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$AlCl_3$-Catalyzed Tandem Acetylation of Hydroarylated [60]Fullerenes

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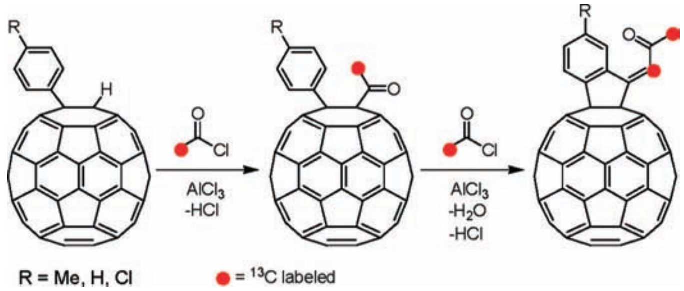
ABSTRACT



The $AlCl_3$-catalyzed acetylation of 1,2-hydrophenylated [60]fullerenes, HC_{60}-Ar, proceeded via a sequential manner involving the acetylation at the hydrogenated fullerene carbon, the following intramolecular cyclization with the adjacent aryl group, the facile loss of water, and the second acetylation of the generated indenylidene double bond. However, the similar reaction of the hydrobiphenylated analogue brought about the normal acetylation at the terminal aromatic ring prior to the same sequential reactions as did hydrophenylated fullerenes.

Chemical modification of fullerenes has attracted significant attention in view of the biological and electronic applications.[1] Although such modification has been well documented for nucleophilic additions and cycloadditions like Bingel, Prato, Diels−Alder, and Huisgen reactions, little is known on electrophilic addition such as Friedel−Crafts hydroarylation.

In 1991, Olah et al. reported that the $AlCl_3$-catalyzed Friedel−Crafts reaction of C_{60} with aromatic compounds gave a mixture of multihydroarylated fullerenes for which the detailed structural analysis was not done.[2,3] Over 15 years later, Nakamura et al. and our group independently clarified the structures of mono-, bis-, and trishydroarylated adducts.[4,5] Recently, various types of monohydroarylated fullerenes have been exclusively synthesized by way of a rhodium-catalyzed reaction of organoborons,[6] and thus the desired functionalization of easily accessible hydroarylated fullerenes can be taken as a new strategy for fullerene modification.

In this paper, we report the $AlCl_3$-catalyzed novel reactions of monohydroarylated [60]fullerenes with acetyl chloride depending on the introduced aryl groups, i.e., (1) for HC_{60}-C_6H_4R (R = *p*-Me, H, *p*-Cl), the direct acetylation at the hydrogenated fullerene carbon followed by the intramolecular cyclization with the adjacent aromatic ring and the loss of water and the subsequent acetylation of the generated indenylidene double bond and (2) for R = *p*-C_6H_5, the preceding normal Friedel−Crafts acetylation at the terminal *p*-position and the following tandem acetylation as above (1).

The 1,2-hydrophenylated fullerenes **2a−c** (R = Me, H, and Cl) at the [6,6]-conjunct bond were prepared by the modified Olah method[5] using 3 equiv of both aromatic compounds and $AlCl_3$ relative to C_{60}. The reactions were carried out in *o*-dichlorobenzene (*o*-DCB) at 30−60 °C under argon atmosphere for 30−80 min to give **2a−c** in 28−42%

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(1) Hirsch, A.; Brettreich, M. *Fullerenes*; Wiley-VCH: Weinheim, 2005.

(2) Olah, G. A.; Bucsi, I.; Lambert, C.; Aniszfeld, R.; Trivedi, N. J.; Sensharma, D. K.; Prakash, G. K. S. *J. Am. Chem. Soc.* **1991**, *113*, 9387.

(3) Olah, G. A.; Bucsi, I.; Ha, D. S.; Aniszfeld, R.; Lee, C. S.; Prakash, G. K. S. *Fullerene Sci. Technol.* **1997**, *5*, 389.

(4) Iwashita, A.; Matsuo, Y.; Nakamura, E. *Angew. Chem., Int. Ed.* **2007**, *46*, 3513.

(5) Tochika, S.; Kato, M.; Kuang, C.; Kokubo, K.; Oshima, T. *Abstracts of the 31st Fullerene-Nanotubes General Symposium* **2006**, 62.

