1,3-Dipolar Cycloadditions to Bicyclic Olefins. V. The Stereo- and Regiochemistry of 1,3-Dipolar Cycloadditions to Several Unsymmetrical Bicyclic Olefins[1,2]

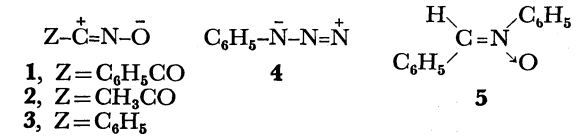
Hisaji TANIGUCHI, Toshikazu IKEDA, and Eiji IMOTO

Department of Applied Chemistry, College of Engineering, University of Osaka Prefecture, Mozu-Umemachi, Sakai, Osaka 591

(Received December 12, 1977)

Each of the 1,3-dipolar cycloadditions of phenylglyoxylonitrile oxide (**1**), methylglyoxylonitrile oxide (**2**), benzonitrile oxide (**3**), and phenyl azide to 2-phenylsulfonyl-2-azabicyclo[3.2.1]octa-3,6-diene (**6**) occurs only to the C_6–C_7 double bond, affording two exo regioisomers. Each of the cycloadditions of **1**, **2**, and **3** to 2-phenylsulfonyl-2-azabicyclo[3.2.1]oct-3-ene (**7**) gives only one exo adduct. The cycloaddition of *C,N*-diphenylnitrone to 2-methylenenorbornane (**8**) gives a mixture of two exo adducts. These results show that the "exo rule" can be extended to the 1,3-dipolar cycloadditions to the bicyclic olefins, **6**, **7**, and **8**. Tentative explanations are offered to account for the exo stereoselectivity and the regio-selectivity in these cycloadditions.

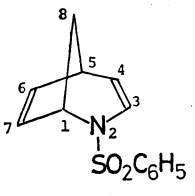
1,3-Dipolar cycloadditions to norbornenes follow the "exo rule."[3] However, a previous paper reported that those to norbornadienes do not follow this rule.[4] This reactivity difference has been ascribed to the presence of homoconjugation in norbornadiene.[4] These results and the assumption prompted us to ascertain to what cases the "exo rule" could be extended. We undertook to study it through 1,3-dipolar cycloadditions to the following three kinds of bicyclic olefins: (i) 2-phenylsulfonyl-2-azabicyclo[3.2.1]octa-3,6-diene (**6**), which has a formally different homoconjugation from norbornadiene;[5] (ii) 2-phenylsulfonyl-2-azabicyclo[3.2.1]oct-3-ene (**7**), which has an unsaturated bridge larger by one nitrogen atom than that of norbornene, and (iii) 2-methylenenorbornane (**8**), whose double bond is of the exo type. The 1,3-dipolar cycloadditions of phenylglyoxylonitrile oxide (**1**), methylglyoxylonitrile oxide (**2**), benzonitrile oxide (**3**), and phenyl azide (**4**) to **6** or **7** and the 1,3-dipolar cycloaddition of α,*N*-diphenylmethanimine *N*-oxide (**5**) to **8** were carried out. Since all the bicyclic olefins used here were unsymmetrical, the regiochemistry of these cycloadditions was also studied.



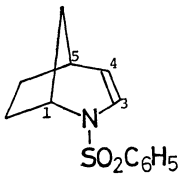
1, $Z=C_6H_5CO$
2, $Z=CH_3CO$
3, $Z=C_6H_5$

