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1,3-DIPOLAR CYCLOADDITION AS A METHOD FOR SYNTHESIS OF FULLERENE C_{60} DERIVATIVES CONTAINING HETEROCYCLIC MOIETIES

M. A. Yurovskaya and A. A. Ovcharenko

We generalize literature data and our own experimental data on using 1,3-dipolar cycloaddition reactions for synthesis of fullerene C_{60} derivatives containing annelated heterocyclic moieties.

The availability of fullerene C_{60} in macroscopic amounts in recent years has opened up unprecedented possibilities in the new field of "three-dimensional chemistry." In less than 10 years, fullerene has become one of the most popular structural units in organic chemistry. Modification of the fullerene nucleus has attracted the attention of researchers because it can be used as the basis for obtaining fundamentally new materials with valuable biological and technological properties. Fullerene derivatives with annelated heterocyclic moieties should be especially interesting from this standpoint.

The possibilities for chemical modifications of the fullerene C_{60} molecule are due to its pronounced electron-acceptor ability, and hence the chemical reactions which are most typical of it are reactions of nucleophilic, radical, and cycloaddition.

One of the most promising routes for annelation of heterocyclic moieties to the C_{60} molecule is the use of [3+2]-cycloaddition processes involving diverse 1,3-dipoles. In 1995, Hirsch's work was published [1] on reactions of addition to fullerene C_{60}. The detailed review by A. Hirsch includes material on [3+2]-cycloaddition reactions as one of the chapters. Analysis of the literature in the last two years suggests that interest in this area of organic chemistry is as high as ever before. At a symposium on the chemistry of large carbon clusters in 1992, it was reported for the first time that C_{60} was capable of playing the role of a 1,3-dipolarophile [2].

Even though the subject of this report is synthesis of fullerene C_{60} derivatives containing heterocyclic moieties, to begin with we should focus our attention on obtaining methanofullerenes by reaction of C_{60} with different diazo compounds. This is first of all because the process proceeds with intermediate formation of fullerenopyrazolines and secondly because it is specifically in these examples that the possibility of obtaining both closed 6,6- and open 5,6-monocycloadducts in the reaction of fullerene with 1,3-dipoles was demonstrated for the first time. In the first case, cycloaddition proceeds with breaking of the 6-6 double bond; in the second case, it proceeds formally with breaking of the σ bond between five-membered and six-membered rings of the fullerene framework.

Thus, a very broad range of diverse methanofullerenes became available as a result of the reaction of C_{60} with different diazomethanes [3-13], diazoacetates [14, 15], diazoketones [16], and diazoamides [17].

The first step in addition of diazo compounds to the 6-6 double bond is formation of fullerenopyrazolines I. When diazomethane (IIa) was used, the pyrazoline intermediate Ia [4] was isolated and characterized. Extrusion of the nitrogen from the pyrazoline leads to formation of both the closed 6,6 structure III and the open 5,6 structures IV in the form of a mixture of diastereomers in different ratios. In the case of addition of diazo compounds $R^1R^2CN_2$ with $R^1 = R^2$, formation of two bridge structures is possible with the radical R^1 located above the six-membered or five-membered rings of the fullerene.

The open 5,6 isomer IVa, is formed exclusively when thermal extrusion of the nitrogen from the pyrazoline molecule Ia occurs, while in photolysis the major reaction product is the closed 6,6 form IIIa. The isomeric structures are assigned based on NMR spectra [12].

M. V. Lomonosov Moscow State University, Moscow 119899, Russia. Translated from Khimiya Geterotsiklicheskikh Soedinenii, No. 3, pp. 291-297, March, 1998. Original article submitted January 28, 1998.

