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Acyl Radical Reactions in Fullerene Chemistry: Direct Acylation of [60]Fullerene through an Efficient Decatungstate-Photomediated Approach

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Abstract: A versatile and highly efficient photochemical methodology for the direct acylation of C_{60} has been developed. This approach utilizes a wide variety of acyl radicals derived from aldehydes through a hydrogen atom abstraction process mediated by tetrabutylammonium decatungstate [$(n\text{-}Bu_4N)_4W_{10}O_{32}$]. The single addition reaction of these acyl radicals to [60]fullerene proceeded selectively to afford a novel class of previously unexplored fullerene-based materials. Product analysis of this reaction showed that decarbonylation and acylation pathways compete when a tertiary or phenylacetyl aldehyde is the starting material. However, a decrease of the reaction temperature was found to be effective in overcoming the decarbonylation encountered in certain acyl radical additions to C_{60}; the carbonyl radical addition precedes decarbonylation even in the cases where the decarbonylation rate constant exceeds 10^6 s^{-1} (i.e., phenylacetaldehyde). The regiochemistry of the *t*-butyl radical addition was also found to be thermally controlled. The present methodology is directly applicable even in the cases of the cyclopropyl-substituted aldehydes, where rapid rearrangement of the cyclopropyl acyl radical intermediate can potentially occur. A mechanistic approach for this new reactivity of C_{60} has been also provided, based mainly on intra- and intermolecular deuterium isotope effect studies.

Introduction

Ever since discovered, fullerenes have attracted great attention; their chemical modification has apparently emerged as a formidable challenge to synthetic organic chemistry. Their broad biological potential and applications in material sciences has stimulated the synthesis of many different classes of fullerene derivatives.[1] In this context, the development of an effective method for the direct synthesis of fullerene derivatives bearing a variety of functional groups is of crucial importance; it provides the basis to exploit the different chemical/physical properties anticipated.

Among the several reactions employed for the fullerene functionalization, the radical reactions appear to be less explored. This is evidently due to the high reactivity of radicals toward C_{60}. Typically, radical additions to C_{60} have led to a complex mixture of multiadducts[2,3] while the corresponding monoadducts have been detected only by mass spectrometric analyses or electron spin resonance (ESR) studies in the early stages of the radical reactions.[3] The chemical reactivity of C_{60} with acyl radicals, however, remained virtually unexplored. Additionally, and despite the widespread applications of acyl radicals in organic chemistry and the great synthetic potential of the ketone group, there have been no systematic studies providing methods for the carbonyl derivatization of [60]fullerene.[4−6] Herein we report a new approach that utilizes acyl radicals for the direct acylation of [60]fullerene affording selectively a novel class of monofunctionalized fullerene compounds. This method utilizes the tetrabutylammonium decatungstate (TBADT) as photocatalyst.[7−9] We demonstrate that, under appropriate conditions, the carbonyl radical addition precedes decarbonylation

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(1) (a) Hirsch, A.; Brettreich, M. *Fullerenes, Chemistry and Reactions*; Wiley-VCH: Weinheim, Germany, 2005. (b) Bonifazi, D.; Enger, O.; Diederich, F. *Chem. Soc. Rev.* **2007**, *36*, 390–414. (c) Thilgen, C.; Diederich, F. *Chem. Rev.* **2006**, *106*, 5049–5135. (d) Martin, N. *Chem. Commun.* **2006**, 2093–2104. (e) Wudl, F. *J. Mater. Chem.* **2002**, *12*, 1959–1963.

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(4) For a comprehensive review on acyl radical chemistry, see: (a) Chatgilialoglu, C.; Crich, D.; Komatsu, M.; Ryu, I. *Chem. Rev.* **1999**, *99*, 1991–2069.

(5) For reviews on radical carbonylations, see: (a) Ryu, I. *Chem. Soc. Rev.* **2001**, *30*, 16–25. (b) Ryu, I.; Sonoda, N. *Angew. Chem., Int. Ed. Engl.* **1996**, *35*, 1050–1066. (c) Ryu, I.; Sonoda, N.; Curran, D. P. *Chem. Rev.* **1996**, *96*, 177–194.

(6) For recent examples of acyl radical reactions, see: (a) Uenoyama, Y.; Fukuyama, T.; Ryu, I. *Org. Lett.* **2007**, *9*, 935–937. (b) Inoue, M.; Ishihara, Y.; Yamashita, S.; Hirama, M. *Org. Lett.* **2006**, *8*, 5801–5804. (c) Jensen, C. M.; Lindsay, K. B.; Taaning, R. H.; Karaffa, J.; Hansen, A. M.; Skrydstrup, T. *J. Am. Chem. Soc.* **2005**, *127*, 6544–6545. (d) For the carbonylation methodology for the generation of acyl radicals, see: Schiesser, C. H.; Wille, U.; Matsubara, H.; Ryu, I. *Acc. Chem. Res.* **2007**, *40*, 303–313.

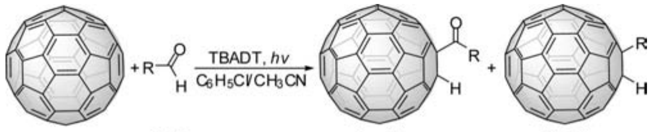
(7) (a) Tanielian, C. *Coord. Chem. Rev.* **1998**, *178−180*, 1165–1181. (b) Duncan, D. C.; Netzel, T. L.; Hill, C. L. *Inorg. Chem.* **1995**, *34*, 4640–4646.

(8) At the same time as this work was in progress, the decatungstate-photocatalyzed activation of aldehydes was independently reported. Esposti, S.; Dondi, D.; Fagnoni, M.; Albini, A. *Angew. Chem., Int. Ed.* **2007**, *46*, 2531–2534.

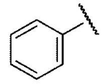
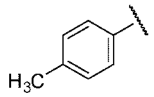
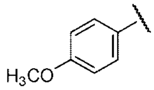
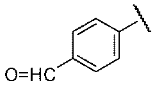
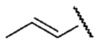
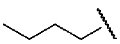
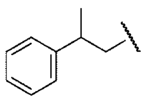
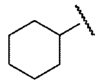
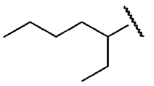
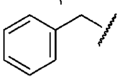
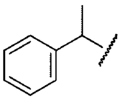
10.1021/ja808658b CCC: $40.75

of the intermediate radical even in the case of phenylacetaldehyde, where the decarbonylation rate constant is high ($k_d > 10^6$ s^{-1}).[10] Finally, a series of experiments has been performed to elucidate the mechanism underlying this new functionalization of C_{60}.