4

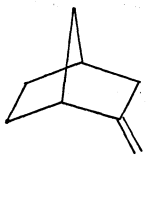
5



6



7



8

Results

1,3-Dipolar Cycloadditions. The slow addition of a dilute THF solution of triethylamine (TEA) to a stirred solution of **6** and α-chloro-α-hydroxyiminoacetophenone (**9**), which is a precursor of **1**, in THF cooled in an ice bath gave two exo adducts, 8-phenylsulfonyl-5-benzoyl-2,6-*exo*-3-oxa-4,8-diazatricyclo[5.3.1.$0^{2,6}$]-undeca-4,9-diene (**10**) and 10-phenylsulfonyl-5-benzoyl-2,6-*exo*-3-oxa-4,10-diazatricyclo[5.3.1.$0^{2,6}$]undeca-4,8-diene (**11**). The cycloadditions of **2** to **6** and **3** to **6** were carried out by a method like that described above. The reaction of **2** to **6** afforded two exo adducts, 5-acetyl-8-phenylsulfonyl-2,6-*exo*-3-oxa-4,8-diazatricyclo-[5.3.1.$0^{2,6}$]undeca-4,9-diene (**12**) and 5-acetyl-10-phenylsulfonyl-2,6-*exo*-3-oxa-4,10-diazatricyclo[5.3.1.$0^{2,6}$]-undeca-4,8-diene (**13**). Moreover, the reaction of **3** with **6** also produced two exo adducts, 8-phenylsulfonyl-5-phenyl-2,6-*exo*-4,8-diazatricyclo[5.3.1.$0^{2,6}$]undeca-4,9-diene (**14**) and 10-phenylsulfonyl-5-phenyl-2,6-*exo*-4,10-diazatricyclo[5.3.1.$0^{2,6}$]undeca-4,8-diene (**15**). All the adducts obtained in the above reactions are produced by the addition of the nitrile oxides, **1**—**3**, to the C_6=C_7 double bond of **6**. The adducts which were to be produced by the addition of the nitrile oxides to the other carbon-carbon double bond (C_3=C_4 double bond) of **6**, the endo adducts, and the bisadducts were not detected at all.

The reaction of the azide, **4**, with an equiv of **6** in dry benzene at room temperature led to the formation of two exo monoadducts, 10-phenylsulfonyl-5-phenyl-2,6-*exo*-3,4,5,10-tetraazatricyclo[5.3.1.$0^{2,6}$]undeca-3,8-diene (**16**) and 8-phenylsulfonyl-5-phenyl-2,6-*exo*-3,4,5,8-tetraazatricyclo[5.3.1.$0^{2,6}$]undeca-3,9-diene (**17**). Similary, the adducts which were to be produced by the attack of **4** on the C_3=C_4 double bond of **6**, the endo adducts, and the bisadducts were not detected at all.

The yields of the adducts obtained in the reactions of **1**—**4** with **6** and the product compositions are summarized in Table 1.

The cycloadditions of the nitrile oxides, **1**—**3**, to **7** was carried out in a manner similar to that described above. Each of the three reactions gave only one exo adduct, 2-phenylsulfonyl-6-benzoyl-3,7-*exo*-4-oxa-2,5-diazatricyclo[6.2.1.$0^{3,7}$]undec-5-ene (**18**), 6-acetyl-2-phenylsulfonyl-3,7-*exo*-4-oxa-2,5-diazatricyclo[6.2.1.$0^{3,7}$]-undec-5-ene (**19**), or 2-phenylsulfonyl-6-phenyl-3,7-*exo*-4-oxa-2,5-diazatricyclo[6.2.1.$0^{3,7}$]undec-5-ene (**20**). When these reactions were carried out at 0 °C, the yields of the adducts were low. When the reaction temperature was raised to 66 °C, the yields of the adducts (**18**, **19**) increased, but no other product was

TABLE 1. THE YIELDS OF ADDUCTS AND PRODUCT COMPOSITIONS IN THE REACTIONS OF **1**—**4** WITH **6**

1,3-Dipole	Adduct	Yield (%)	Composition (%)	Recovery of **6** (%)
1	**10**	97[a]	67	0
	11		33	
2	**12**	94[a]	76	0
	13		24	
3	**14**	96[a]	71	0
	15		29	
4	**16**	78[b]	87	8
	17		13	

a) At 0 °C in THF. b) At r.t. for one week in C_6H_6.