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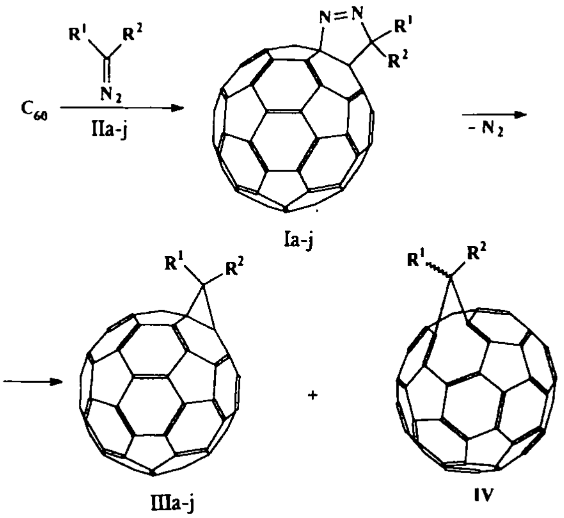
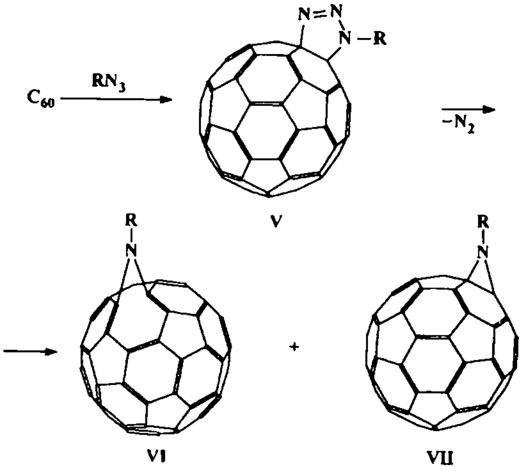
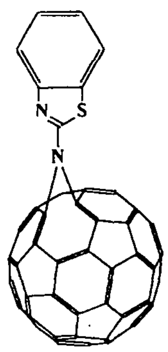


The reaction conditions depend significantly on the structure of the diazo compounds. Thus, addition of diphenyldiazomethane (IIb) is done at room temperature, while boiling in toluene is necessary when using diazoacetates (for example, IIe, f) and diazoamides (for example, IIg). Formation of the open structures IV is considered to be a kinetically controlled process. The closed 6,6 isomers are thermodynamically more stable, so the diastereomeric open 5,6 methanofullerenes may be in equilibrium with the closed 6,6 forms after boiling in toluene for several hours. In the opinion of the authors of [12], thermal isomerization is an electrocyclic process with a [1,5]-sigmatropic shift of the bridging carbon atom.

Cycloaddition of alkylazides to C_{60} in boiling chlorobenzene occurs analogously, through the intermediate triazoline V, which after extrusion of the N_2 rearranges to the open 5,6 aza-bridged isomer VI with the closed 6,6 isomeric adduct VII as an impurity [18].

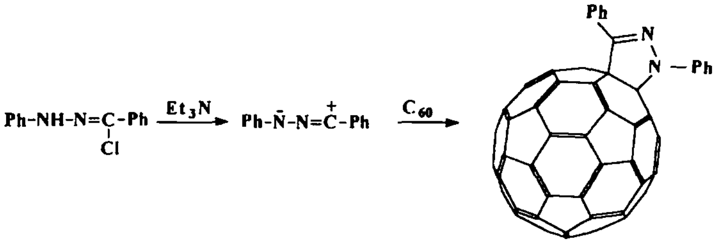


When using arylazides, it was possible to isolate and characterize the triazoline structures V (R = Ph and p-NCC_6H_4). As in the preceding case, thermal extrusion of nitrogen leads to formation of the open aza-bridged structures VI, while the photochemical process yields the closed aziridinofullerenes VII exclusively and isomerization of the fulleroid (open) structures to fullerene (closed) structures is observed under ultraviolet irradiation [19]. Based on FAB [fast atom bombardment] mass spectrometry and ^{13}C NMR spectra, it was observed that addition of 2-azidobenzothiazole to fullerene C_{60} in boiling chlorobenzene leads to formation of the N-hetaryl-substituted π-azidofulleroid VIII and the open bis-adduct π-bisazidofulleroid [20].