Table 1. TBADT-Mediated Reaction of Aldehydes **1**−**12** with C_{60}[a]



1-12 **1a-11a** **9b-12b**

entry	substrate	R	irradiation time (min)[b]	yield (%)[c]		k_d (s^{-1})[d]
				a	**b**	
1	**1**		30	35	–	–
2	**2**		50	35	–	–
3	**3**		80	35	–	–
4	**4**		25	40	–	–
5	**5**		80	40	–	–
6	**6**		90	50	–	$\sim 10^2$[g]
7	**7**		60	45	–	–
8	**8**		60	45	–	–
9[e]	**9**		80	40	2	1.4×10^4
10[e,f]			80	35	-	
11	**10**		50	10	18	8.3×10^5
12[f]			25	35	3	
13	**11**		60	10	20	5.3×10^6
14[f]			70	35	–	
15	**12**		120	–	30	4.9×10^7

[a] For general considerations see the Supporting Information. [b] The optimal time of the reaction with maximum conversion and minimal multiadducts formation. [c] Isolated yield. [d] The rate constants for the decarbonylations of acyl radicals are cited in ref 5b. [e] 0.4 equiv of TBADT were used. [f] The reaction was performed at $T = -50$ to -40 °C; for experimental details, see the Supporting Information. [g] The rate constant for the decarbonylation of valeraldehyde is considered to be in the same order of magnitude with the corresponding k_d for dodecanal.

Results and Discussion

Initially, the reaction of C_{60} with benzaldehyde in the presence of TBADT was investigated (Table 1, entry 1). This reaction was carried out simply by irradiating a solution of C_{60} with 100 equiv of benzaldehyde and 0.2 equiv of TBADT in a mixture of chlorobenzene/CH_3CN (85:15), using a 300 W xenon lamp. To our delight, under these conditions benzaldehyde afforded the corresponding monofunctionalized fullerene derivative **1a** in moderate yield. Subsequently, the scope of this reaction was explored by studying a series of para-substituted benzyl aldehydes **2**−**4**. Indeed, the acylation of [60]fullerene proceeded efficiently to afford the corresponding monoacylated fullerene derivatives in good yields (Table 1, entries 2−4). Additionally, it was recently shown that TBADT can abstract a hydrogen atom from the $-CH_3$ and $-OCH_3$ groups of toluene and anisole, respectively, affording the corresponding fullerene adducts in good yields.[9a] However, in the present case, although substrates **2** and **3** possess a $-CH_3$ and a $-OCH_3$ substituent in the para position of the aromatic ring, respectively, only the carbonyl hydrogen atom was preferentially abstracted from these aldehydes affording the corresponding adducts **2a** and **3a**, thus rendering this reaction highly chemoselective. It is also interesting to mention here that in a recent study, the TBADT-photomediated acylation of electrophilic olefins was found essentially ineffective with aromatic aldehydes;[8] however, in our case the acylation of [60]fullerene was effective even when using benzyl aldehydes, presumably due to the different experimental conditions used. Likewise, the photocatalyzed reaction between an allylic aldehyde, namely crotonaldehyde **5**, and C_{60} gave the enone **5a** in 40% yield (Table 1, entry 5).

The scope of this reaction was further explored by studying the reaction of C_{60} with two pairs of primary and secondary aldehydes, such as **6**, **7** and **8**, **9**, respectively (Table 1, entries 6−9). Indeed, following the previous photocatalytic procedure, the corresponding intermediate acyl radicals were efficiently trapped by C_{60} to yield selectively the monofunctionalized fullerene derivatives **6a**−**9a**, respectively, in good yields, thus validating the versatility and efficiency of this method. However, as seen in the case of 2-ethylhexanal **9** (Table 1, entry 9), some acyl radicals possess the inherent ability to undergo decarbonylation, yielding a new carbon-centered radical and carbon monoxide.[4] The facility of this degradation step can be unambiguously correlated to the stability of the newly generated radical upon decarbonylation,[4,11,12] the temperature,[12] and the solvent.[13] Hence, acyl radical addition reactions have, in general, been restricted to carbonyl radicals exhibiting low decarbonylation rates (k_d typically less than 10^4 s^{-1}). On the other hand, addition reactions of acyl radicals with higher decarbonylation rate constants (e.g., greater than 10^4 s^{-1}), commonly leads to products subjected to loss of CO. This is consistent with the slight decarbonylation of 2-ethylhexanal **9** observed herein (Table 1, entry 9) and becomes even more evident when pivalaldehyde, phenylacetaldehyde, or 2-phenylpropionaldehyde (substrates **10**, **11**, and **12**, respectively) are being employed in the title reaction (Table 1, entries 11, 13, 15). In these cases the monoadducts **10b**, **11b**, and **12b** were obtained as the major or only addition products, respectively; they were apparently derived from the decarbonylation of the corresponding parent acyl radicals. This decarbonylation reaction, however, should

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(9) For recent examples of TBADT-mediated reactions, see: (a) Tzirakis, M. D.; Orfanopoulos, M. *Org. Lett.* **2008**, *10*, 873–876. (b) Tzirakis, M. D.; Lykakis, I. N.; Panagiotou, G. D.; Bourikas, K.; Lycourghiotis, A.; Kordulis, C.; Orfanopoulos, M. *J. Catal.* **2007**, *252*, 178–189.

(10) Tsentalovich, Y. P.; Fischer, H. *J. Chem. Soc. Perkin Trans. 2* **1994**, 729–733.

(11) Fischer, H.; Paul, H. *Acc. Chem. Res.* **1987**, *20*, 200–206.

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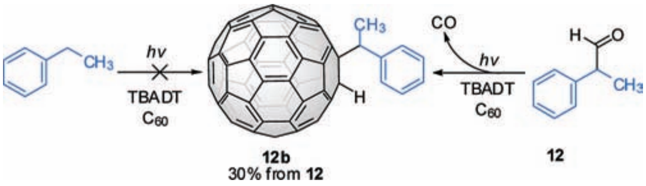
(13) Kurnysheva, O. A.; Gritsan, N. P.; Tsentalovich, Y. P. *Phys. Chem. Chem. Phys.* **2001**, *3*, 3677–3682.