TABLE 2. THE YIELDS OF ADDUCTS IN THE REACTIONS OF **1**—**3** WITH **7** IN THF

1,3-Dipole	Temp (°C)	Adduct	Yield (%)	Recovery of **7** (%)
1	0	**18**	12	73
	66	**18**	56	27
2	0	**19**	10	79
	66	**19**	45	39
3	0	**20**	33	50
	66	**20**	33	52

obtained (Table 2).

A solution of **4** and **7** in dry benzene was allowed to stand in the dark for one week at room temperature; however, this treatment gave no adduct.

When a solution of the nitrone, **5**, in toluene containing two equiv. of **8** was refluxed, a 1:1 mixture of two exo adducts, 1′-*exo*,3′-*endo*-2′,3′-diphenylspiro[norbornane-2,5′[1′]oxa[2′]azacyclopentane] (**21**) and 1′-*exo*,3′-*exo*-2′,3′-diphenylspiro[norbornane-2,5′[1′]oxa[2′]azacyclopentane] (**22**), was obtained in an 83% yield.

The above results show that the "exo rule" can be extended to the 1,3-dipolar cycloadditions to the bicyclic olefins, **6**, **7**, and **8**.

The separation or the isolation of the adducts from the reaction mixture was carried out using column chromatography on silica gel or alumina.

*Determination of Configurations of Adducts. a) Adducts (**10**—**17**) obtained in Cycloadditions to **6***: The structural assignments of the adducts were made on the basis of the NMR chemical shifts (Table 3), the coupling constants (Table 4), the spin-spin decouplings, and the nuclear Overhauser effects (NOE).[6]

In each adduct, the signal which appeared as a double doublet in the region of δ 6.50—6.66 was assigned to the vinyl proton, 9-H. This was confirmed by the spin-decoupling technique; the vinyl proton was coupled to the adjacent vinyl proton (J=8.0 or 7.5 Hz) and to the bridgehead proton which neighbors on the nitrogen atom (J=1.0 or 1.5 Hz). This finding indicates that all the adducts (**10**—**17**) are produced by the addition of 1,3-dipoles to the C_6=C_7 double bond of **6**.

The signals of the 2-H and the 6-H in each adduct appeared as simple doublets. The coupling constant between the 2-H (or 6-H) and the adjacent bridgehead proton was 0 Hz, as is shown in Table 4. This finding shows that all the adducts are produced by the attack of 1,3-dipoles on **6** from the exo side.

Each adduct pair, **10** and **11**, **12** and **13**, **14** and **15**, or **16** and **17**, consists of regioisomers to each other. The distinction between the **12** and **13** regioisomers was achieved by NOE experiments. Irradiation at the frequency of the 1-H of the adduct, **12**, caused a 24% increase in the integral of the multiplet (δ=5.00—5.12, 2-H and 6-H), but brought about no increase in the integral of the doublet (6-H). The saturation of the 7-H of the adduct, **13**, gave rise to a 20% enhancement of the integral of the 8-H and a 5% enhancement of that of the 6-H. These findings show that the oxygen atom of the isoxazoline moiety in the **12** adduct is on the opposite side of the molecule from the *N*-phenylsulfonyl group, while the corresponding oxygen atom of the adduct, **13**, is on the same side of the molecule as the *N*-phenylsulfonyl group. The difference in the chemical

TABLE 4. COUPLING CONSTANTS IN ADDUCTS (**10**—**17**)[a,b]

Adduct	$J_{1,2}$	$J_{2,6}$	$J_{6,7}$	$J_{7,8}$	$J_{8,9}$	$J_{9,10}$	$J_{10,1}$	$J_{7,9}$	$J_{1,9}$
10	0	8.5	0	—	—	8.0	8.0	1.0	0
11	0	8.5	0	8.0	8.0	—	—	0	1.0
12	0	8.5	0	—	—	8.0	8.0	1.5	0
13	0	8.5	0	8.0	8.0	—	—	0	1.0
14	0	8.5	0	—	—	8.0	8.0	1.0	0
15	0	8.5	0	8.0	8.0	—	—	0	1.0
16	0	9.5	0	7.5	7.5	—	—	0	1.0
17	0	9.5	0	—	—	7.5	7.5	1.0	0

a) The spectra were recorded at 60 MHz. b) J values in Hz.

