated isomers.

The introduction of biphenyl (**2**) as co-donor showed a marked enhancement in all of the reactions investigated (see entries 4 and 5 in Table 1 as examples). Biphenyl (**2**) has a half-wave oxidation potential, $E_{1/2}^{\text{ox}}$, of 1.85 V vs SCE (CH₃CN).⁹ This implies a free energy for photoinduced electron transfer, ΔG_{PET} , of -75 kJ mol^{-1} for step 3a, Scheme 1.

NaCl) ν (cm⁻¹) 831 (s), 1176 (w), 1299 (w), 1326 (w), 1413 (w), 1446 (w), 1503 (m), 1606 (s), 2227 (s), 2859 (m), 2931 (s), 3021 (w); MS (EI) *m/z* 183 (M⁺, 100%), 168 (82), 154 (89), 140 (58), 129 (55), 115 (86); M⁺, 183.1058, C₁₃H₁₃N requires M, 183.1048.

(6) (a) Kojima, M.; Kakehi, A.; Ishida, A.; Takamuku, S. *J. Am. Chem. Soc.* **1996**, *118*, 2612. (b) Kojima, M.; Ishida, A.; Kuriyama, Y.; Oishi, S. *Bull. Chem. Soc. Jpn.* **2000**, *73*, 1557.

(7) (a) Arnold, D. R.; Wong, P. C.; Maroulis, A. J.; Cameron, T. S. *Pure Appl. Chem.* **1980**, *52*, 2609. (b) Borg, R. M.; Arnold, D. R.; Cameron, T. S. *Can. J. Chem.* **1984**, *62*, 1785.

(8) It has been estimated that a photoinduced electron-transfer process will proceed at a diffusion-controlled rate when the free energy is less than -20 kJ mol^{-1} .

(9) Arnold, D. R.; Du, X. *Can. J. Chem.* **1994**, *72*, 403.

Table 2. Free Energies for the Photoinduced Electron Transfer between **1** and Alkenes **5–10** (ΔG_{PET}) and for the (Charge-Shift) Electron Transfer between $2^{+\bullet}$ and **5–10** (ΔG_{ET})

alkene	$E_{1/2}^{\text{ox}}$ (V) ^a	ΔG_{PET} (kJ mol ⁻¹) ^b	ΔG_{ET} (kJ mol ⁻¹) ^c	alkene	$E_{1/2}^{\text{ox}}$ (V) ^a	ΔG_{PET} (kJ mol ⁻¹) ^b	ΔG_{ET} (kJ mol ⁻¹) ^c
5a	1.55	-104	-29	5b	1.70	-89	-14
6a	1.87	-73	+2	6b	2.08	-52	+22
7a	1.87	-73	+2	7b	2.40	-22	+53
8a	2.00	-60	+14	8b	2.44	-18	+56
9a	2.40	-22	+53	9b	2.54	-8	+67
10a	2.42 ^d	-20	+53	10b	2.44	-18	+57

^a Oxidation potentials were measured by cyclic voltammetry in a three-electrode electrochemical cell equipped with a spherical platinum working electrode, a platinum coil counter electrode, and a saturated calomel reference electrode (SCE). Deoxygenated acetonitrile was used as solvent and 0.1 M tetraethylammonium perchlorate was the supporting electrolyte. The voltammograms were acquired at a scan rate of 100 mV s⁻¹ and calibrated against the ferrocene/ferrocenium oxidation potential of 0.51 V. In all cases, the electron transfer was irreversible and $E_{1/2}^{\text{ox}}$ was taken as 0.03 V before the peak potential.⁹ ^b Determined by means of the Weller equation:⁴ $\Delta G_{\text{PET}} = F(E_{1/2}^{\text{ox}} - E_{1/2}^{\text{red}} - e/\epsilon\alpha) - E_{0,0}$ where $E_{1/2}^{\text{red}}(\mathbf{1}) = -1.66$ V vs SCE (CH₃CN), $E_{0,0}(\mathbf{1}) = 408$ kJ mol⁻¹ and the Coulombic attraction term $Fe/\epsilon\alpha$ is estimated as 5.4 kJ mol⁻¹ in acetonitrile.^{7b} ^c Determined using: $\Delta G_{\text{ET}} = F(E_{1/2}^{\text{ox}} - E_{1/2}^{\text{red}})$ where $E_{1/2}^{\text{red}}(2^{+\bullet}) = 1.85$ V vs SCE (CH₃CN).⁹ ^d Could not be determined experimentally. $E_{1/2}^{\text{ox}}(\mathbf{10a})$ was estimated from a Hammett plot of $E_{1/2}^{\text{ox}}$ vs σ^+ ($\rho^+ = -10.4$, $R^2 = 0.995$) using our experimentally determined $E_{1/2}^{\text{ox}}$ values.