Scheme 1. TBADT-Mediated Decarbonylation of 2-Phenylpropionaldehyde **12** as an Indirect Approach for the Free-Radical Functionalization of C_{60}

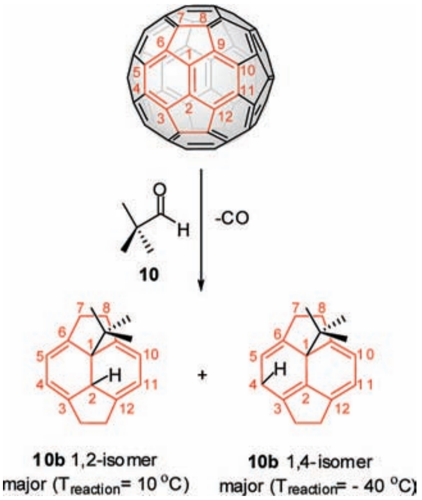


be considered as an indirect approach for the functionalization of C_{60} with some organic moieties (i.e., secondary benzyl), which are otherwise inaccessible. For instance, the reaction of ethylbenzene with C_{60} (Scheme 1) afforded only traces of adduct **12b**,[14] whereas by taking advantage of this method a 30% yield for **12b** was achieved under milder conditions (Table 1, entry 15). At this point, it is worth mentioning that fullerene adducts **1a**, **3a**, and **11a** have been previously synthesized over seven steps starting from the parent [60]fullerene in a rather low overall yield.[15] Our method provides an alternative one-step and higher yield synthesis of these derivatives.

It is also important to mention here that the decarbonylation rate constant k_d increases upon going from the primary aldehyde **6** (Table 1, entry 6) to 2-phenylpropionaldehyde **12** (Table 1, entry 15). Consequently, the product distribution in this series of reactions (Table 1, product **a** vs **b**) should reflect the aforementioned facility of the intermediate radical decarbonylation. Indeed, the relative yield of the decarbonylation-derived adducts **9b**−**12b** increases with increasing k_d. In principle, the observed decarbonylation process strongly suggests that this reaction involves an acyl radical. The generation of a relatively stable tertiary or benzyl radical is the driving force in these reactions. Moreover, as first suggested by Fischer and Paul,[11] the rate constants of decarbonylation (k_d) are a linear function of the R−CO bond dissociation energy, $BDE_{(R-CO)}$. One of the strongest bonds is that of benzoyl (Ph−CO), which has an estimated value of $BDE_{(R-CO)} = 26$ kcal/mol. The decarbonylation rate constant at ambient temperature for this radical is exceedingly slow $k_d = 10^{-7}\ s^{-1}$ (a lifetime of several days),[16,17] and accordingly, no decarbonylation is observed for benzyl aldehydes **1**−**4**. This may be realized in terms of a highly unstable forming σ-localized phenyl radical in the transition state.[17]

In the next stage, we examined the possibility of suppressing the decarbonylation observed in certain acyl radical addition reactions where the intermediate acyl radicals are prone to rapid decarbonylation. To this purpose we examined the photocatalyzed reaction of C_{60} with aldehydes **9**−**11**, for the first time in fullerene chemistry, in temperatures below −40 °C (Table 1, entries 10, 12, 14). Indeed, essentially no decarbonylation-derived fullerene adducts were detected when aldehydes **9**−**11** were used. As shown by the results in Table 1, the low-temperature coupling protocol proved successful even with phenylacetaldehyde **11** where the decarbonylation rate constant of the corresponding acyl radical surpass $10^6\ s^{-1}$ (Table 1, entry 14). The otherwise fast decarbonylation of tertiary acyl and phenylacetyl radicals, **10** and **11**, respectively, was only slightly observed for **10** under the lower temperature conditions (reaction temperature −40 to −50 °C; Table 1, entries 12 and 14, respectively). Previous attempts to minimize the fast decarbonylation process in the TBADT-photocatalyzed addition of pivaloyl radical to an electron-poor olefin were rather insufficient.[8] The present result provides a neat example of thermally controlled decarbonylation. To our knowledge, this is also the first instance whereby addition of a tertiary acyl radical onto an electron-deficient polyolefin, such as [60]fullerene, was obtained and more importantly, in exceptional selectivity. Another important result obtained from this experiment concerns the regioselective addition of *t*-butyl radical to [60]fullerene, affording the corresponding adduct **10b**. When the reaction was performed at ca. 10 °C, both 1,2- and 1,4-isomers were obtained; in this case, the thermodynamically more stable 1,2-isomer **10b** was predominantly formed.[18] However, the kinetically favored 1,4-adduct **10b** was the major product, when the reaction was performed at −40 °C (see Supporting Information).

Scheme 2. Temperature-Dependant Regioselective Addition of *t*-Butyl Radical to [60]Fullerene[a]



[a] The pyracylene unit where the addition occurs is depicted in red.

To the best of our knowledge, this is the first example concerning the thermal control of a regioselective addition to C_{60}, which may lead to further applications in C_{60} chemistry; it also provides an elegant support of the previously reported theoretical calculations concerning the regiochemistry of the *t*-butyl group addition to C_{60}.[18c] Moreover, 1,4-isomer of **10b** was stable in the solid form, while in solution a small amount converts to the thermodynamic product, over several hours, presumably due to the presence of trace impurities.[19]

To further probe the reactivity of the acyl radical additions to C_{60}, the cyclopropanecarboxaldehydes **13** and **14** were prepared (Scheme 3). The reaction was carried out under similar conditions outlined for aldehydes **1**−**12** using 90 equiv of cyclopropanecarboxaldehydes **13** and **14** and 0.5 equiv of TBADT.

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(14) The reaction was run under various conditions using 0.2−1 equiv of TBADT and 200−1500 equiv of ethylbenzene for 2−15 h of irradiation.

(15) Tada, T.; Ishida, Y.; Saigo, K. *Org. Lett.* **2007**, *9*, 2083–2086, and references cited therein.

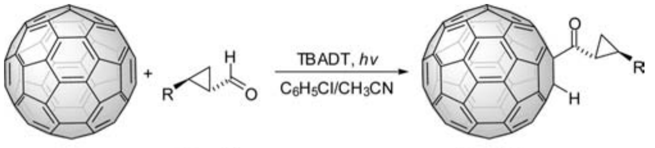
(16) Solly, R. K.; Benson, S. W. *J. Am. Chem. Soc.* **1971**, *93*, 2127–2131.

(17) Garcia-Garibay, M. A.; Campos, L. M. Decarbonylation of Acyl Radicals. In *CRC Handbook of Organic Photochemistry and Photobiology*, 2nd ed.; Horspool, W., Lenci, F., Eds.; CRC Press: Boca Raton, FL, 2004; pp 48/8−48/10.