TABLE 3. CHEMICAL SHIFTS OF ADDUCTS (**10**—**17**)[a,b]

Adduct	1-H	2-H	6-H	7-H	8-H	9-H	10-H	$\Delta\delta$[c]
10	2.70	5.00	3.77	4.88	—	6.60	5.14	1.23
11	4.54	4.92	4.20	2.73	5.38	6.50	—	0.72
12	2.69	5.00	3.49	4.68	—	6.60	5.12	1.51
13	4.53	4.93	3.96	2.63	5.34	6.52	—	0.97
14	2.70	5.12	4.10	4.50	—	6.64	5.22	1.02
15	4.52	4.91	4.21	2.55	5.37	6.57	—	0.70
16	*ca.* 4.7	4.82	4.25	2.60	5.28	6.64	—	0.57
17	2.88	5.12	4.28	*ca.* 4.4	—	6.66	5.49	0.84

a) The spectra were recorded at 60 MHz. b) Expressed in δ ppm units, with TMS as the internal standard, in $CDCl_3$ soln. c) The shift difference between the 2-H and the 6-H.

shift between the 2-H and the 6-H of the **12** adduct is greater by 0.54 ppm than the corresponding difference between the 2-H and the 6-H of the **13** adduct. Such a chemical-shift difference was applied to the distinction between the **10** and **11**, or **14** and **15** regioisomers (Table 3).

The distinction between the **16** and **17** regioisomers was also achieved by observing the NOE. Irradiation at the frequency of the bridgehead proton, 7-H, of the **16** adduct brought about an increase of 9% in the integral of the doublet (6-H) and an increase of 9% in the integral of the vinyl proton, 8-H, but caused no increase in the integral of the doublet (2-H). Also, the empirical data[7] suggest that the high-field doublet of the two doublet is due to the 6-H which is adjacent to the phenyl group. These findings show that the phenyl group is on the opposite side of the molecule from the *N*-phenylsulfonyl group, as is shown in the structure (**16**). In the case of the **17** adduct, it was confirmed by irradiation at the frequency of the bridgehead proton, 1-H, of this adduct that the phenyl group is on the same side of the molecule as the *N*-phenylsulfonyl group. An increment of 25% was observed in the integral of the multiplet, which consisted of a low-field doublet (2-H) and a triplet (10-H).

Table 5. The NMR data of adducts (**18**—**20**)[a,b]

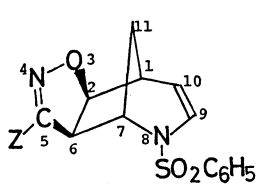
Adduct	1-H	3-H	7-H	8-H	$J_{3,7}$	$J_{7,8}$
18	4.01	6.65	3.72	2.58	10	0
19	4.00	6.58	3.52	—	9.5	0
20	4.00	6.60	3.65	2.32	9.5	0

a) The spectra were recorded at 60 MHz. b) The chemical shifts are expressed in δ ppm units, with TMS as the internal standard, in $CDCl_3$ soln. J values in Hz.

