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Stereoelectronic Effects in Diastereoselective Formation of Fulleroids

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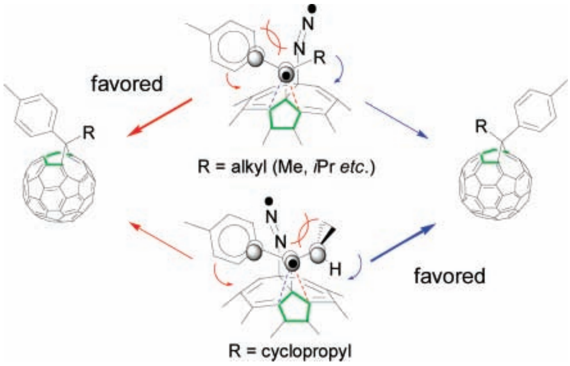
ABSTRACT



The substituent effects on diastereoselective formation of fulleroids in the reactions of C_{60} with various unsymmetrical diazoalkanes were investigated. The steric demand on the stereochemical course of reactions dominated the diastereoselectivity for diazoalkanes bearing aliphatic as well as monosubstituted π-resonating groups, whereas the stereoelectronic effects of coexisting π-resonating aromatic and cyclopropyl groups played a crucial role in the ring closure of the radical intermediates, overriding the steric demand.

It is well-known that C_{60} easily undergoes a variety of addition reactions due to the low-lying LUMO level.[1] In particular, 1,3-dipolar cycloadditions of C_{60} with diazoalkanes have been extensively studied since the pioneering work by Wudl et al. in 1991.[2] The reactions of unsymmetrical diazoalkanes (**1**, $R^1R^2CN_2$, $R^1 \neq R^2$) produce two diastereoisomers of [6,5]open fulleroids (**2** and **3**) and the [6,6]closed methanofullerenes **4** via a nitrogen extrusion of intermediate [6,6]closed pyrazolinofullerenes,[3] depending on the identities of diazoalkanes. In general, these reactions preferentially yield fulleroids in which the bulky group is located above the five-membered ring (pentagon) of the bridged fullerene subunit.[4] In the case of monoaryldiazoalkanes, it was also found that fulleroids bearing an aryl group above the pentagon were predominantly obtained.[5] Such a diastereoselectivity was rationalized by Hirsch et al. on the basis of

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[1] (a) Hirsch, A. *Top. Curr. Chem.* **1999**, *199*, 1−65. (b) Wilson, S. R.; Schuster, D. I.; Nuber, B; Meier, M. S.; Maggini, M.; Prato, M.; Taylor, R. *Fullerene, Chemistry, Physics and Technology*; John Wiley & Sons Inc.: New York, 2000; pp 91−176. (c) Nakamura, Y.; O-Kawa, K.; Nishimura, J. *Bull. Chem. Soc. Jpn*. **2003**, *76*, 865−882. (d) Hirsch, A.; Brettreich, M. *Fullerenes, Chemistry and Reactions*; Wiley-VCH: Weinheim, Germany, 2005; Chapter 4, pp 101−172.

[2] Suzuki, T.; Li, Q.; Khemani, K. C.; Wudl, F.; Almarsson, O. *Science* **1991**, *254*, 1186−1188.

[3] Suzuki, T.; Li, Q.; Khemani, K. C.; Wudl, F. *J. Am. Chem. Soc.* **1992**, *114*, 7301−7302.

[4] (a) Isaacs, L.; Wehrsig, A.; Diederich, F. *Helv. Chim. Acta* **1993**, *76*, 1231−1250. (b) Skiebe, A.; Hirsch, A. *J. Chem. Soc., Chem. Commun.* **1994**, 335−336. (c) Schick, G.; Hirsch, A. *Tetrahedron* **1998**, *54*, 4283−4296. (d) Nakamura, Y.; Inamura, K.; Oomuro, R.; Laurenco, R.; Tidwell, T. T.; Nishimura, J. *Org. Biomol. Chem.* **2005**, *3*, 3032−3038.

[5] (a) Prato, M.; Lucchini, V.; Maggini, M.; Stimpfl, E.; Scorrano, G.; Eiermann, M.; Suzuki, T.; Wudl, F. *J. Am. Chem. Soc.* **1993**, *115*, 8479−8480. (b) Hummelen, J. C.; Knight, B. W.; LePeq, F.; Wudl, F. *J. Org. Chem.* **1995**, *60*, 532−538. (c) Martin, N.; Sanchez, L.; Guldi, D. M. *Chem. Commun.* **2000**, 113−114. (d) Hall, M. H.; Lu, H.; Shevlin, P. B. *J. Am. Chem. Soc.* **2001**, *123*, 1349−1354. (e) Hall, M. H.; Shevlin, P.; Lu, H.; Gichuhi, A.; Shannon, C. *J. Org. Chem.* **2006**, *71*, 3357−3363.