(18) (a) Fagan, P. J.; Krusic, P. J.; Evans, D. H.; Lerke, S. A.; Johnston, E. *J. Am. Chem. Soc.* **1992**, *114*, 9697–9699. (b) Hirsch, A.; Soi, A.; Karfunhel, H. R. *Angew. Chem., Int. Ed. Engl.* **1992**, *31*, 766–768. (c) Kitagawa, T.; Tanaka, T.; Takata, Y.; Takeuchi, K.; Komatsu, K. *J. Org. Chem.* **1995**, *60*, 1490–1491.

(19) Banim, F.; Cardin, D. J.; Heath, P. *Chem. Commun.* **1997**, 25–26.

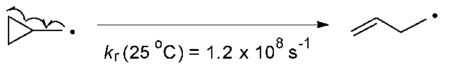
Scheme 3. TBADT-Mediated Reaction of C_{60} with Cyclopropanecarboxaldehydes **13**−**14**



13, R = H
14, R = Ph

13a, 40%
14a, 40%

The cyclopropyl group has been used in the past as a mechanistic trap for other radical intermediates, since it involves the rapid cyclopropylcarbinyl to homoallylcarbinyl radical rearrangement (eq 1).[20] In our case, the rapid cyclopropyl acyl radical opening could similarly lead to β-ketene alkyl radical, as shown in eq 2, which may react further.[21]



(1)

(2)

13, R = H
14, R = Ph

However, no rearranged products were detected in the reaction of C_{60} with aldehyde **13** (Scheme 3). The presence of a phenyl group on the cyclopropane ring in substrate **14** did not alter this result. Intriguingly, this reaction proceeded in good yield, affording **14a** as the only product. This important result indicates that the coupling rate of C_{60} with the newly formed phenylcyclopropyl formyl radical is greater than the rate of phenyl cyclopropyl ring opening ($k_{\text{coupling}} > k_{\text{opening}}$). The rate constant for the opening of the corresponding phenyl substituted cyclopropylcarbinyl radical is k_{opening} (25 °C) = 3×10^{11} s^{-1} to form the corresponding allylcarbinyl radicals.[20b] Apparently, these results indicate that a direct acylation of C_{60} can occur even in the cases where rapid rearrangement of the intermediate cyclopropyl acyl radical is potentially possible.

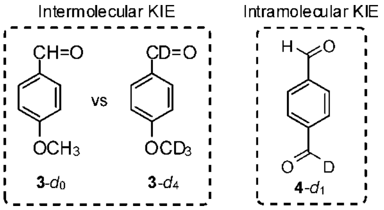
The reaction conditions adopted throughout this work have been carefully optimized by examining the reaction of C_{60} with **1**−**14** under various conditions. The experimental conditions applied are probably the most critical factor in determining the efficiency of this selective monofunctionalization. For example, prolonged irradiation of the reaction mixture increased dramatically the multiple addition products. From a synthetic point of view, the yields obtained herein are reasonable considering that C_{60} (as a starting material) reactions exhibit comparatively low yields, especially in radical addition reactions where the monoaddition product is anticipated. This reaction is also attractive because of the simplicity of the procedure, the mild reaction conditions used, and the readily available starting materials. Furthermore, the reaction of an electron-deficient polyolefin with an electron-deficient group, namely [60]fullerene with the carbonyl carbon correspondingly, is already per se a remarkable result.

The structures of compounds **1a**−**14a** were unequivocally characterized by UV−vis, FTIR, ^{1}H and ^{13}C NMR spectroscopic techniques, as well as by mass spectrometry (see Supporting Information). As diagnostic signals in the ^{1}H NMR spectra ($CDCl_3/CS_2$) the protons attached on the fullerene core resonate at 7.23−7.80 ppm, the highest value ever observed for similar C_{60} protons. This low-field shift is attributed principally to the deshielding effect[22] of the neighboring carbonyl group. More importantly, the ^{13}C NMR spectra reveal that ketones **1a**−**6a**, **8a**, **10a**, **11a**, and **13** possess C_s symmetry, indicating that the addition has taken place across the [6,6]-ring junction in C_{60}. Accordingly, there are 30 ^{13}C NMR signals for the sp^2 carbons of the C_{60} core and two signals for the sp^3-hybridized fullerenyl carbons. The latter appears at 53.55−54.23 (C_{60}−H) and 60.05−60.90 ppm (C_{60}−C(O)R), respectively. On the other hand, each of the compounds **7a**, **9a**, **12b**, and **14a** bears at least one stereogenic center and, as such, the symmetry of these adducts is expected to be reduced from C_s to C_1. Indeed, their ^{13}C NMR spectra consist of at least 45 signals for the fullerene carbons. The addition reaction has taken place again to the 6,6-junction bond of C_{60}, as evidenced by their UV−vis spectra; all of the compounds **1a**−**14a** showed a weak absorption around 432 nm, which is diagnostic for 1,2-adducts of fullerene (while 1,4-adducts exhibit a broad absorption band at ca. 445 nm).

In order to elucidate the mechanism underlying this reaction, additional experiments were performed. Initially the origin of the fullerenyl hydrogen in adducts **1a**−**14a** was investigated by performing the photocatalyzed reaction of **6** with C_{60} first in a mixture of dry C_6H_5Cl/CD_3CN (85:15) and then in a mixture of C_6H_5Cl/CH_3CN containing 1% D_2O. No measurable deuteration resulted in the first case, while the product **6a** was obtained with high deuterium incorporation on the C_{60} core under the latter set of conditions, suggesting the intermediacy of the fullerene anion in the reaction mechanism (see Supporting Information). Given the inherent acidity of the C_{60}−H proton in **6a**, the H/D exchange could potentially occur after the formation of **6a**. However, this possibility was excluded since no H/D exchange observed (^{1}H NMR) when a deaerated solution of **6a** was irradiated in the presence of TBADT and 1% D_2O, under the same experimental conditions (see Supporting Information).

To gain further insight into the reaction mechanism, we measured the intra- and intermolecular kinetic isotope effects (KIE). In general, deuterium isotope effects are a powerful tool to probe the transition state and provide valuable information on the extent of bond breaking and bond making.[23] To this end, we prepared 4-methoxybenzaldehyde-d_4 (**3**-d_4) and benzene-1,4-dicarboxaldehyde-d_1 (**4**-d_1), respectively (Chart 1). Substrate 4-methoxybenzaldeyde (**3**-d_0) is commercially available.