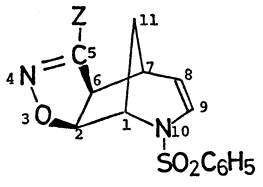
b) Adducts (18—20) Obtained in Cycloadditions to 7: The structural assignments of the **18**—**20** adducts were carried out by means of their NMR data (Table 5). Each spectrum of these adducts showed two simple doublets at δ *ca.* 3.6 and *ca.* 6.6 (Table 5). The high-field doublet in each spectrum was assigned to the 7-endo H by making a comparison between its spectrum and the spectrum of the exo adduct (**25**)[4] formed in the cycloaddition of **1** to norbornadiene; in the spectrum of Compound **25**, the 6-endo H appears at δ 3.78 ppm as a simple doublet.[4] From the fact that the coupling constant between the 7-H and the adjacent bridgehead proton, 8-H, in each adduct is 0 Hz, it can be said that each adduct is an exo adduct; the dihedral angle between the 7-H and the 8-H is close to 90°.

c) The 21 and 22 Adducts: Since no hydrogen atom is attached to the 2-carbon atom of the **8** olefin, it is impossible to determine the structure of the 1 : 1 adducts obtained in the cycloaddition of **5** to **8** on the basis of the NMR spectrum alone. A solid obtained in this cycloaddition consisted of the two exo adducts **21** and **22**, not of the endo adducts, **23** and **24**. This was confirmed by the following observations. (i) The NMR spectrum of a mixture of **21** and **22** showed the signal of their 5′-methylene protons at δ 2.2—2.9 as a multiplet. This chemical-shift value indicated that these adducts are produced by the attack of the oxygen atom in the nitrone, **5**, on the 2-carbon atom in the olefin, **8**. (ii) It was revealed by the double-resonance technique that the solid obtained in this cycloaddition consisted of two adducts. Each 4′-H of the two adducts (**21** and **22**) has the same chemical shift (δ=4.61). When their 4′-H's were irradiated with an additional radio frequency at the resonance position, the multiplet which appeared at δ 2.2—2.9 was transformed into eight sharp peaks, which consisted of two sets of AB quartets (J_{AB}=11.0 and 14.0 Hz) assigned to 5′-methylene protons in **21** and to those in **22**. (iii) The hydrogenolysis of the solid which consisted of **21** and **22** gave only 2-phenethyl-2-*exo*-norbornanol (**26**) in a 79% yield. The structure of this alcohol was established by comparison with the corresponding endo alcohol (**27**), which had been prepared by a method like that described in the literature.[8]

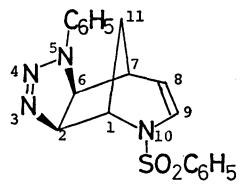
These findings (i—iii) indicate that the solid obtained in this cycloaddition consists of the two exo adducts, **21** and **22**.



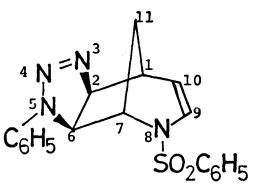
10, Z=C_6H_5CO
12, Z=CH_3CO
14, Z=C_6H_5



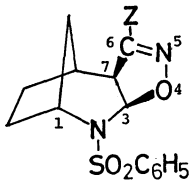
11, Z=C_6H_5CO
13, Z=CH_3CO
15, Z=C_6H_5



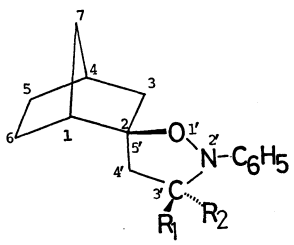
16



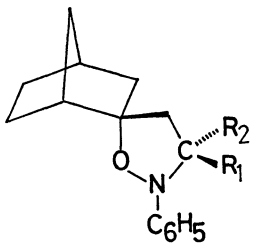
17



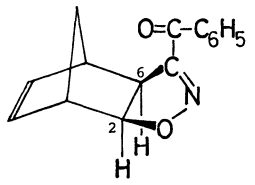
18, Z=C_6H_5CO
19, Z=CH_3CO
20, Z=C_6H_5



