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STEREOSELECTIVITY IN CYCLOADDITION OF PHENYLGLYOXYLONITRILE OXIDE TO 7-SUBSTITUTED NORBORNADIENES AND 8-SUBSTITUTED 2-AZABICYCLO[3.2.1]OCT-3,6-DIENES

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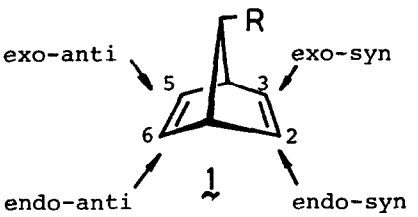
Summary: The cycloaddition of phenylglyoxylonitrile oxide to the 7-substituted norbornadienes 1a-c gives predominantly the endo isomers, but that to the 8-substituted 2-azabicyclo[3.2.1]oct-3,6-dienes 2a,b the exo isomers.

Norbornadiene has been known to exhibit exo selectivity in some reactions with dienes and 1,3-dipoles.[1] On the other hand, recent studies have disclosed that the prevalent formation of endo adducts is observed in the reactions of 7-tert-butoxynorbornadiene with phenyl azide,[2] diphenyldiazomethane,[3] and cyclopentadienes,[4] 7-chloronorbornadiene with diazomethane and diazoethane,[5] and 1,2,3,4,7-pentachloro- and 1,2,3,4,7,7-hexachloronorbornadiene with 1,3-dipoles.[6] These results are discussed on the basis of steric and electronic effects of the 7-substituents. However, the effect of the interaction between two π bonds on the endo prevalence is still uncertain. We have compared the size of the exo/endo ratio in the cycloaddition of phenylglyoxylonitrile oxide to the 7-substituted norbornadienes 1a-c with that to the 8-substituted 2-azabicyclo-[3.2.1]oct-3,6-dienes 2a,b, of which the π-π interaction must be much smaller than that of compounds 1a-c. We report herein that compounds 1a-c undergo preferential endo addition on both anti and syn sides, but compounds 2a,b exo addition on anti side.

The compounds 1a-c and 2a,b were prepared according to the methods described in the literatures.[7] The reactions were carried out as follows: a



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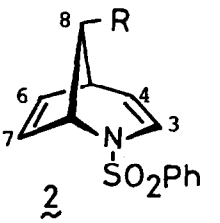
a; R = PhCOO
b; R = Bu^{t}O
c; R = HO



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a; R = PhCOO
b; R = HO

solution of triethylamine (3.6 mmol) in THF (7 ml) was added dropwise to a stirred solution of a mixture of compound 1 or 2 (3 mmol) and α-chloro-α-hydroxyiminoacetophenone (3 mmol), used as a precursor of phenylglyoxylonitrile oxide, in THF (15 ml) at 0 °C for 1 h, and then the mixture was stirred at 0 °C for 2 h. The products were isolated in the usual manner and their structures were determined by elemental analysis and IR and NMR spectra.[8] The results are summarized in Tables 1 and 2.

The cycloaddition of phenylglyoxylonitrile oxide to 1a-c gave mainly three adducts 3a-c, 5a-c, and 6a-c with a prevalence of the endo anti and endo syn isomers, as Table 1 shows. This phenomenon of the endo prevalence is similar to

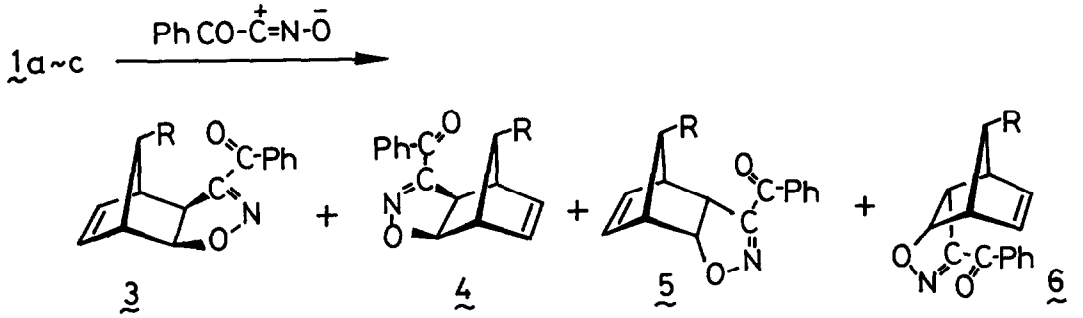


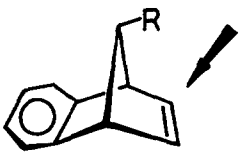
Table 1. The isomer ratios in the cycloaddition of phenylglyoxylonitrile oxide to compounds 1a-c

R	Sum of yield of isomer (%)	Isomer ratio 3	4	5	6	Exo/Endo ratio syn	anti
PhCOO	76	13	6	41	40	0.31	0.15
Bu^tO	75	23	0	37	40	0.62	0
HO	66	12	0	29	59	0.41	0

the results reported recently for the cycloadditions of the electron-rich 1,3-dipoles to 7-chloronorbornadiene and polychloronorbornadienes.[5,6] When the phenyl and p-chlorophenyl groups were used as the substituent(R) at the 7-position of 1, the cycloaddition of phenylglyoxylonitrile oxide resulted in preferential formation of the exo adduct: the yields of the exo-syn, exo-anti, and endo-syn or anti isomers in the cases of R = C_6H_5 and R = p-ClC_6H_4 were 0 and 0, 63 and 63, and 22 and 26 % respectively and the exo/endo ratio 2.4-2.8. This fact indicates that an electron-withdrawing effect of the 7-substituent brings about the endo attack of 1,3-dipoles on the C_2-C_3 and C_5-C_6 double bonds.

