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Hydroxyalkylation of [60]fullerene: free radical addition of alcohols to $C_{60}\dagger\ddagger$

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A new general reaction for the preparation of isomerically pure hydroxyalkylated C_{60} monoadducts, *via* the free radical photochemical addition of alcohols to [60]fullerene, is described.

Free-radical reactions were one of the first investigated reactions in fullerene chemistry,¹ although the high affinity of free-radicals with [60]fullerene (a "radical sponge") has limited their utility as a practical tool for the selective functionalization of C_{60} . However, under appropriately controlled conditions a single-addition of free-radicals to C_{60} can be achieved. For example, we have recently shown that tetrabutylammonium decatungstate [TBADT, $(n-Bu_4N)_4W_{10}O_{32}$], a well-established free-radical initiator with several applications in organic synthesis,² can be utilized for the selective, radical mono-functionalization of C_{60} .³ Building upon this work, we report herein a powerful free-radical method for the preparation of structurally diverse hydroxyalkylated [60]fullerene mono-adducts, thus broadening the scope of TBADT complex as an efficient catalyst in fullerene chemistry.

synthesis of hydroxyl-containing [60]fullerene The derivatives is an area of intense research interest, due to the great application potential that this class of compounds possess in materials science and medicinal chemistry.⁴ These compounds can be roughly divided into two types based on their motifs: (i) polyhydroxylated fullerenes (fullerenols) where the -OH group is located on the C₆₀ core,⁵ and (ii) hydroxyalkyl(aryl)fullerenes (HAFs) where the hydroxyl group is located on the organic addend bound to the fullerene core.^{6,7} Although synthetic methods for the preparation of fullerenols have been extensively investigated,⁵ hydroxyalkylation of C₆₀ is still in its infancy; to the best of our knowledge this is the first example concerning a general method for the selective, and yet direct mono-hydroxyalkylation of C60 from commercially available alcohols.

Initially, the potential of the aforementioned monohydroxyalkylation of [60]fullerene was assessed by studying the TBADT-photocatalyzed reaction of C_{60} with one of the simplest commercially available alcohols, namely MeOH (1). This reaction involved irradiation of a degassed solution of C_{60} in a mixture of chlorobenzene/CH₃CN (85:15), 0.5 equiv. TBADT, and 200 equiv. of MeOH (1) under an argon atmosphere. Gratifyingly, hydroxyalkylfullerene (HAF)

monoadduct 1a was obtained in moderate yield after 30 min of irradiation (Table 1, entry 1). Encouraged by this initial result, we further explored the scope of this novel transformation with a series of structurally diverse alcohols, including primary alcohols (2-3), a secondary alcohol (4), propargyl alcohol (5), and benzyl alcohol (6), under the same reaction conditions. Indeed, these reactions proceeded rapidly to afford the corresponding HAF monoadducts 2a-6a in good yields. At longer reaction times an increase of the multi-addition byproducts was observed. A summary of the reaction times and yields is given in Table 1. The low yield observed for alcohol 6a is essentially due to further side-reactions that produce $C_{60}H_2$ (at *ca*. 20% yield).⁸ The formation of this side-product ($C_{60}H_2$) may be rationalized by the *in situ* conversion of **6a** to $C_{60}H_2$, *via* a base catalyzed elimination of benzaldehyde from 6a.^{9,10} In this case, C_{60}^{-} anion acts as a good leaving group by virtue of its increased electrophilicity. At this point, it is worth mentioning that C₆₀H₂ has been also detected, albeit in a low yield (up to 5% based on HPLC analysis), during the reaction of C_{60} with alcohols 1–5.

The structure of compounds **1a–6a** was unambiguously established by ¹H NMR, ¹³C NMR and UV-vis spectroscopy, as well as by MALDI mass spectrometry. The ¹H NMR spectra showed the expected proton coupling pattern for these C_1 or C_s symmetric fullerene derivatives. As a diagnostic signal, compounds **1a–6a** exhibit the characteristic fullerenyl C₆₀-H proton resonance at 6.60–6.98 ppm. The C_a-H protons

Table 1 TBADT-photocatalyzed reaction of alcohols 1-6 with C₆₀



| Entry | Substrate | R ¹ R ² CHOH | Irradiation time/min | Yield $(\%)^a$ |
|--------|-----------|--|----------------------|--------------------|
| 1 2 | 1 2 | CH ₃ OH CH ₃ CH ₂ OH | 30 25 | 30 (70) 30 (70) |
| 3 | 3 | ∽∽ОН | 20 | 30 (65) |
| 4 | 4 | OH | 10 | 25 (60) |
| 5 | 5 | ≡ ^{OH} | 40 | 35 (65) |
| 6 | 6 | ОН | 25 | 15 (35) |
| | | | | |

^{*a*} Isolated yield. Yield in parentheses is based on consumed C₆₀.

