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Novel Cycloaddition Reaction of [60]Fullerene with Carbonyl Ylides Generated from Epoxides

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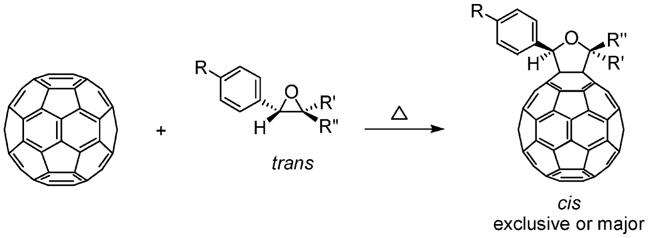
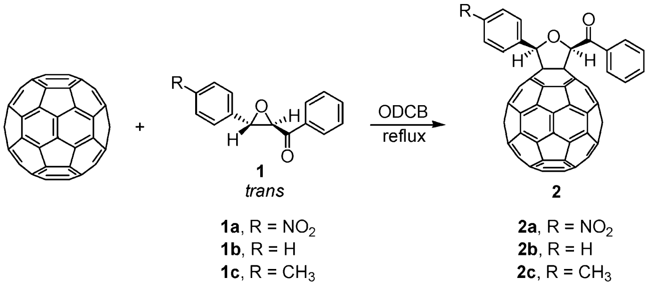


The thermal reaction of [60]fullerene (C_{60}) with the carbonyl ylides generated in situ from *trans*-epoxides to give C_{60}-fused tetrahydrofuran derivatives has been investigated. The reaction of C_{60} with *trans*-2-benzoyl-3-aryloxiranes afforded only cis-products, while the reaction of C_{60} with 2-cyano-2-ethoxycarbonyl-3-aryloxiranes gave exclusively or predominantly cis isomers. The isomeric distributions of the latter reactions were drastically affected by the substituent on the phenyl ring.

Various types of reactions of fullerenes have been developed to synthesize a great diversity of fullerene compounds,[1] some of which have seen potential applications in material sciences and medicinal chemistry.[2] Among the methodologies for functionalizing fullerenes, the 1,3-dipolar cycloaddition reaction is one of the most commonly used protocols, and a variety of 1,3-dipoles including azomethine ylides, diazo compounds, azides, nitrile oxides, nitrile ylides, nitrile imine, pyarazolinium ylides have been reported to react with fullerenes.[1] However, the reaction of [60]fullerene (C_{60}) with carbonyl ylides has not received much attention. Nair and co-workers reported the reaction of C_{60} with five- and six-membered cyclic carbonyl ylides generated in situ from diazo ketones in the presence of $Rh_2(OAc)_4$, while the reaction of C_{60} with a seven-membered cyclic carbonyl ylide failed.[3] Wudl and co-workers described a similar reaction of C_{60} with diazo imides catalyzed by $Rh_2(pbf)_4$ (pbf = perfluorobutyrate).[4] Nevertheless, the products were unstable and were easily reversed to C_{60}, even at room temperature. The formation of these cyclic carbonyl ylides from diazo ketones and diazo imides required the expensive Rh(II) as the catalyst. To the best of our knowledge, there was only one example of the reaction of C_{60} with a noncyclic carbonyl ylide, that is, that from tetracyanoethene oxide.[5] Other carbonyl ylides as 1,3-dipoles applied to the functionalization of C_{60} are yet to be explored. In continuation of our interest in fullerene chemistry,[6] herein we report the novel reaction of C_{60} with *trans*-epoxides to afford exclusively or predominantly the cis-isomers of C_{60}-fused tetrahydrofuran derivatives containing functional groups such as ketone, ester, and cyano groups.

SCHEME 1. Reaction of C_{60} with *trans*-Oxiranes 1a−c



Epoxides undergoing thermal or photochemical 1,3-dipolar cycloaddition via carbonyl ylides with alkenes,[7] alkynes,[8] benzylidene anilines,[9] thioketones,[10] and phosphaalkynes[11] have been well-documented. Due to the electron-deficient-alkene property of C_{60}, we therefore investigated the reaction of C_{60} with epoxides.