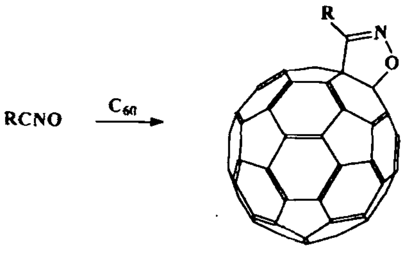


VIII

While 1,3-dipolar cycloaddition of diazo compounds and azides to fullerene C_{60} does not yield stable adducts but rather leads to decomposition of heterocyclic intermediates to methanofullerene and aziridinofullerene and fulleroids, using 1,3-diphenylnitrilimine as the 1,3-dipole (generated *in situ* from N-(α-chlorobenzylidene)-N′-phenylhydrazine when treated with triethylamine) allows us to obtain a stable closed 6,6 product of annelation of a pyrazoline nucleus to fullerene [21].



Analogous derivatives of fullerene C_{60} with an annelated isoxazoline moiety can be obtained by using 1,3-dipolar cycloaddition at the 6-6 bond of nitriloxides [22-25].



R= Me, Et, CO_2Et, p-C_6H_4OMe, p-C_6H_4CHO, $(CH_2)_4CO_2Me$, anthryl

The x-ray diffraction data for isoxazolinofullerene with R = anthryl fully confirms the closed 6,6 fullerene form of the monoadduct formed.

Using active 1,3-dipoles, azomethinylides of general formula $(R^1R^2)C=N^+(R^3)\text{-}C^-\,(R^4R^5)$, makes it possible to obtain pyrrolidinofullerenes [26-29]. Azomethinylides are typically generated *in situ* from easily available precursors. For example, azomethinylide (obtained by decarboxylation of N-methylglycine in the presence of paraform in boiling toluene) when reacted with C_{60} forms N-methylpyrrolidinofullerene in 41% yield [26].

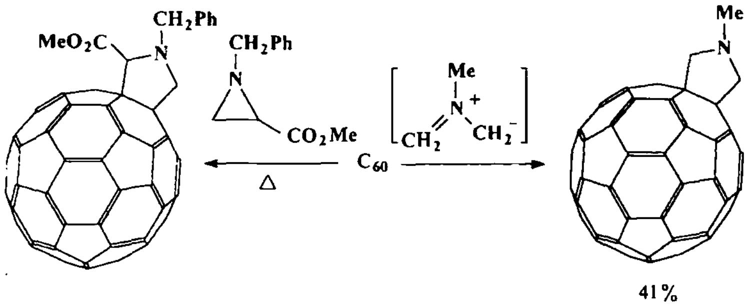


TABLE 1. Reactions of Diazo Compounds with C_{60}

Diazo compound			Condition*	Yield, %	Reference
II	R^1	R^2			
a	H	H	A	44	[4]
b	Ph	Ph	B	-	[3]
c	p-$MeOC_6H_4$	p-$MeOC_6H_4$	B	73	[5]
d	H	p-t-$BuO_2CC_6H_4$	B	-	[10]
e	EtO_2C	EtO_2C	A	10	[12]
f	H	p-t-$BuO_2CC_6H_4$	A	25	[15]
g	H	CO-N-morpholyl	A	25	[17]
h	H	COPh	A	18	[16]
i	H	$COCH{=}CHCO_2CH_3$	A	18	[16]

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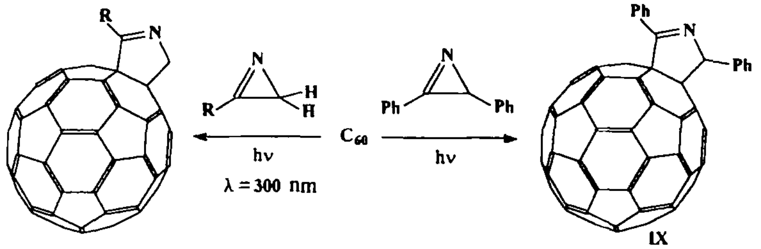
*A) Boiling in toluene; B) reaction in toluene at room temperature.

In addition to the chemical generation route, thermal opening of the aziridine ring may be used to obtain azomethinylides [27]. Data is available on the considerable acceleration of the process of cycloaddition of azomethinylides to C_{60} when treated with microwave radiation [29].