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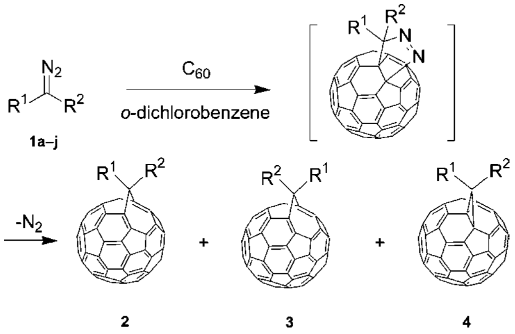
steric demand in the nitrogen evolution step of pyrazoline intermediate.[4c]

However, a detailed study of the steric and electronic effects governing the diastereoselectivity has not been hitherto carried out. Hence, in the present work on the reactions of C_{60} with various unsymmetrical diazoalkanes, we have investigated the substituent effects on the diastereoselective formation of fulleroids to provide more insight into the mechanism and the stereochemical course of these reactions. Here, we wish to report the decisive electronic effects of coexisting aryl and cyclopropyl substituents which reverse the diastereoselectivity deduced from only the steric demand in the fulleroid formation.

The reactions of C_{60} with various diazoalkanes **1a**−**j** were carried out under conditions at ambient temperature as depicted in Table 1. The unstable diazoalkanes **1a**−**c** and **1g**,**h** were generated in situ from the corresponding hydrazones with silver oxide to just undergo rapidly 1,3-dipolar cycloaddition with C_{60} in *o*-dichrolobenzene solution. The reactions of relatively stable aryl-substituted diazoalkanes were performed by adding their toluene solution of **1d**−**f** and **1i**,**j** (<1 equiv), which were prepared by oxidation of hydrazones, into the stirred *o*-dichlorobenzene solution of C_{60}. Purification of the reaction mixtures was made by HPLC on a Buckeyprep column to give a mixture of monoadducts of **2**, **3**, and **4**.[6]

Table 1. Product Distributions of the Reaction of C_{60} with Various Diazoalkanes



entry	1	R¹	R²	product ratio[a] [%]			total yield[b] [%]
				2	3	4	
1	**1a**	Et	Me	65	35		31
2	**1b**	*i*Pr	Me	91	9		23
3	**1c**	*t*Bu	Me	91	5	4	19
4	**1d**	*p*-tolyl	Me	80	10	10	23
5	**1e**	*p*-tolyl	*i*Pr	83	*c*	17	42
6	**1f**	*p*-tolyl	cyclopropyl	26	43	31	35
7	**1g**	cyclopropyl	H	>99	*c*		9
8	**1h**	cyclopropyl	Me	48	44	8	36
9	**1i**	*p*-tolyl	Ph	27	46	27	37
10	**1j**	*p*-anisyl	Ph	15	60	25	33

[a] Determined by ^{1}H NMR. [b] Based on used C_{60}. [c] Trace.

The fulleroids and the methanofullerenes were identified by the measurements of UV−vis, ^{1}H NMR, and ^{13}C NMR spectra. The two diastereomers of fulleroids **2** and **3** both with C_s symmetry were assigned on the basis of the ^{1}H NMR chemical shifts of the diagnostic methyl and methine protons as well as the aryl *o*-protons,[7] since the functional groups above pentagon and hexagon were much affected by the strong paramagnetic and the weak diamagnetic currents, respectively.[8] For instance, as shown in Figure 1, the methine proton of the cyclopropyl group of **2f** and **3f** resonates at δ 1.0 and 3.9, whereas their aromatic protons resonate at δ 7.2−7.8 and 7.0, respectively. Here, the fulleroids with larger R^1 substituent above pentagon and hexagon are referred to as **2** and **3**, respectively.