We first examined *trans*-2-benzoyl-3-aryloxiranes (**1a−c**), which were prepared according to the reported procedure[12] and their identities confirmed by the typical coupling constant of 2 Hz for the two methine hydrogens in their ^{1}H NMR spectra.[12] A coupling constant of 4 Hz for the two methine hydrogens in the ^{1}H NMR spectra of the cis isomers was usually observed.[13] Surprisingly, the reaction of C_{60} with *trans*-oxiranes **1a−c** in refluxing 1,2-dichlorobenzene gave the C_{60}-fused tetrahydrofuran derivatives **2a−c** with cis-sterochemistry (Scheme 1).

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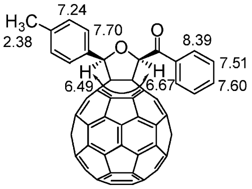

FIGURE 1. Assignment for the chemical shifts of **2c**.

TABLE 1. Reaction Times and Yields for the Reaction of C_{60} with 1a−c

entry	product	R	time (h)	% yield[a]
1	**2a**	NO_2	7	42 (84)
2	**2b**	H	8	39 (76)
3	**2c**	CH_3	7	35 (49)

[a] Isolated yield; that in the parentheses refers to the yield based on consumed C_{60}.

The reaction times and yields for the reaction of C_{60} with *trans*-oxiranes **1a**−**c** in refluxing 1,2-dichlobenzene affording **2a**−**c** are listed in Table 1.

It can be obviously seen from Table 1 that both electron-withdrawing and electron-donating groups on the phenyl ring of the substrates worked well for the reactions shown in Scheme 1. The yields are good and can be up to 84% based on consumed C_{60}. It should be noted that no product was found even after prolonging the reaction time to 24 h when R was a methoxy group. Further study indicated that *trans*-2-benzoyl-3-(4-methoxyphenyl)oxirane decomposed rapidly in refluxing 1,2-dichlorobenzene. Therefore, no 1,3-dipole was generated and the desired product could not be obtained.

The structures of **2a**−**c** were fully identified by their MS, ^1H NMR, ^{13}C NMR, FT-IR, and UV−vis spectra. It was interesting to observe that the reaction of C_{60} with *trans*-oxiranes **1a**−**c** selectively gave cis-products **2a**−**c**. The cis-stereochemistry of **2a**−**c** was substantiated by the NOESY spectrum of **2c**, which clearly showed the NOE between the two methine hydrogens. The NOESY spectrum of **2c** also allowed the assignment of all chemical shifts in its ^1H NMR spectrum in CS_2−$CDCl_3$, as shown in Figure 1.

Encouraged by the good result for the reaction of C_{60} with **1a**−**c**, we extended the substrates to *trans*-2-cyano-2-ethoxycarbonyl-3-aryloxiranes (**3a**−**c**), which were prepared by the procedure reported in the literature.[14] The reaction of C_{60} with *trans*-oxiranes **3a**−**c** in refluxing chlorobenzene was found to afford exclusively cis-isomer (**4a**) or a mixture with cis isomer (**4b**,**c**) as the major product and trans isomer (**5b**,**c**) as the minor product of the C_{60}-fused tetrahydrofuran derivatives (Scheme 2).

The reaction times and yields for the reaction of C_{60} with **3a**−**c** in refluxing chlorobenzene, giving **4a**−**c** and **5b**,**c** are listed in Table 2.

The reaction of C_{60} with **3a**−**c** could proceed in refluxing chlorobenzene, while that with **1a**−**c** required much higher temperature, that is, refluxing 1,2-dichlorobenzene. This can be understood as the two CN and COO groups in **3a**−**c** having a much stronger electron-withdrawing property than a single CO group in **1a**−**c**, thus facilitating the formation of the carbonyl ylides from **3a**−**c**.