Photochemical cleavage of azirine derivatives leads to formation of nitrilylides: another class of 1,3-dipoles whose cycloaddition to fullerene C_{60} leads to annelation of the pyrroline moiety [19, 30]. Thus, photoreaction of C_{60} with a 10-fold excess of 2,3-diphenyl-2H-azirine leads to formation of 6,6-closed 1,2-(3,4-dihydro-2,5-diphenyl-2H-pyrrolo)fullerene [60] (IX) in 31% yield, obtained together with polyaddition products [30].



IX

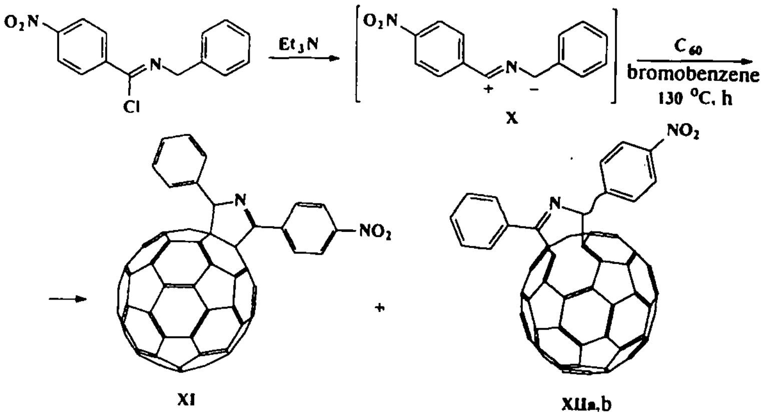
R=Ph (22%), p-ClC_6H_4 (26%), p-$MeOC_6H_4$ (56%)

Mono-substituted aryl-2H-azirines behave similarly [19].

In all cases described previously of annelation of moieties of five-membered heterocycles to fullerene C_{60}, formation of only closed 6,6 fullerene derivatives was observed. Formation of open 5,6 structures was observed only for 1,3-dipolar addition of diazo compounds and azides to fullerene C_{60}, and was considered a secondary result of extrusion of nitrogen from the closed 6,6 heterocyclic intermediates of the pyrazoline or triazoline type.

However, our results suggest that in reactions of 1,3-dipolar cycloaddition of nitrilylides to C_{60}, formation of open 5,6 adducts is also possible. Thus we have shown [31] that cycloaddition of 1-(4-nitrophenyl)-3-phenylnitrilylide (X) (generated *in situ* from N-benzyl-4-nitrophenylimidoyl chloride) to fullerene C_{60} leads not only to formation of 6,6-closed 1,2-[3,4-dihydro-2-phenyl-5-(4-nitrophenyl)-2H-pyrrolo]fullerene [60] (XI), but also to a diastereomeric mixture of two open 5,6 isomers XIIa, b in 2:1 ratio. Furthermore, it has been observed that the double bond in open 5,6 adducts is located at the α position relative to the unsubstituted phenyl ring, while in the closed 6,6 isomer XI it is located α to the nitrophenyl substituent. It has also been established that isomeric structures do not interconvert upon prolonged boiling in bromobenzene.

The reasons for the observed orientation of the observed reactions and the mechanisms for the formation of the closed and open adducts have not yet been conclusively clarified. Further investigations are being carried out on determining the effect of electronic and steric factors on the orientation of the process of 1,3-dipolar cycloaddition of nitrilylides to fullerene C_{60}. But these results cannot be ignored in devising unified theoretical descriptions of the processes of 1,3-dipolar cycloaddition to fullerene.