Chart 1. Aldehydes Used in this Study for KIE Measurements



3-d_0 **3**-d_4 **4**-d_1

To determine the primary isotope effect, a mixture of C_{60} and a 100-fold excess of equimolar quantities of **3**-d_0 and **3**-d_4

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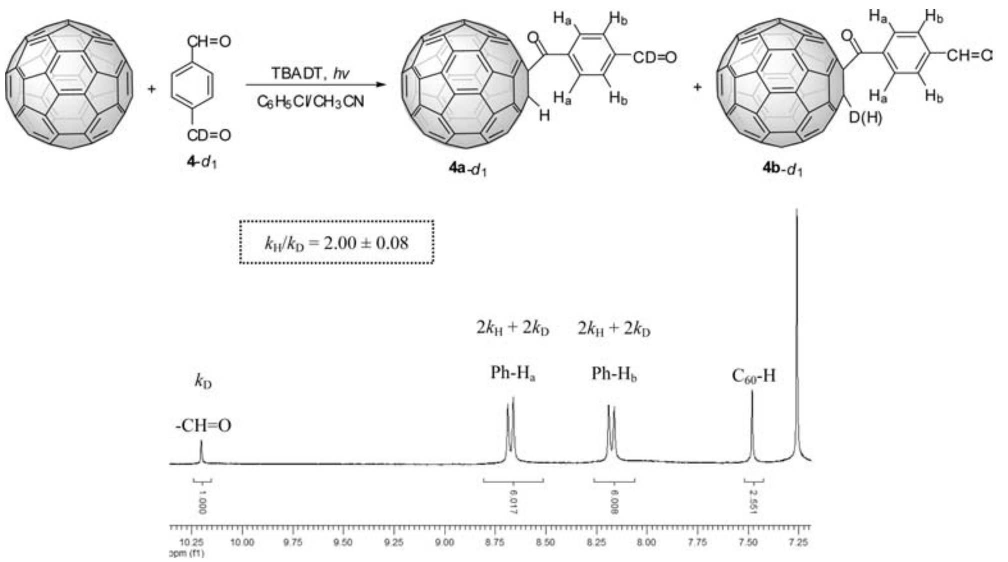
(20) (a) Rudolph, A.; Weedon, A. C. *Can. J. Chem.* **1990**, *68*, 1590–1597. (b) Newcomb, M.; Johnson, C. C.; Manek, M. B.; Varick, T. R. *J. Am. Chem. Soc.* **1992**, *114*, 10915–10921. (c) Adam, W.; Curci, R.; D'Accolti, L.; Dinoi, A.; Fusco, C.; Gasparrini, F.; Kluge, R.; Paredes, R.; Schulz, M.; Smerz, A. K.; Veloza, L. A.; Weinkötz, S.; Winde, R. *Chem. Eur. J.* **1997**, *3*, 105–109.

(21) Boeck, B. D.; Herbert, N. M. A.; Harrington-Frost, N. M.; Pattenden, G. *Org. Biomol. Chem.* **2005**, *3*, 328–339.

(22) Karabatsos, G. J.; Sonnichsen, G. C.; Hsi, N.; Fenoglio, D. J. *J. Am. Chem. Soc.* **1967**, *89*, 5067–5068.

(23) (a) Melander, L.; Saunders, W. H. *Reaction Rates of Isotopic Molecules*; John Wiley and Sons: New York, 1980. (b) Carpenter, B. K. *Determination of Organic Reaction Mechanisms*; John Wiley and Sons: New York, 1984.

Scheme 4. Determination of the Intramolecular Primary KIE in the Reaction of **4**-d_1 with C_{60} by ^1H NMR Spectroscopy

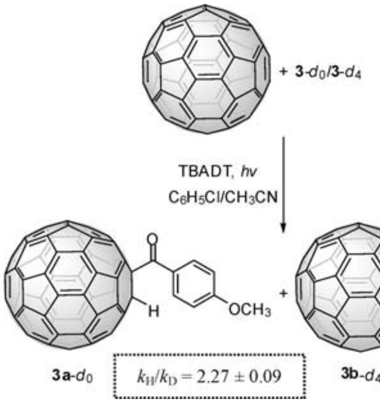


(intermolecular KIE), as well as **4**-d_1 (intramolecular KIE) in separate experiments, was dissolved in a mixture of dry C_6H_5Cl/CH_3CN (85:15) with 0.4 equiv of the TBADT catalyst. The experimental conditions were identical to those described above. The kinetic isotope effects were determined by the ^1H NMR integration of the appropriate proton signals of the products.

In the case of the intramolecular isotopic competition between the *p*-formyl substituents of **4**-d_1, the primary isotope effect is proportional to the ratio of **4a**-d_1/**4b**-d_1 (Scheme 4). Integration of the H_a or the H_b phenyl hydrogens of both **4a**-d_1 and **4b**-d_1 at 8.67 and 8.18 ppm, respectively, as well as the aldehyde hydrogen signal of **4b**-d_1 at 10.20 ppm, determines the intramolecular isotope effect k_H/k_D (**4a**-d_1/**4b**-d_1 = $k_H/k_D = 2.00 \pm 0.08$, Scheme 4).

In a similar manner, the intermolecular KIE in the reaction of C_{60} with **3**-d_0/**3**-d_4 was found to be $k_H/k_D = 2.27 \pm 0.09$ (see also Supporting Information). Integration of the methoxy hydrogens of **3a**-d_0, as well as the phenyl hydrogens of both **3a**-d_0 and **3b**-d_4, determines the intermolecular primary isotope effect k_H/k_D (**3a**-d_0/3**b**-d_4 = $k_H/k_D = 2.27 \pm 0.09$, Scheme 5).

Scheme 5. Intermolecular Primary KIE in the Reaction of **3**-d_0/**3**-d_4 with C_{60}



The substantial primary isotope effects shown in Table 2, indicate a rate-determining C−H(D) bond breaking in the transition state of the first slow carbonyl radical forming step. This is a typical primary isotope effect value ($k_H/k_D \approx 2-3$), indicating the limiting step in several organic reactions.[23] Notably, in both cases the adducts **4b**-d_1 and **3b**-d_4, from which the k_D is derived, are partially deuterated (regarding the C_{60}−H hydrogen atom). This result provides further support that the intermediate RC_{60}^- can also be trapped by a proton originated from the reaction moisture; it is consistent with the deuteration observed in the reaction of **6** with C_{60}, in the presence of 1% D_2O.