A survey of Table 1 indicates the following points: (1) aliphatic diazoalkanes **1a**−**c** raised the diastereoselectivity (i.e., **2**/**3** ratio = 2 to 18) with increasing the bulkiness of R_1 in conformity with the steric demand (entries 1−3); (2) *p*-tolyl-substituted **1d** and **1e** also attained the high **2**/**3** ratios as the above aliphatic diazoalkanes (entries 4 and 5); (3) surprisingly, however, the replacement of the R_2 = *i*Pr group of **1e** by a smaller cyclopropyl group reversed the **2**/**3** ratio (=0.6) as found for **1f** (entry 6); (4) but cyclopropyl diazomethane **1g** and diazoethane **1h** obeyed the usual steric demand (entries 7 and 8); (5) also of interest is that the diaryldiazomethanes **1i** and **1j** exhibited the notable diastereoselectivity where the more electron-donating aromatic nucleus tended to locate above the hexagon (entries 9 and 10); (6) in addition, the aromatic diazoalkanes, **1d**−**f**, **1i**, and **1j** provided rather a considerable amount of methanofullerenes **4** (10−31%).

Mechanistically, the N_2-extrusion of pyrazoline intermediates is generally argued to proceed via a concerted orbital controlled $[{}_{\pi}2_s + {}_{\pi}2_s + {}_{\sigma}2_s + {}_{\sigma}2_a]$ rearrangement (path a)[9] or a stepwise biradical pathway (path b),[4c,10] with both paths initially generating the transient [6,5]closed methanofullerenes capable of undergoing a facile valence tautomerisation (V.T.) into [6,5]open fulleroids **2** and **3** (Scheme 1).

Here, it should be noted that the methanofullerenes **4** are only formed in the latter radical mechanism. However, the diazenyl diradical process is needed so as to involve the protruding azenyl radical terminus for the diastereoselective formation of fulleroids since the prior N_2-extrusion would result in the loss of steric discrimination on the radical coupling step (vide infra).

Since the **1a**−**c** provided the high **2**/**3** ratios with a negligible amount of radical product **4**, the reactions of **1a**−**c** are expected to proceed mainly via the concerted mechanism. Therefore, the lager substituent (R_L) tends to locate in the *quasi*-equatorial position of the enveloped pyrazoline ring in conformer A rather than in the axial position in conformer

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(6) Further recycle HPLC treatment provided the pure **4** for diazoalkanes **1d**−**f**, **1h**−**j** and also brought about the enrichment of isomer **2** or **3** for diazoalkanes **1a**, **1f**, and **1h**.

(7) Smith, A. B., III; Strongin, R. M.; Brard, L.; Furst, G. T.; Romanow, W. J.; Owens, K. G.; Goldschmidt, R. J.; King, R. C. *J. Am. Chem. Soc.* **1995**, *117*, 5492−5502.

(8) (a) Pasquarello, A.; Schluter, M.; Haddon, R. C. *Science* **1992**, *257*, 1660−1661. (b) Prato, M.; Suzuki, T.; Wudl, F.; Lucchini, V.; Maggini, M. *J. Am. Chem. Soc.* **1993**, *115*, 7876−7877.

(9) Wallenborn, E.-U.; Haldimann, R. F.; Klärner, F.-G.; Diederich, F. *Chem. Eur. J.* **1998**, *4*, 2258−2265.

(10) (a) Cases, M.; Duran, M.; Mestres, J.; Martin, N.; Solá, M. *J. Org. Chem.* **2001**, *66*, 433−442. (b) Engel, P. S. *Chem. Rev.* **1980**, *80*, 99−150.