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REFERENCES

1. A. Hirsch, Synthesis, No. 8, 895 (1995).
2. F. Wudl, A. Hirsch, K. C. Khemani, T. Suzuki, P.-M. Allemand, A. Koch, H. Eckert, G. Srdanov, and H. M. Webb, Fullerenes: Synthesis, Properties, and Chemistry of Large Carbon Clusters, G. S. Hammond and V. J. Kuck (eds.), ACS Symposium Series 468, Washington (1992), p. 161.
3. T. Suzuki, Q. Li, K. C. Khemani, F. Wudl, and O. Almarsson, Science, **254**, 1186 (1991).
4. T. Suzuki, Q. Li, K. S. Khemani, and F. Wudl, J. Am. Chem. Soc., **114**, 7301 (1992).
5. S. Shi, K. C. Khemani, Q. Li, and F. Wudl, J. Am. Chem. Soc., **114**, 10656 (1992).
6. A. B. R. M. Smith III, L. Strongin, G. T. Bzard, W. J. Furst, K. G. Romanov, R. C. Owens, and J. King, J. Am. Chem. Soc., **115**, 5829 (1993).
7. M. Prato, T. Suzuki, F. Wudl, V. Lucchini, and M. Maggini, J. Am. Chem. Soc., **115**, 7876 (1993).
8. M. Prato, V. Lucchini, M. Maggini, E. Stimpfl, G. Scorrano, M. Eiermann, T. Suzuki, and F. Wudl, J. Am. Chem. Soc., **115**, 8479 (1993).
9. L. Issacs and F. Diederich, Helv. Chim. Acta, **76**, 2454 (1993).
10. M. Prato, A. Bianco, M. Maggini, G. Scorrano, C. Toniolo, and F. Wudl, J. Org. Chem., **58**, 5578 (1993).
11. F. Diederich, L. Isaacs, and D. Philp, J. Chem. Soc., Perkin Trans. II, No. 3, 391 (1994).
12. F. Diederich, L. Isaacs, and D. Philp, Chem. Soc. Rev., No. 3, 243 (1994).
13. J. Osterodt, A. Zett, and F. Vogtle, Tetrahedron, **52**, 4949 (1996).
14. F. Wudl, Accts. Chem. Res., **25**, 157 (1992).
15. L. Issacs, A. Wehrsig, and F. Diederich, Helv. Chim. Acta, **76**, 1231 (1993).
16. H. J. Bestmann and C. Moll, Synlett., No. 8, 729 (1996).
17. A. Skiebe and A. Hirch, J. Chem. Soc., Chem. Commun., No. 3, 335 (1994).
18. M. Prato, Q. Li, F. Wudl, and V. Lucchini, J. Am. Chem. Soc., **115**, 1148 (1993).
19. J. Averdung and J. Mattay, Tetrahedron, **52**, 5407 (1996).
20. N. Jagerovic, J. Elguero, and J.-L. Aubagnac, Tetrahedron, **52**, 6733 (1996).
21. Y. Matsubara, H. Tada, S. Nagase, and Z-I. Yoshida, J. Org. Chem., **60**, 5372 (1995).
22. M. S. Meier and M. Poplawska, J. Org. Chem., **58**, 4524 (1993).
23. H. Irngartinger, C. M. Kohler, U. Huber-Patz, and W. Kratschmer, Chem. Ber., **127**, 581 (1994).
24. M. S. Meier and M. Poplawska, Tetrahedron, **52**, 5043 (1996).
25. V. N. Drozd, V. N. Knyazev, F. M. Stoyanovich, F. M. Dolgushin, and A. I. Yanovskii, Izv. Akad. Nauk, Ser. Khim., No. 1, 118 (1997).
26. M. Maggini, G. Scorrano, A. Biianco, C. Toniolo, R. P. Sijbesma, F. Wudl, and M. Prato, J. Chem. Soc., Chem. Commun., No. 3, 305 (1994).
27. M. Maggini, G. Scorrano, and M. Prato, J. Am. Chem. Soc., **115**, 9798 (1993).

28. M. Prato, M. Maggini, C. Giacometti, G. Scorrano, G. Sandona, and G. Farina, Tetrahedron, **52**, 5221 (1996).

29. P. de la Cruz, A. de la Hoz, F. Langa, B. Illescas, and N. Martin, Tetrahedron, **53**, 2599 (1997).

30. J. Averdung, E. Albrecht, J. Lauterwein, J. Mattay, H. Mohn, W. H. Muller, and H. U. ter Meer, Chem. Ber., **127**, 787 (1994).

31. A. A. Ovcharenko, V. A. Chertkov, A. V. Karchava, and M. A. Yurovskaya, Tetrahedron Lett., **38**, 6933 (1997).