Although most of the conjugated alkenes have a $E_{1/2}^{\text{ox}}$ that is higher than that of **2**, suggesting an endergonic electron transfer in step 3b, Scheme 1 (Table 2), an enhanced yield of radical ions is still observed. This phenomenon is commonly noticed in co-donor mediated reactions.^{9,10} The underlying mechanism is not fully understood. The formation of alkene radical cations, despite an endergonic electron-transfer process, is generally attributed to the existence of an equilibrium between $2^{+\bullet}$ and the alkene radical cation. Rapid consumption of the alkene radical cation drives the reaction forward. Alternatively, this may be viewed as the formation of a complex between $2^{+\bullet}$ and the alkene. This complex imparts substantial positive charge onto the alkene. It should be kept in mind that the second electron-transfer process (steps 3b and 3c, Scheme 1) is a charge-shift electron transfer that may behave differently from the more common and better understood charge-separation process (step 3a, Scheme 1). The overall enhancement in the co-donor mediated reaction is a consequence of the slower rate of back electron transfer (BET) for the $1^{-\bullet}/2^{+\bullet}$ pair as opposed to that of the $1^{-\bullet}$ /alkene radical cation pair.³ This is attributed to a smaller solvent reorganization energy for $2^{+\bullet}$ going back to **2**.

One of the crucial steps in the reaction is the selective consumption of the conjugated alkene over its nonconjugated tautomer. Clearly, free energy considerations in the initial photoinduced electron transfer between **1** and the alkene (step 2, Scheme 1) cannot account for the selectivity. In most cases, the electron transfer is expected to be diffusion-controlled for both tautomers. In the biphenyl-mediated mechanism, however, the situation is different. The second electron transfer (steps 3b and 3c, Scheme 1) is not diffusion-controlled. It will thus be sensitive to the redox potentials of the constituents, favoring electron transfer from the alkene of lower oxidation potential. In the extreme case of the cyano

derivative the reaction is slow and the selectivity for the formation of the nonconjugated isomer is poor (entry 8, Table 1). Here, both tautomers **10a** and **10b** have exceedingly high and very similar oxidation potentials. It has been argued that, should the radical cation of the deconjugated tautomer form, it would undergo rapid electron transfer from the ground-state conjugated alkene. This would occur even in the absence of **2**, provided that the oxidation potential of the conjugated isomer is sufficiently lower than that of its tautomer.² In fact, in the current study, an enrichment of the nonconjugated tautomer is generally observed in the absence of **2**, although the selectivity is lower than in the co-donor mediated reaction (entry 5, Table 1).

Despite a highly exergonic electron transfer, the methoxy derivative **5a** does not undergo an efficient deconjugation reaction (entry 1, Table 1). The radical cation of **5a** is expected to exhibit the lowest thermodynamic acidity among the alkenes studied. It has been well established that the radical cations of 1-arylalkene systems bearing strongly electron-donating groups are relatively inert toward any type of reaction that involves the cationic site.^{6b,11,12} The structurally similar 1-phenylpropene radical cation was reported to have a pK_a of -12 ;² the pK_a of $5a^{+\bullet}$ can thus be estimated as ca. -4 ,¹³ which, however, is still acidic enough to be deprotonated by collidine ($pK_a = 16.8$).

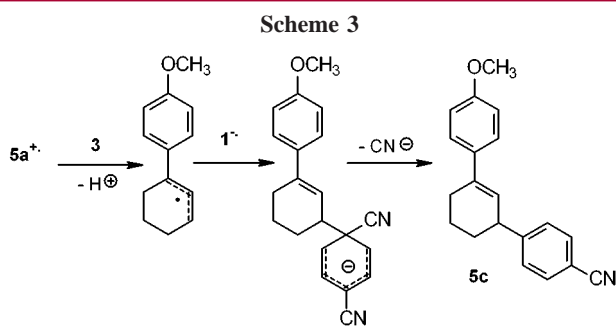
The acidity of the alkene radical ions increases with oxidation potential, with the cyano derivative **10a** having an estimated pK_a of approximately -22 . The introduction of collidine (**3**) is crucial for a successful deconjugation reaction, even though most of the alkene radical ions in this study are acidic enough to be deprotonated by acetonitrile ($pK_a = \text{ca. } -11$). However, in the absence of **3**, the deconjugation reaction is slow and other reactions dominate

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(entries 5 and 6, Table 1).⁶ The optimal collidine (**3**) concentration was found to be ca. 0.05 M. Higher concentrations led to an increasingly inefficient reaction. We have evidence that this is most likely due to quenching by **3** of the 1,4-dicyanobenzene excited state, probably via an electron-transfer mechanism.