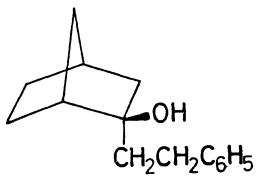
21
22



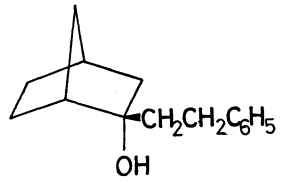
23
24



25



26



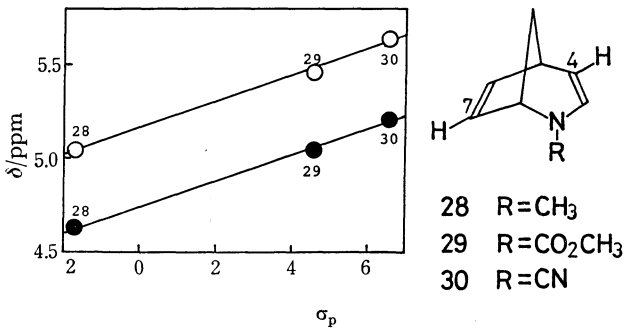
27

Discussion

This kind of 1,3-dipolar cycloaddition has been shown to be a kinetically controlled reaction.[4,9]

A Tentative Explanation of the exo Stereoselectivity. In view of the results obtained in previous work,[2,4] it may be suggested that the dipoles used here, **1**—**5**, act as electron-accepting 1,3-dipoles toward the olefins, **6**—**8**. This indicates that the present 1,3-dipolar cycloadditions may be classified as LU-controlled reactions.[10] On the other hand, it has been suggested by the orbital mixing rule that the highest occupied molecular orbital (HOMO) of norbornene extends more to the exo side than to the endo side because of the interaction beteen the HOMO of the carbon-carbon double bond and the strained methano-bridge orbital.[11] Each olefin used here has a strained methano-bridge such as norbornene. Similarly, it can be predicted by the orbital mixing rule that the HOMO of the carbon-carbon double bond in each olefin extends more to the exo side than to the endo side.[12] Consequently, the dipoles, **1**—**5**, attack the olefins, **6**—**8** from their exo sides.

Attacking Site of 1,3-Dipoles on 6. Although the **6** olefin has two double bonds which are to be attacked by 1,3-dipoles, cycloaddition occurs only to the C_6=C_7 double bond, not to the enamine-type double bond (C_3=C_4 double bond). This phenomenon may be ascribed to the following factors (i—iii): (i) In the 2-azabicyclo[3.2.1]octa-3,6-diene system (**28**,[5] **29**,[13] and **30**[5]), the signals of the 4-H and the 7-H shift to lower fields with an increase in the value of Hammett's σ_p[14] of the *N*-substituent, *R* (Fig. 1). Also, both the 4-H and the 7-H appear at higher fields than the 6-H. These findings indicate that not only the 4-carbon atom, but also the 7-carbon atom, is under the influence of the electron-donating character of the nitrogen atom. (ii) From the structural consideration of **6**, the interaction of the HOMO of the C_6=C_7 double bond with the methano-bridge orbital is assumed to be greater than that of the HOMO of the C_3=C_4 double bond with the methano-bridge orbital, so that the extension of the HOMO of the C_6=C_7 double bond into the exo side may be greater than that of the HOMO of the C_3=C_4 double bond.[15] (iii) The bulky *N*-substituent (phenylsulfonyl group) may hinder the approach of 1,3-dipoles to the C_3=C_4 double bond. From the fact that phenyl azide addition to bicyclo[3.2.1]octa-2,6-diene (**31**) occurs only to the C_6=C_7 double bond from the exo side,[16] however, this factor seems less probable.



28 R=CH_3
29 R=CO_2CH_3
30 R=CN

Fig. 1. Chemical shifts (TMS as an internal standard, in CCl_4 solutions) of vinyl protons of 2-azabicyclo-[3.2.1]octa-3,6-diene system *vs.* Hammett's σ_p.
○: 7-H, : ●4-H.