Table 2. Primary Intra- and Intermolecular Isotope Effects for the Reaction of C_{60} with **4**-d_1 and **3**-d_0/**3**-d_4

substrate	k_H/k_D[a]
4-d_1	2.00 ± 0.08 (intramolecular)
3-d_0/**3**-d_4	2.27 ± 0.09 (intermolecular)

[a] The isotope effects were determined by ^1H NMR integration of the appropriate hydrogen absorptions. The error was 0.04. Each value is the average of three consecutive measurements.

Scheme 6 depicts a mechanistic approach of this carbonyl functionalization of fullerene C_{60}, consistent with the results described in the preceding discussion. The process should be initiated by the photoexcited TBADT ($W_{10}O_{32}^{4-*}$) through a hydrogen atom abstraction (HAT) from the aldehyde substrate.[24] In addition, control experiments showed that in the absence of TBADT and/or *hv* no reaction occurred for aldehydes **5**−**14** for several hours. Consequently, it is reasonable to assume that the fullerene anion is formed via an electron transfer process from the reduced TBADT ($W_{10}O_{32}^{5-}$) catalyst to the triplet excited state of C_{60}.[9a,25,26] The validity of this assumption is further confirmed when comparing the relative redox potential order of the involving species; the redox potential of the couple $W_{10}O_{32}^{4-}/W_{10}O_{32}^{5-}$ ($E_{red} = -0.97$ V/NHE or -1.215 V vs SCE)[24b] is more negative than the first reduction potential of $^3C_{60}^*$ ($E_{red} = 1.14$ V vs SCE),[25a] and as such, the electron transfer from $W_{10}O_{32}^{5-}$ to $^3C_{60}^*$ is expected to proceed spontaneously. Subsequently, the carbonyl radical is trapped by the C_{60} radical anion affording, after protonation, the observed fullerene adducts.[27]

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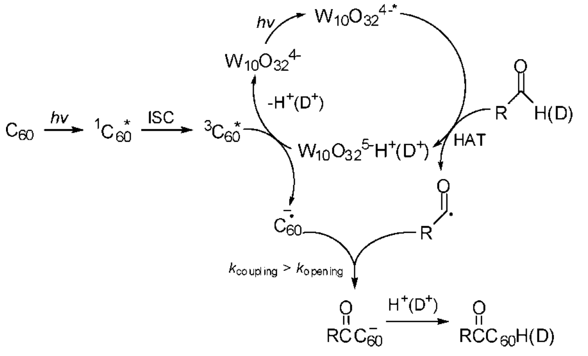
(24) For selected examples, regarding further details on the photoexcitation mechanism of TBADT and its interaction with organic substrates, see: (a) Duncan, D. C.; Fox, M. A. *J. Phys. Chem. A* **1998**, *102*, 4559–4567. (b) Texier, I.; Delaire, J. A.; Giannotti, C. *Phys. Chem. Chem. Phys.* **2000**, *2*, 1205–1212. (c) Tanielian, C.; Seghrouchni, R.; Schweitzer, C. *J. Phys. Chem. A* **2003**, *107*, 1102–1111, and references cited therein. See also refs 7−9.

Scheme 6. Proposed Mechanism for the TBADT-Catalyzed Reaction of Aldehydes with Fullerene C_{60}



It is worth mentioning the unique structure of the resultant ketones **1a**−**14a**, in which an electron-withdrawing group, i.e., the carbonyl group, is directly connected to the [60]fullerene core. This is expected to alter significantly the chemical/physical properties of the [60]fullerene moiety; the resulting C_{60}-based compounds exhibit a remarkable electron-accepting ability,[28] and as such, they could be applied for the construction of [60]fullerene-based donor−acceptor dyad systems.[29] They also possess great synthetic potential due to the presence of a ketone group.

Conclusions

In conclusion, we have developed a straightforward method for the direct acylation of C_{60} which includes the novel reaction of C_{60} with carbonyl radicals mediated by the TBADT catalyst. This free-radical acylation method was found to be highly effective when using a wide range of aldehydes (e.g., aromatic or alkyl); it is directly applicable even in the cases of the cyclopropyl-substituted aldehydes, where rapid rearrangement of the intermediate cyclopropyl acyl radical is potentially possible. We have also established a simple, low-temperature, approach for overcoming decarbonylations encountered in certain acyl radical addition reactions where the acyl radical intermediates are prone to undergo rapid decarbonylation. Further studies were also conducted to gain mechanistic insight into this reaction. On the basis of these results, a mechanistic approach has been provided that rationalizes all the experimental data. This method not only broadens the scope of the fullerene chemistry, thereby opening a new route to a wide variety of previously unexplored fullerene-based materials, but also represents a new strategy of inorganic catalysis in nanocarbon chemistry. Further studies directed to the generality of this methodology for the functionalization of C_{60} are currently underway.

Experimental Section

Some representative experimental procedures are described here. Full experimental details and spectral data for all compounds can be found in the Supporting Information.

General Considerations. Unless otherwise noted, all materials including dry solvents were obtained from commercial suppliers and used without further purification. TBADT was prepared according to procedure reported in the literature.[7b] ^1H and ^{13}C NMR spectra were recorded on Bruker AMX-500 MHz (125 MHz for ^{13}C) and DPX-300 MHz (75 MHz for ^{13}C) spectrometers, in $CDCl_3$, $CDCl_3/CS_2$, or ODCB-d_4 solutions. Chemical shifts are reported in ppm downfield from Me_4Si by using the residual solvent peak as internal standard. FT-IR spectra were recorded on a PerkinElmer Fourier transform infrared spectrometer, using KBr pellets. UV−vis spectra were performed on a Shimadzu MultiSpec-1501 UV/visible spectrometer. HPLC analysis was conducted on a Marathon III instrument equipped with a 5C18-MS (4.6 × 250 mm, Nacalai Tesque) reversed-phase column with detection at 310 nm. A mixture of toluene/acetonitrile (1:1 v/v) was used as eluent at 1 mL/min flow rate. Semipreparative HPLC was performed with a Marathon III instrument equipped with a Cosmosil 5PBB column (10 × 250 mm, Nacalai Tesque) with detection at 310 nm. A mixture of toluene/acetonitrile (4:1 v/v) was used as eluent (unless otherwise noted) at 5 mL/min flow rate. Flash column chromatography was carried out on SiO_2 (silica gel 60, SDS, 230−400 mesh ASTM). Evaporation of the solvents was accomplished with a rotary evaporator or by high vacuum distillation. Negative-ion MALDI spectra were recorded for all the new compounds using DCTB as the matrix. GC-MS analysis was performed on a Shimadzu GC MS-QP5050A apparatus equipped with a Supelco capillary column (MDN-5, 30 m × 0.25 mm, 0.25 μm film thickness) and a 5971A MS detector. Photochemical reactions were carried out by using a 300-W xenon lamp as the light source.