The next step in the proposed mechanism, that is, the reduction of the allylic radical to the corresponding anion by **1**⁻, is more likely to be the reason for the poor yield of deconjugation product **5b**. The reduction potential is expected to be too high for the allylic radical derived from **5a** as a result of the electron-donating effect of the methoxy group destabilizing the anion.¹⁴ The inability of the allylic radical derived from **5a** to be reduced is confirmed by the isolation of 3-(4-cyanophenyl)-1-(4-methoxyphenyl)cyclohexene **5c** in good yield. This product is thought to arise via coupling of the allylic radical with the radical anion of **1**, followed by expulsion of cyanide anion as driven by rearomatization (Scheme 3). The identity of product **5c** has been firmly established by spectroscopic techniques.¹⁵

Electron-withdrawing groups raise the reduction potential of the radical, promoting reduction by the sensitizer radical

(14) $E_{1/2}^{\text{red}}$ for the 4-methoxybenzyl radical is -1.82 V vs SCE, which implies a free energy of $+15$ kJ mol⁻¹ for its reduction by **1**⁻. In comparison, $E_{1/2}^{\text{red}}$ for the benzyl radical is -1.43 V vs SCE, giving a free energy of -22 kJ mol⁻¹ for its reduction by **1**⁻.¹⁶

(15) **5c**: oil; ¹H NMR (250.13 MHz, CDCl₃, TMS) δ 1.52–2.51 (m, 4H), 2.47–2.51 (m, 2H), 3.59–3.66 (m, 1H), 3.81 (s, 3H), 5.99 (br. s, 1H), 6.86–7.39 (m, 4H, AA'BB'), 7.34–7.64 (m, 4H, AA'BB'); ¹³C NMR (62.9 MHz, CDCl₃) δ 21.5 (t), 27.3 (t), 32.0 (t), 42.7 (d), 55.3 (q), 109.9

anion **1**⁻.¹⁶ Therefore, the influence of this step on the reaction outcome is marginal when the substituents are electron-withdrawing or weakly electron-donating. Consequently, the formation of adducts similar to **5c** is less favorable.

In summary, the photochemical electron-transfer deconjugation of conjugated aromatic alkenes has been extended to include 1-arylcyclohexenes with a range of substituents on the aromatic ring. This reaction constitutes a simple and straightforward synthetic method for converting the readily available conjugated alkenes to the corresponding 3-arylcyclohexenes that are not as easily accessible. The observed substituent effects on the reaction follow the predictions made on the basis of the mechanism proposed. For a successful reaction outcome there are several key steps that have to be satisfied: formation of radical ions, deprotonation of the alkene radical cation, reduction of the allylic radical, and selective consumption of the conjugated alkene relative to the nonconjugated isomer. The introduction of strongly electron-donating substituents (e.g., methoxy) inhibits the reaction as the result of an inefficient reduction of the alkene-derived allylic radical to the corresponding anion. On the other hand, strongly electron-withdrawing substituents (e.g., cyano) hinder the initial formation of radical ions and reduce the selectivity toward the formation of the deconjugated tautomer because of similar oxidation potentials for both conjugated and nonconjugated isomers.

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(s), 113.7 (d), 119.1 (s), 124.1 (d), 126.2 (d), 128.6 (d), 132.2 (d), 134.3 (s), 138.3 (s), 152.4 (s), 158.9 (s); IR (film, NaCl) ν (cm⁻¹) 824 (m), 1036 (m), 1181 (m), 1249 (s), 1513 (s), 1607 (m), 2227 (m), 2832 (w), 2932 (m), 3036 (w); MS (EI) m/z 289 (M⁺, 100%), 261 (46), 121 (43); M⁺, 289.1445, C₂₀H₁₉NO requires M, 289.1467.

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