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INAPPLICABILITY OF THE "EXO RULE" TO THE 1,3-DIPOLAR CYCLOADDITIONS TO NORBORNADIENES

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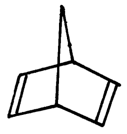
1,3-Dipolar cycloadditions of phenylglyoxylonitrile oxide, benzonitrile-N-phenylimine, or N-phenyl-C-p-nitrophenylnitrone to norbornadiene and 2,3-disubstituted norbornadienes gave the endo-adducts together with the exo-adducts. These observations show that 1,3-dipolar cycloadditions to norbornadienes do not follow the "exo rule" of Alder and Stein.

The "exo rule" was deduced by Alder and Stein from the facts that the 1,3-dipolar cycloadditions of phenyl azide to bicyclic olefins having a moiety of bicyclo-[2.2.1]hydrocarbon skeleton afforded only exo-adducts.[1] Thereafter, many papers have shown that cycloadditions of any 1,3-dipole other than phenyl azide to norbornenes follow the "exo rule". Similarly many 1,3-dipolar cycloadditions to norbornadiene have been reported to follow the "exo rule". For example, the cycloadditions of 1,3-dipoles such as diphenyldiazomethane,[2] dimethyl phenyldiazomethylphosphonate,[3] C,N-diphenylnitrone,[4] N-methyl-C-phenylnitrone,[4] C-propyl-N-cyclohexylnitrone,[4] 3,4-dihydroisoquinoline 2-oxide,[4] benzonitrile-N-phenylimine,[5] and formonitrile oxide,[6] to norbornadiene have always afforded only exo-adducts. A survey of the literature, however, showed that a small amount of the endo-adduct had been obtained together with the exo-adduct in the cycloaddition of phenyl azide to norbornadiene,[7] and that the formation of the endo-adduct in the reaction of benzonitrile oxide with norbornadiene had been assumed.[8] Now, one must consider either that the above two cases are special exceptions which do not follow the "exo rule", or that the "exo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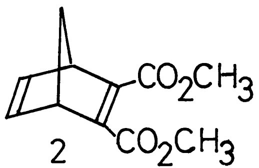
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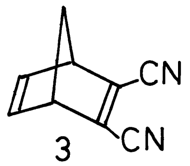
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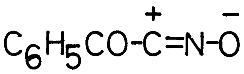
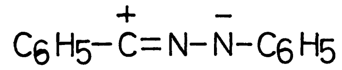
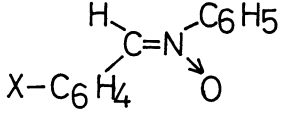

$C_6H_5CO\text{-}\overset{+}{C}{=}N\text{-}\overset{-}{O}$

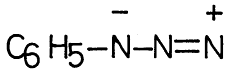
4


$C_6H_5\text{-}\overset{+}{C}{=}N\text{-}\overset{-}{N}\text{-}C_6H_5$

5


6a X = H

6b X = p-NO$_2$

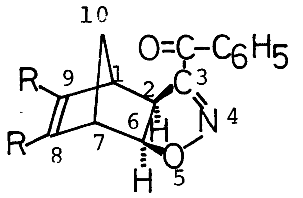

$C_6H_5\text{-}\overset{-}{N}\text{-}N{=}\overset{+}{N}$

7

rule" is not applicable to 1,3-dipolar cycloadditions to norbornadiene. In order to determine either the former or the latter, we carried out the 1,3-dipolar cycloadditions of phenylglyoxylonitrile oxide(4), benzonitrile-N-phenylimine(5), C,N-diphenylnitrone(6a), or N-phenyl-C-p-nitrophenylnitrone(6b) to norbornadiene(1), 2,3-bis(methoxycarbonyl)norbornadiene(2) and 2,3-dicyanonorbornadiene(3), and we isolated the endo-adducts in these 1,3-dipolar cycloadditions.

The reaction of 4 with 1 was carried out in the following manner. To a stirred solution of α-chloro-α-hydroxyiminoacetophenone(1.84g, 10.0 mmol) and norbornadiene (2.00g, 21.8 mmol) in THF(30 cm^3) in an ice bath, a solution of triethylamine(1.30g, 13.0 mmol) in THF(20 cm^3) was added dropwise over one hour. Usual work up of the reaction mixture afforded a mixture of monoadducts and bisadducts(See Table I). The separation of these mono- and bisadducts was carried out by use of column chromatography on silica gel. As Table I shows, other cycloadditions of the 1,3-dipoles (4,5,6a,6b) to the norbornadienes(1,2,3) also gave the endo-adducts together with the exo-adducts.

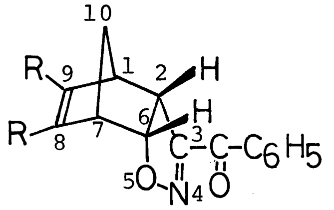
Each isolated adduct had the appropriate composition(by combustion analysis)



8a R = H

8b R = CO_2CH_3

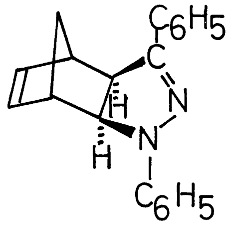
8c R = CN



9a R = H

9b R = CO_2CH_3

9c R = CN



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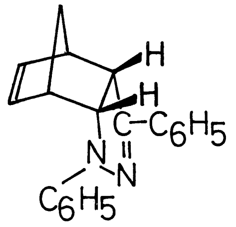