(6) Nambo, M.; Noyori, R.; Itami, K. *J. Am. Chem. Soc.* **2007**, *129*, 8080.

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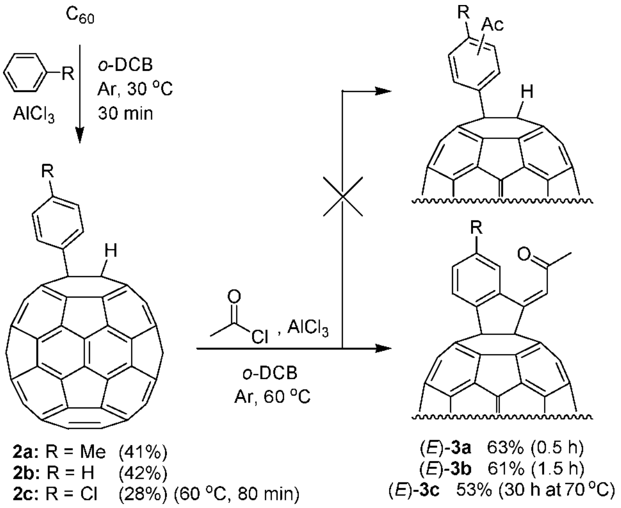
yields. These adducts **2a**−**c** were then treated with 10 equiv of acetyl chloride in the presence of 10 equiv of $AlCl_3$ in *o*-DCB at elevated temperature (60−70 °C) under argon atmosphere for 0.5−30 h (Scheme 1).

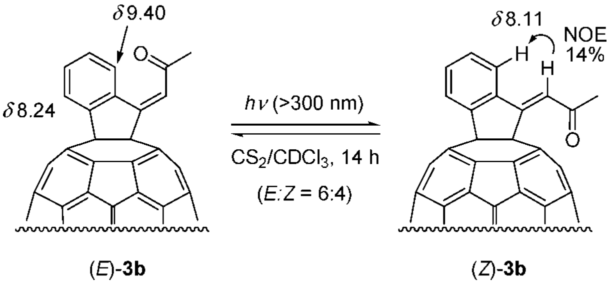
Scheme 1. Synthesis of Hydroarylated Fullerenes **2a**−**c** and the Following $AlCl_3$-Catalyzed Acetylation



It is very interesting that these reactions brought about no Friedel−Crafts acetylation on the introduced phenyl ring but instead provided β-acetyl-substituted fullereno-indenylidenes **3a**−**c** in moderate to good yields (53−63% relative to **2** used). The ^{1}H NMR spectrum of **3b** indicated the presence of an *o*-phenylene bridge (two dd at δ 7.67 and 7.78 and two d at 8.24 and 9.40) and the acetyl Me (δ 2.53) and the vinyl H (7.72). It was also confirmed from the ^{13}C NMR (δ 32.4 and 197.2) and LCMS (m/z = 864) that **3b** has the structure of a β-acetyl-substituted fullerenoindenylidene with C_s symmetry.[7]

On the basis of the differential NOE measurement of **3b**, we attempted to determine the geometry of the olefinic double bond. However, no recognizable correlation was observed between the aromatic proton and either the vinyl or the methyl proton. However, we can suppose its structure as *E*-form from the unusual downfield shift of one aromatic proton (δ 9.40), probably because this proton strongly suffers the deshielding effect of the conformationally restricted facing carbonyl group. Another downfield shift for the *o*-proton (δ 8.24) may be rationalized by the strong paramagnetic current due to the underlying pentagon ring.[8] This geometrical assignment was unequivocally confirmed by the observation of *E*−*Z* photoisomerization of (*E*)-**3b** by irradiation with a medium-pressure mercury lamp (>300 nm) for 14 h to afford a 6:4 mixture of *E* and *Z* at the photostationary state (Scheme 2). The *Z*-isomer demonstrated the NOE correlation between the aryl and the vinyl proton in addition to the noticeable upfield shift of the relevant aromatic proton (δ 9.40 → 8.11).