General Procedure for the TBADT-Catalyzed Photochemical Reactions of Aldehydes 1−14 with C_{60}. Unless otherwise noted in the individual procedures described in the Supporting Information, a solution of C_{60} (20 mg, 0.028 mmol) in a mixture of chlorobenzene/acetonitrile 85:15 (80 mL) was added in a 150-mL glass flask containing a magnetic stirring bar. This solution was degassed by performing three freeze−pump−thaw cycles under argon, and then TBADT (18.5 mg, 0.0056 mmol) and the aldehyde substrate (2.7 mmol) were added. The resulting solution was serum-capped and purged for 20 min with argon. This solution was subsequently irradiated at 5−10 °C using an ice water bath, while a constant, slow argon stream was maintained over the solution (the progress of all reactions was monitored by HPLC). Then, the solvent and the aldehydes **1**−**14** were distilled from the reaction mixture under reduced pressure, and the remaining crude product was centrifuged three times with acetonitrile HPLC grade. The isolated product was further purified by flash column chromatography (hexane/toluene 4:1 v/v) and/or semipreparative HPLC (toluene/acetonitrile 4:1 v/v, 5 mL/min flow rate, detection at 310 nm) to afford the final fullerene adducts.

Synthetic Procedure and Spectral Data of 4-Methoxybenzaldehyde-*d*$_4$ (3-*d*$_4$). Methyl 4-Methoxybenzoate-*d*$_3$. Methyl 4-hydroxybenzoate (1.00 g, 6.57 mmol) was dissolved in 12 mL of dry DMF, under an Ar atmosphere. The solution was cooled to 0 °C, and 315 mg (7.88 mmol) of NaH (60% in mineral oil) was added. The mixture was stirred at room temperature for 30 min, and 0.9 mL of CD_3I was added at 0 °C. Stirring was continued at room temperature for 30 min, and then Et_2O (30 mL) was added to the reaction mixture. The mixture was washed three times with brine, dried over $MgSO_4$, and concentrated in vacuo to afford the desired methyl 4-methoxybenzoate-d_3 (1.00 g, 90%). ^1H NMR (500 MHz,

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(25) The lowest excited singlet state ($^1C_{60}^*$) of the fullerene C_{60} almost quantitively decays via intersystem crossing (ISC) to the energetically lower-lying triplet excited state of C_{60} ($^3C_{60}^*$). See: (a) Arbogast, J. W.; Foote, C. S.; Kao, M. *J. Am. Chem. Soc.* **1992**, *114*, 2277–2279. (b) Arbogast, J. W.; Darmanyan, A. P.; Foote, C. S.; Rubin, Y.; Diederich, F. N.; Alvarez, M. M.; Anz, S. J.; Whetten, R. L. *J. Phys. Chem.* **1991**, *95*, 11–12.

(26) Many of the known photochemical reactions involving [60]fullerene have taken advantage of the excited triplet state of [60]fullerene formed by intersystem crossing (ISC) from the singlet excited state. However, the possibility of an electron transfer from $W_{10}O_{32}^{5-}$ to the ground state of C_{60} cannot be excluded.

(27) On the basis of similar studies, the radical coupling/protonation route may be more plausible than the protonation/radical coupling route. See: (a) Alam, M. M.; Sato, M.; Watanabe, A.; Akasaka, T.; Ito, O. *J. Phys. Chem. A.* **1998**, *102*, 7447–7451. (b) Mikami, K.; Matsumoto, S.; Ishida, A.; Takamuku, S.; Suenobu, T.; Fukuzumi, S. *J. Am. Chem. Soc.* **1995**, *117*, 11134–11141.

(28) (a) Martín, N.; Altable, M.; Filippone, S.; Martín-Domenech, A.; Poater, A.; Solà, M. *Chem. Eur. J.* **2005**, *11*, 2716–2729. (b) Keshavarz-K, M.; Knight, B.; Srdanov, G.; Wudl, F. *J. Am. Chem. Soc.* **1995**, *117*, 11371–11372.

(29) Guldi, D. M.; Maggini, M.; Martin, N.; Prato, M. *Carbon* **2000**, *38*, 1615–1623.

$CDCl_3$): 7.99 (d, $J = 8.5$ Hz, 2H), 6.91 (d, $J = 8.5$ Hz, 2H), 3.88 ppm (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$): 166.60, 163.23, 131.43, 122.44, 113.44, 54.36 ppm (hept, $J_{C-D} = 22$ Hz), 51.59; MS: *m/z* = 169 (M − 31, 138).

4-Methoxybenzyl Alcohol-*d*$_5$. To a solution of methyl 4-methoxybenzoate-*d*$_3$ (1.00 g, 5.91 mmol) in anhydrous THF (60 mL) under an Ar atmosphere at 0 °C was added lithium aluminum deuteride $LiAlD_4$ (126 mg, 3 mmol). The reaction was then warmed to room temperature and stirred for 90 min. The mixture was treated with H_2O and 10% NaOH and extracted twice with Et_2O. The layers were separated and the organic phase dried ($MgSO_4$) and concentrated in vacuo to afford the desired 4-methoxybenzyl alcohol-*d*$_5$ (762 mg, 90%). ^1H NMR (500 MHz, $CDCl_3$): 7.27 (d, $J = 8.5$ Hz, 2H), 6.91 ppm (d, $J = 8.5$ Hz, 2H); ^{13}C NMR (125 MHz, $CDCl_3$): 158.64, 132.94, 128.33, 113.49, 63.27 (pent, $J_{C-D} = 21.5$ Hz), 54.04 ppm (hept, $J_{C-D} = 21.75$ Hz); MS: *m/z* = 143 (M − 30, 113).

4-Methoxybenzaldehyde-*d*$_4$ (3-*d*$_4$). 4-Methoxybenzyl alcohol-*d*$_5$ (600 mg, 4.2 mmol) was oxidized to 4-methoxybenzaldehyde-*d*$_4$ (**3**-*d*$_4$) with PCC (1.08 g, 5.0 mmol) in dry CH_2Cl_2 (30 mL) at room temperature (3−4 h), under an Ar atmosphere. The reaction mixture was filtered through a plug of Celite/silica gel to afford 4-methoxybenzaldehyde-*d*$_4$ (**3**-*d*$_4$) (530 mg, 90%). ^1H NMR (500 MHz, $CDCl_3$): 7.83 (d, $J = 8.5$ Hz, 2H), 7.10 ppm (d, $J = 8.5$ Hz, 2H); ^{13}C NMR (125 MHz, $CDCl_3$): 189.92 (t, $J_{C-D} = 26.25$ Hz), 164.20, 131.45, 129.47 (t, $J_{C-D} = 3.37$ Hz), 113.90, 54.30 ppm (hept, $J_{C-D} = 22$ Hz); MS: *m/z* = 138 (M − 60, 78).