TABLE 6. CHEMICAL SHIFTS OF VINYL PROTONS IN **6** AND **7**[a]

Olefin	3-H	4-H	6-H	7-H
6	6.30	5.1—5.5	6.14	5.1—5.5
7	6.37	5.19		

a) The spectra were recorded at 60 MHz. Expressed in δ ppm units, with TMS as the internal standard, in $CDCl_3$ soln.

Regioselectivity. In the **6** diene, the δ values of its vinyl protons (Table 6)[17] suggest the π electron-cloud on the C_6–C_7 double bond is polarized. This may be caused by the electron-donating character of the nitrogen atom, as has been described above, and by the structural characteristics of the bicyclic dienes with a bicyclo[3.2.1]octane skeleton.[19] In the **7** olefin, the π electron-cloud on the C_3=C_4 double bond may be polarized because of the electron-donating character of the nitrogen atom (see Table 6). In the **8** ofefin, the calculations of Houk *et al.* for the HOMO of ethylenes substituted by alkyl groups[21] suggest that the π electron-cloud of the double bond is polarized. As far as the present cycloadditions are concerned, it may be concluded from the product compositions (Table 1) and the structures of the adducts that the orientation in which the plus poles of 1,3-dipoles attack the minus poles of dipolarophiles is preferred.[22]

Conclusion

The "exo rule" can be applied to 1,3-dipolar cycloadditions to bicyclic olefins with a moiety of the bicyclo-[*n*.2.1]alkane(*n*=2 and 3) skeleton, except for norbornadienes, and can also be applied to such a cycloaddition to 2-methylenenorbornane.

Experimental

Materials. The precursors of the nitrile oxides (**9**),[23] α-chloro-α-hydroxyiminoacetone (**32**),[24] and *N*-hydroxybenzenecarboximidoyl chloride (**33**)[25] and the 1,3-dipoles

(**4**[26] and **5**[27]) were prepared by methods described in the literature. The olefines, **6**,[18] **7**,[18] and **8**,[28] were also prepared by methods described in the literature.

*Cycloaddition of **1** to **6**.* Into a stirred solution of 6 (494 mg, 2.0 mmol) and **9** (367 mg, 2.0 mmol) in dry THF (10 cm³) cooled in an ice bath, a solution of triethylamine (TEA) (250 mg, 2.5 mmol) in dry THF (5 cm³) was added, drop by drop, over a period of 1 h. After an additional 1 h's stirring at the same temperature, the resulting triethylammonium chloride was removed by filtration. The filtrate showed, on TLC with benzene–ether (97: 3), two spots at R_f 0.40 (**11**) and at R_f 0.33 (**10**). The evaporation of the solvent left a residue. The residue was chromatographed on silica gel (200—300 mesh). Elution with benzene–ether (97: 3) gave **11** (252 mg, 32%) and **10** (513 mg, 65%), in that order.

Adduct **10**: mp 119—121 °C (colorless cubic crystals from EtOH); IR(KBr) 1650 (C=O), 1642, 1570, 1453, 1362, 1340, 1255, and 1175 cm^{-1} (SO_2).

Found: C, 64.12; H, 4.64; N, 7.20%. Calcd for $C_{21}H_{18}N_2O_4S_1$: C, 63.94; H, 4.61; N, 7.10%.

Adduct **11**: mp 124—125 °C (colorless needles from 95% EtOH); IR (KBr) 1660 (C=O), 1640, 1575, 1450, 1360, 1340, and 1173 cm^{-1} (SO_2).

Found: C, 64.07; H, 4.57; N, 7.20%. Calcd for $C_{21}H_{18}O_4S_1$: C, 63.94; H, 4.61; N, 7.10%.

*Cycloaddition of **2** to **6**.* A solution of **6** (494 mg, 2.0 mmol) and **32** (250 mg, 2.0 mmol) in dry THF (10 cm³) was treated with TEA (250 mg, 2.5 mmol) in dry THF (5 cm³) as has been described above. A similar work-up of the reaction mixture and evaporation of the solvent produced a viscous oil, which was solidified by the addition of a few drops of CCl_4. The solid was separated by filtration and dried under a vacuum to give 621 mg (94%) of a mixture of **12** and **13**. The NMR spectrum of the mixture showed that the **12**/**13** product ratio was 76/24. The mixture was chromatographed on silica gel. Elution with benzene–ether (97: 3) gave **13** and **12**, in that order.