TABLE 2. Reaction Times and Yields for the Reaction of C_{60} with 3a−c

entry	product	R	time (h)	% yield[a]	
				4 (cis)	**5** (trans)
1	**4a**	NO_2	40	38 (93)	0 (0)
2	**4b** + **5b**	H	14	34 (58)	8 (14)
3	**4c** + **5c**	OCH_3	1.5	23 (34)	20 (30)

[a] Isolated yield; that in the parentheses refers to the yield based on consumed C_{60}.

From Table 2, it can be seen that both electron-withdrawing and electron-donating groups on the phenyl ring gave satisfactory yields. The combined yields of **4** and **5** were 64−93% based on converted C_{60}. The isomeric distribution of **4** and **5** was dramatically affected by the electronic property of the substituent on the phenyl ring. Only cis-isomer **4a** was formed for the strong electron-withdrawing nitro group, while **4b** was the major product for the nonsubstituted phenyl ring. In contrast, nearly equal amounts of **4c** and **5c** were obtained for the electron-donating methoxy group.

The structures of **4a**−**c** and **5b**,**c** were characterized by their MS, ^1H NMR, ^{13}C NMR, FT-IR, and UV−vis spectra. The ^1H NMR and ^{13}C NMR spectral patterns of isomeric **4** and **5** were very similar, the only noticeable difference was a downfield shift of 0.5−0.7 ppm for the methine hydrogen of **5** (**4b** vs **5b** and **4c** vs **5c**) in the ^1H NMR spectra and a downfield shift of 2−3 ppm for the COO group of **5** (**4b** vs **5b** and **4c** vs **5c**) in the ^{13}C NMR spectra. The attempt to determine the stereochemistry of **4c** and **5c** by their NOESY spectra failed because no NOE between the methine group and the distant ethoxy group was observed for both **4c** and **5c**. However, an AM1 calculation indicated that a hydrogen bond may exist between the methine hydrogen and carbonyl oxygen in the lowest-energy trans-isomer (**5c**), as their distance (2.56 Å) is shorter than the sum of their van der Waals radii (2.72 Å). This hydrogen bond caused the downfield shifts[15] for the methine hydrogen and carbonyl carbon in the NMR spectra of trans-isomers relative to the cis-isomers. Therefore, adducts **4a**−**c** are cis-isomers and compounds **5b**,**c** are trans-isomers. The hydrogen bond can also explain the observed red shift for the absorption of the carbonyl group in compounds **5b**,**c** relative to **4b**,**c** (1757 cm^{-1} for **5b**,**c** vs 1773−1774 cm^{-1} for **4b**,**c**).[15] Similar phenomena for the ^1H and ^{13}C NMR downfield shifts and IR red shifts have been observed for the trans-isomers of fullerene-fused pyrrolidine derivatives.[16]

The possible mechanism for the exclusive or predominant formation of cis-products from *trans*-oxiranes is shown in Scheme 3. In compliance with Woodward−Hoffmann rules for electrocyclic ring opening in four-electron systems, the thermal conrotatory C−C bond cleavage of the *trans*-oxiranes gives 1,3-dipoles **6**, which react with C_{60} to afford cis-products as the single isomers or as the major products. The thermal disrotatory C−C bond cleavage of the *trans*-oxiranes to generate 1,3-dipoles **7** is prohibited. Nevertheless, the C−O bond rotation of 1,3-dipoles **6** could produce some 1,3-dipoles **7**, which then react with C_{60} to give trans-products as the minor products.

In summary, the thermal reaction of C_{60} with the carbonyl ylides generated in situ from epoxides to give C_{60}-fused tetrahydrofuran derivatives has been investigated. The reaction of C_{60} with *trans*-2-benzoyl-3-aryl oxiranes afforded cis-products, while the reaction of C_{60} with 2-cyano-2-ethoxycar-