Scheme 2. *E*−*Z* Photoisomerization of Cyclized Fullerene **3b**



To gain some information on the mechanism, we conducted an isotope-labeled experiment using a ^{13}C-labeled acetyl chloride at the methyl carbon in the reaction with **2b**. A mass spectrum of the ^{13}C-labeled product (*E*)-**3b** showed the increased molecular ion peak by 2 mass numbers (m/z from 864 to 866), indicating the introduction of two ^{13}C-labeled carbon atoms into the product (*E*)-**3b**. The ^{1}H NMR spectrum of this product exhibited a typical ^{13}C−^{1}H coupling for the methyl proton (J = 127 Hz) and the vinyl proton (151 Hz). On the basis of these results, a possible mechanism for the formation of **3b** is depicted in Scheme 3. Thus, the ^{13}C-labeled carbons were sequentially incorporated as the *exo*-olefinic carbon and the terminal methyl carbon via a novel tamdem acetylation reaction.[9]

According to this mechanism, first the $AlCl_3$-catalyzed direct electrophilic acetylation on the fullerene cage gives the fullerenyl ketone **A**, losing a proton. Then, the acid-catalyzed 5-*exo-trig* cyclization followed by dehydration affords fullerenoindenylidene **B**. The indenylidene **B** can undergo the second acetylation at the terminal methylene carbon to give the β-acetyl indenylidene **3** with *E*-form avoiding the larger steric hindrance with the fullerene surface than with the aromatic ring. The reaction was accelerated by introduction of the electron-donating *p*-substituent in the order of **2a** > **2b** > **2c** (Scheme 1), implying that the rate-determining step is the nucleophilic attack of the adjacent aromatic ring to the carbonyl group in the favorable 5-*exo-trig* cyclization.[10,11]

Here, we have a mechanistic question as to why the hydrophenylated **2b** underwent not the usual Friedel−Crafts acylation but the displacement of the protruding hydrogen atom by an acetyl group. Two reasons are conceivable: (1) the acceptor fullerene core considerably reduces the nucleo-

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(7) The C_s symmetry was confirmed by the presence of 28 peaks (2C) and 2 peaks (1C) for the different sp^2 fullerene carbons, consisting with the 1,2-addition to the [6,6]-bond.

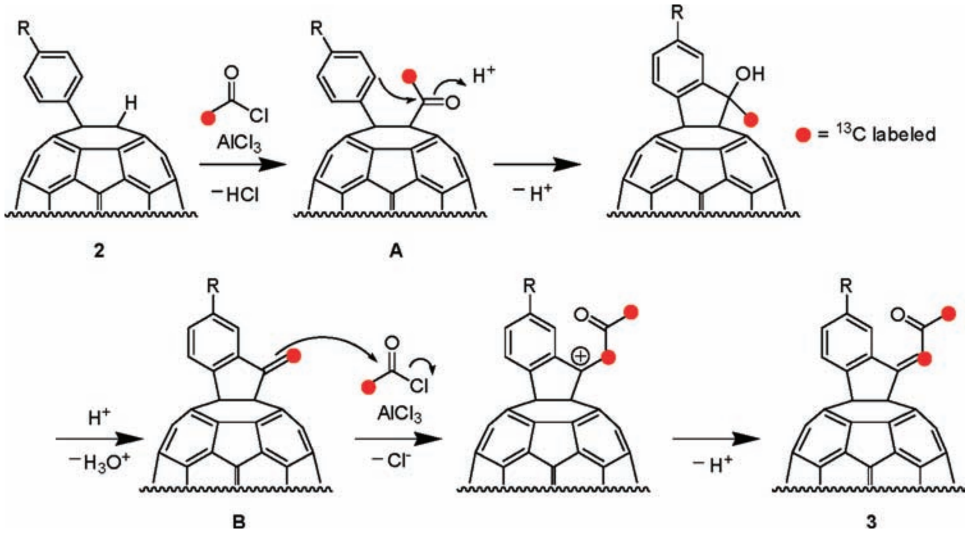
(8) (a) Pasquarello, A.; Schluter, M.; Haddon, R. C. *Science* **1992**, *257*, 1660. (b) Prato, M.; Suzuki, T.; Wudl, F.; Lucchini, V.; Maggini, M. *J. Am. Chem. Soc.* **1993**, *115*, 7876.