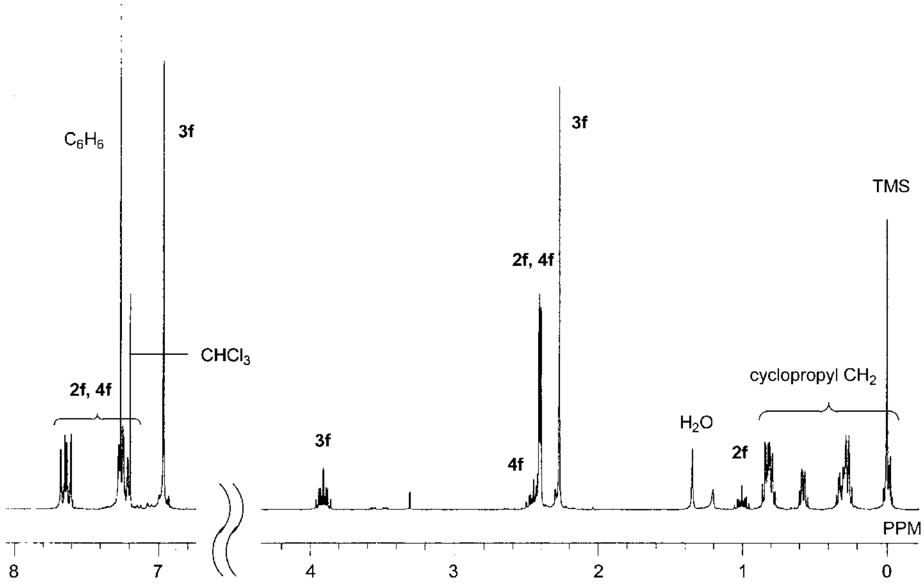
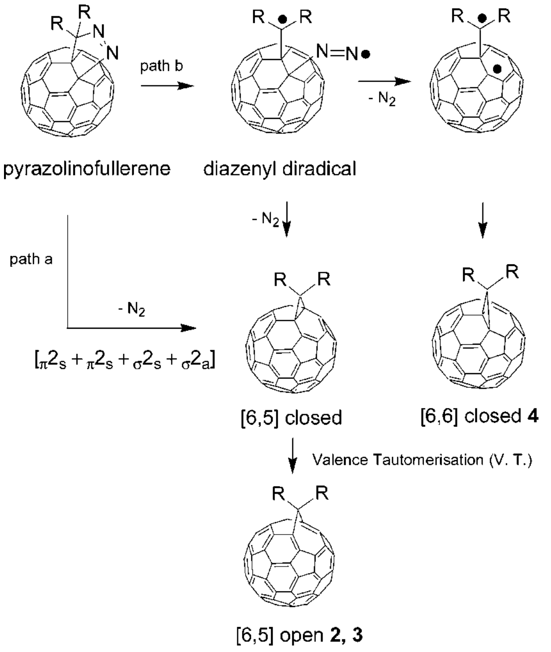


Figure 1. ^1H NMR spectrum of a mixture of **2f**, **3f**, and **4f**.

B (Figure 2a). Hence, the larger equatorial R_L rotates toward the pentagon to give rise to the fulleroid **2**. In contrast, the reactions of **1d**−**f** with a π-resonating tolyl group apparently involve a large extent of radical N_2-extrusion in view of the significant formation of **4** (10−31%). In this possible radical process, as shown in C, the bulky tolyl group (R_L) would rotate away from the azenyl terminus to preferably afford the expected isomer **2** (Figure 2b). However, only the **1f** bearing R^2 = cyclopropyl substituent did give rise to the reverse diastereoselectivity (**2**/**3** = 0.6), although the comparable **1e** bearing the slightly larger R^2 = *i*Pr group exclusively gave the usually expected isomer **2e**. To clarify the peculiar properties of the cyclopropane ring, we carried out the reactions of cyclopropyl-substituted diazomethane **1g** and diazoethane **1h**. However, the observed diastereoselectivity can be explained by the usual steric demand, i.e., cyclopropyl > Me > H, irrespective of whether the N_2-extrusion is concerted or stepwise.

A question is raised on how the cyclopropyl group provided the torque of bringing the coexisting bulky tolyl

Scheme 1. Possible Mechanism of N_2 Extrusion of Pyrazolinofullerene



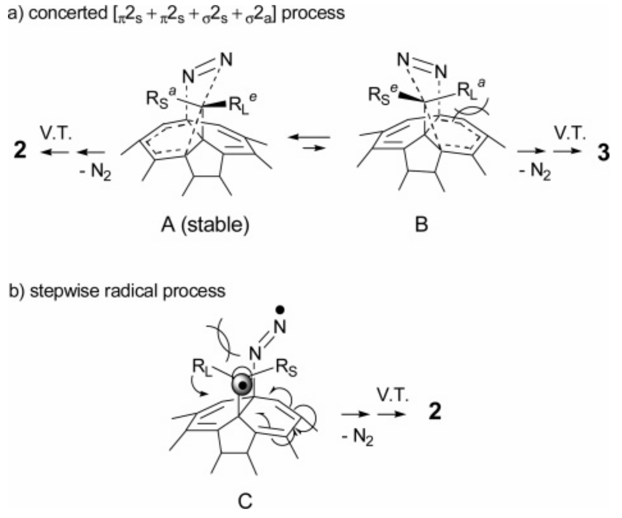


Figure 2. (a) Equilibrated conformers A and B of a concerted transition state: R_L, larger substituent; R_S, smaller substituent; superscripts *a* and *e* represent axial and equatorial, respectively. (b) Radical intermediate C.