In addition to these results, it was found that the cycloaddition of phenylglyoxylonitrile oxide to anti-7-benzoyloxy- and anti-7-tert-butoxy-

benzonorbornadiene (7a,b) gives selectively the exo-syn adducts in 51 and 75 % yields, respectively, with the endo-syn adducts in < 5 % yield. This fact demonstrates that the formation of the endo-syn isomers 5a-c is not merely caused by the steric hindrance of the exo-syn attack. Thus, the $\pi_{2,3}$ and $\pi_{5,6}$ interaction of compound 1 is regarded as an important factor for the endo-syn attack.



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a ; R = PhCOO
b ; R = Bu^{t}O

Next, the cycloaddition of phenylglyoxylonitrile oxide to compounds 2a,b was carried out under the conditions described above. Contrary to the cases of compounds 1a-c, it was found that the exo isomers 8a,b and 9a,b are mainly produced without the formation of the endo isomers, as Table 2 shows. In this reaction, the isomer

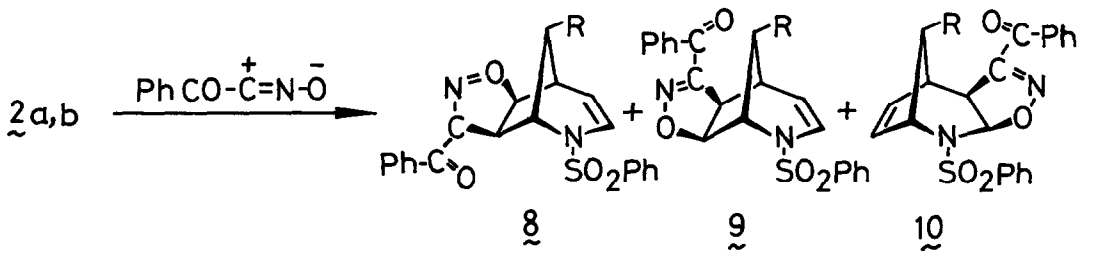


Table 2. The isomer ratios in the cycloaddition of phenylglyoxylonitrile oxide to compounds 2a,b[a]

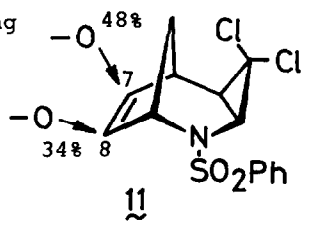
R	Sum of yield of isomer, %	Isomer ratio 8	9	10	Recovery, % 2
PhCOO	64	67	25	8	35
HO	96	75	25	0	0

a. The 1,3-dipolar cycloaddition to the unsubstituted compound 2 (R = H) gave 8 and 9 (R = H) in 65 and 32 % yields respectively.

ratio of 8 to 9, which is in the range of 2.0 – 3.0, would be caused by the homoconjugation of the $\pi_{3,4}$ and $\pi_{6,7}$ bonds, since, in the cycloaddition of phenylglyoxylonitrile oxide to compound 11, the exo adducts having the O-C_7 and O-C_8 bonds are produced in 48 and 34 % yields respectively.

It is worthy of note that the 1,3-dipolar cycloadditions to compounds 2a,b exhibit the exo selectivity in spite of the existence of the electron-withdrawing groups in the methano-bridge. Thus, this fact demonstrates that the interaction between the $\pi_{2,3}$ and $\pi_{5,6}$ bonds of 1a-c is required for the appearance of the electronic effect of the 7-substituent on the endo prevalence. R. Huisgen, et al.[9] have recently reported that norbornene owes its high reactivity only

partially to the strain release, and mentioned that nonequivalent orbital extension[10] would constitute a fitting interpretation of the reactivity in exo cycloaddition. In the cases of the 7-substituted norbornadienes, our results suggest that the endo prevalence is caused by the extension of the $\pi_{2,3}$ and $\pi_{5,6}$ orbitals to the endo side owing to the π-orbital interaction.



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8. The exo/endo orientation of the fused isooxazoline ring was assigned on the basis of the multiplicity of H-2,6: the peaks of the H-2,6 protons of the exo adducts exhibit a doublet ($J_{2,6}$=9.3 Hz), whereas those of the endo adducts a doublet of doublets. The assignment of the syn/anti orientation of the isooxazoline ring was made by the multiplicity of the H-10 proton and the spin-decoupling of the vinyl protons H-8,9: ref. 3 and E. I. Snyder and B. Franzus, J. Am. Chem. Soc., 86, 1166 (1964).
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