(9) Ho, T.-L. *Tandem Organic Reactions*; John Wiley & Sons: New York, 1992.

(10) Baldwin, J. E. *J. Chem. Soc., Chem. Commun.* **1976**, 734.

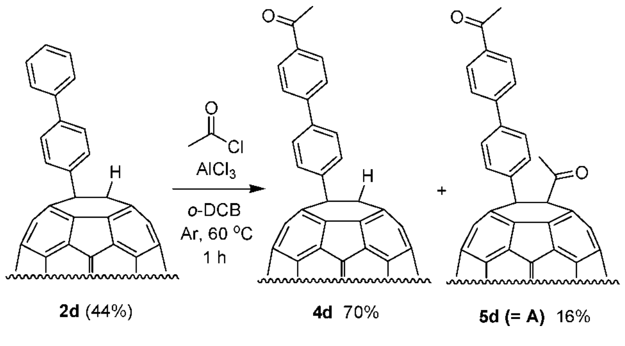
(11) Such a Lewis acid catalyzed 5-*exo-trig* cyclization of the phenyl group to carbonyl function has been reported for electron-deficient ketones such as 1-trifluoromethyl-3-phenylpropanone: Aubert, C.; Bégué, J.-P.; Bonnet-Delpon, D.; Mesureur, D. *J. Chem. Soc., Perkin Trans. 1* **1989**, 395.

Scheme 3. Possible Mechanism for $AlCl_3$-Catalyzed Intramolecular Cyclization of Hydrophenylated Fullerene **2** with Acetyl Chloride



philicity of the introduced phenyl group, and (2) fullerenyl hydrogen is intrinsically active toward the strong electrophile such as an acyl cation. Therefore, according to above (1), we felt that the more remote aromatic ring like in the biphenyl group might allow a possible acylation in the present reaction conditions. Indeed, a similar reaction of hydrobiphenylated fullerene **2d** provided the expected product **4d** in 70% yield along with the further acyl-introduced fullerenyl ketone **5d** (corresponding to **A**) without any cyclized product (Scheme 4). This finding implies that the acceptor fullerene core exerts the appreciable electron withdrawal on the directly connected aromatic ring.

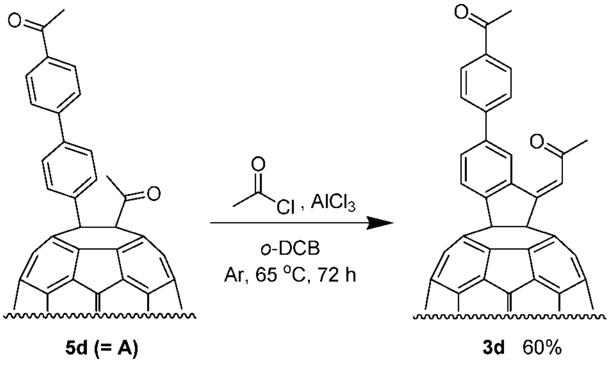
Scheme 4. $AlCl_3$-Catalyzed Acetylation of Hydrobiphenylated Fullerene **2d** with Acetyl Chloride



The structures of **4d** and **5d** were confirmed by ^{1}H and ^{13}C NMR as well as LCMS with the APPI method. Especially, the ^{1}H NMR spectrum of compound **5d** displayed the presence of two acetyl groups (δ 2.58 and 2.63) and two sets of aromatic AB quartet protons. Similar to **2d**, the ^{13}C NMR spectra of **4d** and **5d** apparently indicate the 1,2-addition on the [6,6]-bond with C_s symmetry: 28 peaks (2C) and 2 peaks (1C) for the different sp^2 carbons of the fullerene core. The lower-field shift of one of the fullerene sp^3 carbons of **5d** (δ 81.9 vs 69.9) is strongly suggestive of the direct bonding of the acetyl group on the fullerene surface.

Compared to the possible intermediate **A**, the persistency of **5d** for the 5-*exo*-*trig* reaction may be attributed to the substitution of the *p*-acetylphenyl group which will significantly reduce the nucleophilicity of the parent aromatic ring as in the case of **2c**. However, the prolonged reaction (72 h) led to the formation of the expected **3d** in 60% yield (Scheme 5).