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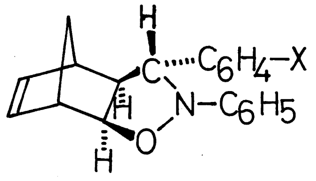
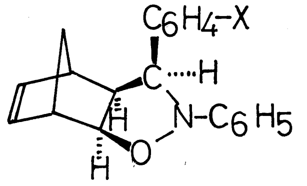


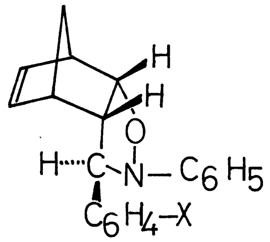
12a X = H

12b X = p-NO_2



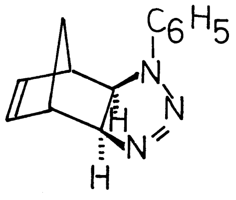
13a X = H

13b X = p-NO_2



14a X = H

14b X = p-NO_2



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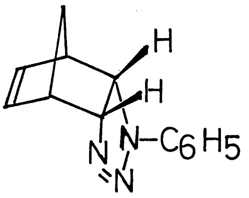

16

Table I : Yield and Product Composition

Olefin	1,3-Dipole	Product						Bisadduct
		Monoadduct						
		Yield[a]	Composition				Exo(%)/Endo(%)	Yield[a]
		(%)	Exo	Mp(°C)	Endo	Mp(°C)		(%)
1	**4**	76	**8a** (74)	65-66	**9a** (26)	53-54	2.8	17
2	**4**	95	**8b** (80)	113-114	**9b** (20)	151-153	4.0	0
3	**4**	90	**8c** (68)	140-141	**9c** (32)	127-127.5	2.1	0
1	**5**	95	**10** (87)	134-135	**11** (13)	110-111	6.7	4
1	**5**	79[b]	**10**[b]	133-135[c]	-- b)			6
1	**6a**	73	**12a** (44) and **13a** (56)	76-77 110-111	**14a** (0)			7
1	**6a**	54[d]	**13a**[d]	111[e]	-- d)			2.8
1	**6b**	76	**12b** (29) and **13b** (67)	153-154 121-122	**14b** (4)	138-140	24	7
1	**7**	67[f]	**15**[f] (92)	55[f]	**16**[f] (8)	124[f]	11[f]	g)

a) The yields are based on the starting 1,3-dipoles. b) The endo-isomer was not obtained in the reaction reported in Ref.5. c) From Ref.5. d) Only **13a** was isolated in the reaction reported in Ref.4. e) From Ref.4. f) From Ref.7. g) A small amount of bisadducts was obtained in the reaction reported in Ref.7.

and IR spectroscopic character. The exo-endo assignments of each isolated adduct were based on the NMR data. In the case of an exo-isomer, the coupling constant between the brigehead proton and the adjacent endo-proton has a value near zero, because the dihedral angle between those protons is nearly a right angle, while the corresponding value for the exo-proton of an endo-isomer is in the range 3-6 Hz.[9)] For example, the two endo-protons(2-H and 6-H) of the exo-adduct(**8a**) appeared as two doublets($J_{2,6}$=9 Hz) at δ 3.78 and 4.99 ppm. The corresponding exo-protons of the endo-adduct(**9a**) appeared as two double doublets($J_{2,6}$=9.5 Hz and $J_{1,2}$=$J_{6,7}$=4 Hz) at δ 4.09 and 5.37 ppm. The 1,3-dipolar cycloaddition of **4** to **2** or **4** to **3** took place on the more electron-rich double bond to give the adducts(**8b** and **9b**, or **8c** and **9c**). The NMR data of these adducts are shown below. **8b**($CDCl_3$): δ 1.66 and 1.90(ABq,2,J=10 Hz,10-CH_2),3.73(broad,2), 3.78(s,3), 3.81(s,3), 4.05(d,1,J=8.5 Hz,2-endo H), 5.19(d,1,J=8.5 Hz,6-endo H), and 7.3-8.3 ppm(m,5). **9b**($CDCl_3$): δ 1.57 and 1.93(ABq,2,J=10 Hz,10-CH_2), 3.33(s,3), 3.71(m,1), 3.78(s,3), 3.82(m,1), 4.40(dd,1,J=10 Hz and J=4 Hz,2-exo H), 5.57(dd,1,J=10 Hz and J=4.5 Hz,6-exo H), and 7.3-8.2 ppm(m,5). **8c**($CDCl_3$): δ 1.89 and 2.05(ABq,2,J=11.5 Hz,10-CH_2), 3.78(broad,1), 3.92(broad,1), 4.06(d,1,J=9.5 Hz,2-endo H), 5.20(d,1,J=9.5 Hz,6-endo H), and 7.2-8.4 ppm(m,5). **9c**($CDCl_3$): δ 1.84 and 1.93 (ABq,2,J=11 Hz,10-CH_2), 3.96(m,2), 4.55(dd,1,J=10 Hz and J=4 Hz,2-exo H), 5.77(dd,1, J=10 Hz and J=4 Hz,6-exo H), and 7.5-8.1 ppm(m,5).

The results show that an endo-adduct can be also obtained even in a 1,3-dipolar cycloaddition to norbornadiene which has been reported to give only exo-adduct. From the above results, we conclude that the "exo rule" is not applicable to 1,3-dipolar cycloadditions to norbornadienes.

The reason why 1,3-dipolar cycloadditions to norbornadienes can afford the endo-adducts together with the exo-adducts, and the experimental details of all of the cycloadditions carried out here will be described later elsewhere.

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