group above the unexpected hexagon. As a consequence, we may rationalize the reverse diastereoselectivity by resorting to the cooperative π-resonating effects of tolyl and cyclopropyl groups. Ideally, the most enhanced radical stabilization will be attained in the coplanar conformation for the tolyl group and the bisected one for cyclopropyl group with respect to the spin-centered sp^2-hyblidized plane as shown in intermediate D (Figure 3).[11] In such a biradical intermediate, the bisected cyclopropane ring will necessarily suffer from the more steric repulsion with the azenyl moiety as compared with the facing tolyl plane. Accordingly, the cyclopropyl group is apt to rotate toward the pentagon. In contrast, the *i*Pr group can approach the azenyl moiety by directing the less hindered methine as denoted in the less congested E (Figure 3).

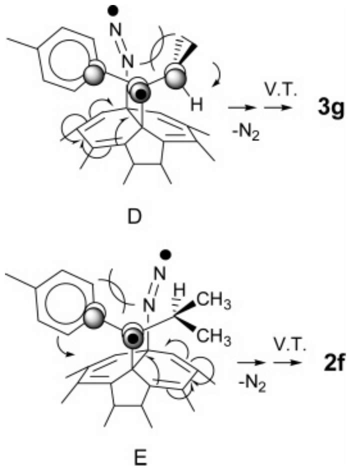


Figure 3. The stereoelectronic effects in diastereoselective ring closure of diazenyl diradical intermediates.

Considering the efficient π-resonating stabilization of the carbon-centered radical, we can regard the reverse diastereoselectivity of diaryl-substituted **1i** and **1j** as strong evidence for the involvement of an electronic effect in the present radical ring-closure.[12] In view of the identical steric bulk of the aromatic portion of the phenyl, *p*-tolyl, and *p*-anisyl substituents, the preferential location of tolyl and anisyl groups above the hexagon can be explained on the basis of the more enhanced radical stabilization by these electron-donating aromatic nuclei. As shown in the equilibrium between F and G (Figure 4), tolyl and anisyl groups are likely to adopt the favorable coplanar conformation with respect to the central sp^2-hybridized plane in order to optimally stabilize the spin center. Hence, the more favored conformer F would provide **3** due to the steric congestion between the less π-resonating phenyl group and the azenyl moiety.

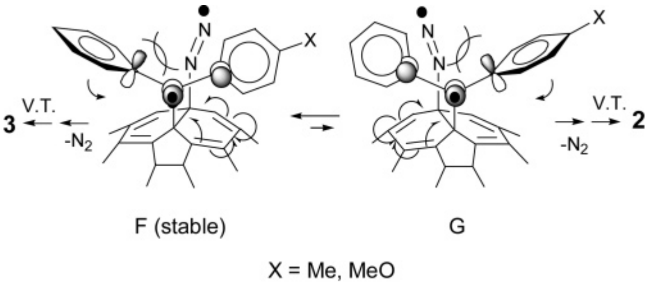


Figure 4. The stereoelectronic effects in diastereoselective ring closure of diazenyl diradical intermediates.

In summary, we found that the steric demand dominates the diastereoselectivity of fulleroid formation for diazoalkanes bearing an aliphatic as well as a monosubstituted π-resonating group, whereas the stereoelectronic effects of coexisting π-resonating groups play an important role in the ring closure of the azenyl radical intermediates, reversing the diastereoselectivity. These findings provide very useful insight into the mechanistic understanding of diazoalkanes−fullerene reactions.

Supporting Information Available: General procedure for the reaction of diazoalkanes with C_{60}, ^1H and ^{13}C NMR spectra of **2**, **3**, and **4**, HPLC charts of the reaction mixtures, ^1H NMR spectra for the determination of product ratios, and $^1H-^1H$ decoupling spectra of the mixture of **2i**, **3i** and **2j**, **3j**. This material is available free of charge via the Internet at http://pubs.acs.org.

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(11) (a) de Meijere, A. *Angew. Chem., Int. Ed. Engl.* **1979**, *18*, 809−886. (b) Engel, P. S.; Nalepa, C. J.; Horsey, D. W.; Keys, D. E.; Grow, R. T. *J. Am. Chem. Soc.* **1983**, *105*, 7102−7107.

(12) Shevlin et al. carried out the similar reaction of diazoalkane **1j** with C_{60} and obtained the mixture of corresponding fulleroids and methanofullerene; see ref 5d.