Synthetic Procedure and Spectral Data of 1a. Compound **1a** has been prepared following the general procedure described above, by using 20 mg (0.0278 mmol) of C_{60}, 18.5 mg (0.0056 mmol) of TBADT, and 295 mg (2.78 mmol) of benzaldehyde, in a mixture of chlorobenzene/acetonitrile 85:15 (80 mL). The progress of the reaction was monitored by analytical HPLC (5C18-MS, 4.6 × 250 mm, 1 mL/min, toluene/acetonitrile 1:1, 310 nm). The reaction mixture was irradiated at 5−10 °C for 30 min, after which time the solvent was evaporated under reduced pressure. Acetonitrile was then added and the resulting suspension was centrifuged at 4100 rpm for 10 min (three times). Further purification of the resulting precipitate by semipreparative HPLC (5PBB, 10 × 250 mm, 5 mL/min, toluene/acetonitrile 8:2, 310 nm) afforded ca. 8.0 mg of **1a** (0.01 mmol, 35%). IR (KBr): ν (cm^{-1}) = 2915, 1672, 1426, 1224, 1180, 1008, 869, 691, 578, 526; UV−vis ($CHCl_3$): λ_{max} (nm) = 255, 323, 433; MS (MALDI, negative, DCTB): *m/z* 826.157; ^1H NMR (300 MHz, $CS_2/CDCl_3$): 7.36 (s, 1H), 7.68−7.80 (m, 3H), 8.70−8.73 ppm (m, 2H); ^{13}C NMR (75 MHz, ODCB-*d*$_4$): 196.92, 151.23, 150.31, 146.70, 146.53, 146.25, 145.69, 145.67, 145.51, 145.50, 145.01, 144.96, 144.76, 144.71, 144.68, 143.97, 143.65, 142.52, 142.26, 142.00, 141.89, 141.41, 141.39, 141.36, 141.03, 140.93, 140.88, 139.87, 139.37, 135.84, 135.35, 135.22, 132.89, 128.50, 76.76, 57.21 ppm.

Synthetic Procedure and Spectral Data of 11a and 11b. Compounds **11a** and **11b** have been prepared following the general procedure described above, by using 20 mg (0.0278 mmol) of C_{60}, 18.5 mg (0.0056 mmol) of TBADT, and 334 mg (2.78 mmol) of phenylacetaldehyde, in a mixture of chlorobenzene/acetonitrile 85:15 (80 mL). The progress of the reaction was monitored by analytical HPLC (5C18-MS, 4.6 × 250 mm, 1 mL/min, toluene/acetonitrile 1:1, 310 nm). The reaction mixture was irradiated at 5−10 °C for 60 min, after which time the solvent was evaporated under reduced pressure. Acetonitrile was then added and the resulting suspension was centrifuged at 4100 rpm for 10 min (three times). Further purification of the resulting precipitate via flash column chromatography on silica (hexane/toluene 8:2) afforded ca. 2.3 mg of **11a** (0.003 mmol, 10%) and ca. 4.5 mg of **11b** (0.0055 mmol, 20%). The same reaction was also carried out by using 20 mg (0.0278 mmol) of C_{60}, 46 mg (0.014 mmol) of TBADT, and 667 mg (5.56 mmol) of phenylacetaldehyde, at $T = -50$ °C. After 70 min, the reaction was concentrated and purified by flash column chromatography on silica (hexane/toluene 8:2) to afford ca. 8.1 mg of **11a** (0.01 mmol, 35%).

11a: IR (KBr): ν (cm^{-1}) = 2916, 1720, 1493, 1426, 1088, 1037, 752, 703, 575, 527; UV−vis ($CHCl_3$): λ_{max} (nm) = 259, 329, 433; MS (MALDI, negative, DCTB): *m/z* 840.067; ^1H NMR (500 MHz, ODCB-*d*$_4$/CS_2): 7.60 (s, 1H), 7.20−7.34 (m, 5H), 4.88 ppm (s, 2H); ^{13}C NMR (125 MHz, ODCB-*d*$_4$/CS_2): 200.90, 153.56, 150.07, 147.78, 147.55, 147.35, 147.28, 146.82, 146.54, 146.47, 146.45, 146.11, 145.94, 145.87, 145.61, 145.52, 145.04, 144.44, 143.57, 143.31, 143.03, 142.92, 142.66, 142.50, 142.36, 142.04, 141.95, 141.77, 140.92, 140.53, 137.02, 135.40, 133.87, 132.72, 129.26, 79.14, 56.24, 46.37 ppm.

11b: IR (KBr): ν (cm^{-1}) = 1493, 1460, 1452, 1427, 1259, 1215, 1181, 1064, 1024, 807, 760, 744, 722, 697, 662, 575, 546, 525, 512, 475; UV−vis ($CHCl_3$): λ_{max} (nm) = 257, 326, 433, 485; MS (MALDI, negative, DCTB): *m/z* 812.015; ^1H NMR (500 MHz, ODCB-*d*$_4$): 7.77 (d, $J = 7.5$ Hz, 2H), 7.45 (dd, $J_1 = J_2 = 7.5$ Hz, 2H), 7.35 (t, $J = 7.5$ Hz, 1H), 6.52 (s, 1H), 4,65 ppm (s, 2H); ^{13}C NMR (75 MHz, $CS_2/CDCl_3$): 155.23, 153.75, 147.45, 147.29, 146.92, 146.41, 146.37, 146.27, 146.24, 146.17, 145.77, 145.49, 145.43, 145.38, 144.70, 144.56, 143.22, 142.56, 142.19, 142.03, 141.97, 141.90, 141.65, 141.58, 140.21, 139.96, 136.33, 136.06, 135.74, 131.39, 128.81, 127.82, 65.85, 59.13, 53.20 ppm.

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Supporting Information Available: Detailed experimental procedures, spectral data, ^1H and ^{13}C NMR, FT-IR, and UV−vis spectra. This material is available free of charge via the Internet at http://pubs.acs.org.

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