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appear at 5.13–5.57 ppm for adducts 1–4. This resonance is low-field shifted at 6.11 and 6.52 ppm, for the propargyl and benzyl protons of **5a** and **6a**, respectively. The ¹³C NMR spectra of C_1 symmetric compounds **2a**, **3a**, **5a**, and **6a** exhibit almost all 60 resonances of the fullerene cage carbons. On the other hand, C_s symmetric compound **4a** exhibits 30 ¹³C NMR signals for the sp² carbons of the C₆₀ core and two signals for the sp³-hybridized fullerenyl carbons. More importantly, the UV-vis absorption spectra of compounds **1a–6a** showed the diagnostic weak absorption of 1,2-adducts of C₆₀ at around 432 nm.

The reaction mechanism was next investigated by performing a series of deuterium labeling experiments. Initially, the origin of the fullerenyl H atom in RC₆₀H was determined by performing the photocatalyzed reaction of **3** with C₆₀ in a mixture of C₆H₅Cl/CH₃CN containing 0.5% D₂O. A high percentage of deuterium incorporation (>80%) at the C₆₀ sp³ carbon of the reaction product **3a** was observed by ¹H NMR spectroscopy.¹¹ Apparently, this result suggests that the reaction mechanism involves the intermediacy of fullerene anion, which can be effectively trapped by D₂O.

To probe this mechanism further and identify the ratelimiting transition state, we measured the intramolecular primary kinetic isotope effect (KIE) of this reaction. To this end, we studied the reaction of C_{60} with butan-1-ol- d_1 (3- d_1) (Scheme 1). This reaction was performed similarly to those described previously in this work. The ratio of products $3a - d_1$ and $3b-d_1$, which is the result of an intramolecular isotopic competition between the C_{α} -H and C_{α} -D bonds of 3- d_1 , is proportional to the primary isotope effect of $k_{\rm H}/k_{\rm D}$. ¹H NMR integration of the methylene $-CH_2$ - signals of both **3a**- d_1 and **3b**- d_1 as well as the C_{α}-H proton of **3b**- d_1 determined the primary isotope effect $k_{\rm H}/k_{\rm D} = 2.23 \pm 0.10$ (Scheme 1). This substantial KIE indicates an extensive C-H(D) bond breaking in the transition state of the first slow radical-forming step. Another important finding from this experiment concerns the source of the fullerenyl hydrogen. Thus, the adduct $3b-d_1$, from which the $k_{\rm D}$ is derived, is partially deuterated (RC₆₀-H/D). This result indicates, in accordance with the D₂O-quenching



Scheme 1 Determination of the intramolecular primary KIE in the reaction of $3-d_1$ with C_{60} by ¹H NMR spectroscopy.

experiment mentioned above, that the intermediate C_{60} anion is mainly trapped by a proton originating from residual moisture in the reaction mixture.

At this point it is worth noting that the reaction of alcohols 1 and 2 with C_{60} has been previously studied under co-sensitization conditions.⁷ In particular, Mattay and coworkers found that irradiation of C₆₀ in the presence of a sensitizer (e.g., DCA) and biphenyl (BP) as co-sensitizer leads to the formation of the radical cation of C_{60} ($C_{60}^{\bullet^+}$), which in turn reacts with alcohols 1 or 2 by abstracting a hydrogen atom from the α -C–H and/or O–H bond of 1 or 2.⁷ In this case, the corresponding adducts 1a and 2a are identical with those observed in the present study. Hence, it was reasonable to assume that a similar mechanism may be operative in the present study, with TBADT acting as a strong photochemical oxidant to produce $C_{60}^{\bullet+}$. This assumption is further supported by considering the relative reduction potential order of the involved species. Thus, photoexcited decatungstate (TBADT*) has a higher reduction potential ($E_{red} = 2.26-2.61$ V vs. SCE)¹² compared to that of ground or excited state $C_{60}[E_{red}(^{3}C_{60}^{*})] =$ 1.14 V vs. SCE or $E_{red}(C_{60}) = -0.42$ V vs. SCE, respectively],¹³ which makes an electron transfer oxidation of C₆₀ by TBADT* energetically feasible. On the other hand, another possible reaction pathway that could also be operative in the present study would involve H-atom abstraction from α -C–H alcohol bond by TBADT* instead of by C₆₀^{•+}.