Scheme 5. $AlCl_3$-Catalyzed Intramolecular Cyclization of Fullerenyl Ketone **5d** with Acetyl Chloride



To the best of our knowledge, only two examples have been so far reported for the synthesis of fullerenyl ketones. Mattay et al. first synthesized a fullerenyl ketone by photoinduced electron transfer reaction of C_{60} with propanal.[12] Recently, Saigo et al. found that the ring-opening reaction of aminomethano[60]fullerenes gives several fullerenyl ke-

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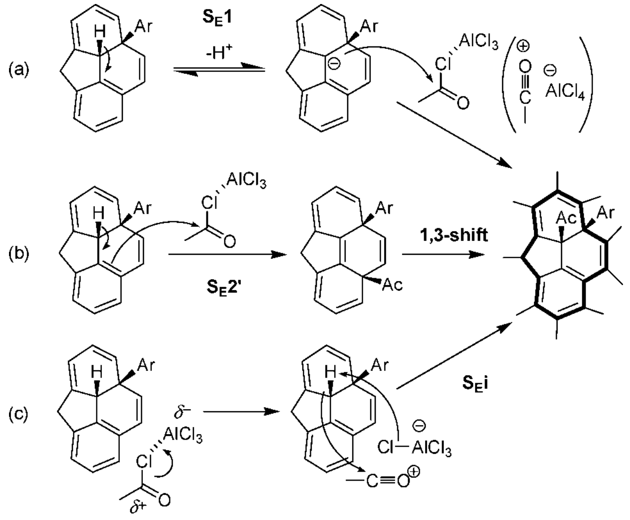
(12) Siedschalag, C.; Luftman, H.; Wolff, C.; Mattay, J. *Tetrahedron* **1997**, *53*, 3587.

tones.[13] Accordingly, the reaction mechanism for the present acetyl substitution of fullerenyl hydrogen C−H is quite interesting since the cage fullerene cannot undergo a S_E2 (back) reaction.[14] Some other conceivable mechanisms (a−c) are shown in Scheme 6. Although a S_E2' reaction[15] (b) seems to be possible, the subsequent thermally forbidden 1,3-acyl-migration is needed. On the other hand, a S_E1 mechanism (a) is likely to occur on the basis of the fact that the fullerene C−H bond has a relatively high dissociation constant (pK_a = 4.7 for $C_{60}H_2$ and 5.7 for t-$BuC_{60}H$).[16] However, owing to the acidic nature of the fullerenyl C−H bond, a possible S_Ei mechanism[17] (c) can not be thoroughly ruled out in the presence of an acylium cation complex with $AlCl_4^-$.

In conclusion, we found two novel acetylation reactions of monohydroarylated fullerenes with acetyl chloride, such as a direct acetylation by substitution of hydrogen on the fullerene moiety and the following tandem acetylation associated with intramolecular cyclization and loss of water. Although the mechanism for the first direct acetylation is still unclear at the present stage, the observed reaction on the fullerene surface is quite unusual and unique.

Scheme 6. Possible Mechanisms for $AlCl_3$-Catalyzed Direct Acetylation on the Fullerene Cage with Acetyl Chloride[a]



[a] Only the reaction site is drawn for clarity.

Supporting Information Available: Experimental procedures and compound data for new compounds (E)-**3a**−**d**, (Z)-**3b**, **4d**, and **5d**. This material is available free of charge via the Internet at http://pubs.acs.org.

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(14) Smith, M. B.; March, J. *March's Advanced Organic Chemistry*, 5th ed.; John Wiley & Sons: New York; Chapter 12, p 760.

(15) Buckle, M. J. C.; Fleming, I.; Gil, S. *Tetrahedron Lett.* **1992**, *33*, 4479.

(16) Niyazymbetov, M. E.; Evans, D. H.; Lerke, S. A.; Cahill, P. A.; Henderson, C. C. *J. Phys. Chem.* **1994**, *98*, 13093.

(17) (a) Winstein, S.; Traylor, T. G.; Garner, C. S. *J. Am. Chem. Soc.* **1955**, *77*, 3741. (b) Abraham, M. H.; Hill, J. A. *J. Organomet. Chem.* **1967**, *7*, 11.