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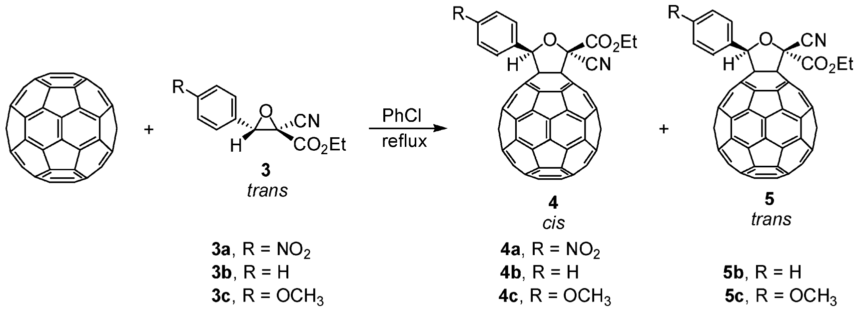
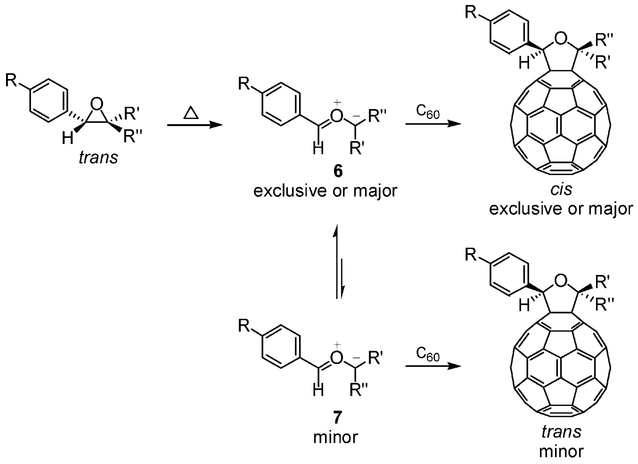
SCHEME 2. Reaction of C_{60} with *trans*-Oxiranes 3a−c



SCHEME 3. Proposed Reaction Mechanism



bonyl-3-aryloxiranes gave only cis-isomer or a mixture of cis- and trans-isomers, for which the isomer distribution was drastically affected by the substituent on the phenyl ring. Further investigation on the inverse of the stereochemistry of the fullerene products relative to the starting *trans*-oxiranes by theoretical calculation is underway.

Experimental Section

Reaction of C_{60} with *trans*-2-Benzoyl-3-aryloxiranes 1a−c. A mixture of C_{60} (54.0 mg, 0.075 mmol) and **1a** (**1b** or **1c**, 0.225 mmol) was dissolved in 1,2-dichlorobenzene (12 mL) and stirred in an oil bath preset at 210 °C for the designated time. The solvent was then evaporated in vacuo, and the residue was separated on a silica gel column eluted with CS_2−toluene mixture to afford unreacted C_{60} and **2a** (**2b** or **2c**). The purities of products **2a**−**c** were checked by HPLC on an Agilent 1100 liquid chromatograph with a diode-array detector using a Cosmosil Buckyprep column (4.6 × 250 mm) with toluene as the eluent at 1 mL/min and were found to be over 98%.

Reaction of C_{60} with *trans*-2-Cyano-2-ethoxycarbonyl-3-aryloxiranes 3a−c. A mixture of C_{60} (54.0 mg, 0.075 mmol) and **3a** (**3b** or **3c**, 0.113 mmol) was dissolved in chlorobenzene (12 mL) and stirred in an oil bath preset at 140 °C for a desired time. The solvent was then evaporated in vacuo, and the residue was separated on a silica gel column eluted with CS_2−toluene mixture to give unreacted C_{60}, **4a** (**4b** or **4c**), and **5b** (**5c**). The purities of adducts **4a**−**c** and **5b**,**c** were checked by HPLC and were found to be over 98%.

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Supporting Information Available: Spectral data of **2a**−**c**, **4a**−**c**, **5b**, and **5c**; MS, ^{1}H NMR, and ^{13}C NMR spectra of compounds **2c**, **4c**, and **5c**; NOESY spectrum of **2c**; AM1-optimized geometries for the lowest-energy conformer of **4c** and **5c** isomers. This material is available free of charge via the Internet at http://pubs.acs.org.

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