In order to clarify this issue, we studied the TBADTcatalyzed reaction of C_{60} with ethylene glycol (7, eqn (1)). This substrate was chosen as a mechanistic probe by virtue of its characteristic product distribution upon reaction with $C_{60}^{\bullet+}$. In particular, as first shown by Mattay and coworkers, the DCA/BP-catalyzed reaction of C_{60} with 7 affords exclusively adduct **1a**.^{7b} The formation of this adduct has been rationalized by considering a H-atom abstraction from the –OH group of 7 by $C_{60}^{\bullet+}$, followed by extrusion of formaldehyde (CH₂O) and coupling of the resultant radical species (•CH₂OH and HC₆₀•) (eqn (1)). Accordingly, the formation of this product in the corresponding TBADT-catalyzed reaction would reveal the formation of $C_{60}^{\bullet+}$.

$$HO-CH_2-CH_2-OH \xrightarrow{C_{60}^{\circ}} HO-CH_2-CH_2-O \xrightarrow{HO-CH_2-CH_2-O} HO-CH_2 \xrightarrow{HC_{60}} HC_{60}CH_2OH$$
7
1a
(1)

In the present study, however, the TBADT-catalyzed reaction of C₆₀ with 7 afforded exclusively product 7a instead of 1a (Scheme 2). This important result indicates that alcohol 7a is derived through a H-atom abstraction from the α -C-H alcohol bond of 7 by TBADT* (*vide infra*). The absence of compound 1a in this case strongly argues against the reaction pathway that would involve the intermediacy of C₆₀^{•+}. Similarly, the otherwise possible TBADT-mediated formation of C₆₀^{•+} can now be safely excluded from the previously reported TBADT-mediated reactions of C₆₀.³ This important conclusion is further supported by the fact that no TBADTcatalyzed reaction of C₆₀ with either propionic acid or methyl formate was observed, although these substrates are known to be reactive with C₆₀ upon DCA/BP catalysis.^{7b} Also, TBADT photocatalyzed oxidation of aryl alkanols to form aryl ketones



Scheme 2 TBADT-photocatalyzed reaction of C₆₀ with 7.

is known to proceed through a hydrogen abstraction mechanism *via* the formation of the coresponding radical intermediate similar to the present case.¹⁴

According to the above-mentioned results, the reaction mechanism of the photocatalyzed hydroxyalkylation of C₆₀ is summarized in Scheme 3. Initially, the excited state of decatungstate ($W_{10}O_{32}^{4-*}$), generated upon light excitation, abstracts a H-atom from the C_a-H bond of alcohol affording the one-electron reduced form of decatungstate ($W_{10}O_{32}^{5-}$) and the corresponding α-hydroxy C-centered radical. Isotope effect studies showed that this step determines the rate of this reaction. The triplet excited state of C₆₀ (³C₆₀*), generated upon light excitation followed by an effective intersystem crossing ($\Phi_{\rm ISC} \approx 1$), regenerates $W_{10}O_{32}^{4-}$ through an electron transfer process, thus closing the catalytic cycle. Since the free energy change of electron transfer (ΔG°_{et}) from W₁₀O₃₂⁵⁻ $[E^{\circ}(W_{10}O_{32}^{4-}/W_{10}O_{32}^{5-}) = -1.215 \text{ V } vs. \text{ SCE}] \text{ to } {}^{3}C_{60}^{*}*$ $(E_{\rm red}^{\circ} = 1.14 \text{ V vs. SCE})^{13}$ is negative ($\Delta G_{\rm et}^{\circ} = -226 \text{ kJ mol}^{-1}$), the electron transfer reduction of ${}^{3}C_{60}$ * is thermodynamically feasible to give $C_{60}^{\bullet-}$. Similarly, however, the electron transfer reduction of ground state C_{60} ($E^{\circ}_{red} = -0.42$ V vs. SCE)¹³ by $W_{10}O_{32}^{5-}$ is also energetically feasible to form $C_{60}^{\bullet-}$ ($\Delta G_{et}^{\circ} = -76.7 \text{ kJ mol}^{-1}$). Finally, radical coupling followed by protonation of the resulting radical anion ($C_{60}^{\bullet-}$) affords the observed fullerene adducts.

In summary, the photochemical addition of α -hydroxy C-centered radicals to C₆₀ represents a powerful method for the hitherto unexplored mono-hydroxyalkylation of C₆₀. Considering the inexpensive catalytic system, the simplicity of this method, the convenient availability of the starting



Scheme 3 Proposed mechanism for the TBADT-catalyzed reaction of alcohols with fullerene C_{60} .

materials, and the unique structure of the final adducts, this new reaction paves the way for the preparation of a variety of new hydroxyalkylated fullerenes of interest in materials science and medicinal chemistry.

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