Adduct **12**: mp 148—149 °C (coloeless leaves from EtOH); IR (KBr) 1693 (C=O), 1639, 1575, 1457, 1362, 1340, and 1172 cm^{-1} (SO_2); MS (80 eV), *m/e* 332, 289, 221, and 80.

Found: C, 57.63; H, 4.65; N, 8.51%. Calcd for $C_{16}H_{16}N_2O_4S_1$: C, 57.81; H, 4.86; N, 8.43%.

Adduct **13**: mp 129—130 °C (colorless needles from EtOH): IR (KBr) 1700 (C=O), 1639, 1580, 1458, 1360, 1345, and 1180 cm^{-1} (SO_2); MS (80 eV), *m/e* 332, 289, 221, and 80.

Found: C, 58.02; H, 4.81; N, 8.63%. Calcd fro $C_{16}H_{16}N_2O_4S_1$: C, 57.81; H, 4.96; N, 8.43%.

*Cycloaddition of **3** to **6**.* A solution of **6** (494 mg, 2.0 mmol) and **33** (311 mg, 2.0 mmol) in dry THF (10 cm³) was treated with TEA (250 mg, 2.5 mmol) in dry THF (10 cm³) by a procedure like that described above. A similar work-up of the reaction mixture and evaporation of the solvent gave 703 mg (96%) of a mixture of **14** and **15**. The NMR spectrum of the mixture showed that the **14**/**15** product ratio was 71/29. The solid was recrystallized from benzene to give colorless, pure **14**. The evaporation of benzene from the mother liquor afforded a residue, which was chromatographed on silica gel with benzene–ether(95: 5) to give **15** and **14**, in that order.

Adduct **14**: mp 214—215 °C (colorless leaves from benzene); IR(KBr) 1635, 1450, 1360, 1335, and 1172 cm^{-1}.

Found: C, 65.68; H, 4.95; N, 7.88%. Calcd for $C_{20}H_{18}N_2O_3S_1$: C, 65.55; H, 4.96; N, 7.65%.

Adduct **15**: mp 151—153 °C (colorless cubic crystals from EtOH–$CHCl_3$); IR (KBr) 1640, 1452, 1360, 1340, and 1172 cm^{-1}.

Found: C, 65.34; H, 4.76; N, 7.64% Calcd for $C_{20}H_{18}N_2O_3S_1$: C, 65.55; H, 4.96; N, 7.65%.

*Cycloaddition of **4** to **6**.* A mixture of **6** (494 mg, 2.0 mmol) and **4** (238 mg, 2.0 mmol) was dissolved in dry benzene (5 cm³). The solution was then allowed to stand in the dark for one week at room temperature. The resulting white solid was separated from the solution by filtration, washed with a small amount of cold benzene, and dried under a vacuum to give pure **16** (343 mg, 47%). The filtrate was evaporated to afford a residue, which was subsequently chromatographed on alumina. Elution with $CHCl_3$ gave **6** (38 mg, recovery 8%), **17** (76 mg, 10%), and an additional amount of **16** (156 mg, 21%), in that order.

Adduct **16**: mp 179—181 °C (from MeOH); IR (KBr) 1632, 1600, 1505, 1488, 1350, and 1177 cm^{-1}.

Found: C, 62.38; H, 4.88; N, 15.25%. Calcd for $C_{19}H_{18}N_4O_2S_1$: C, 62.28; H, 4.95; N, 15.29%.

Adduct **17**: mp 165—167 °C (from MeOH); IR (KBr) 1639, 1603, 1500, 1363, and 1180 cm^{-1}.

Found: C, 62.20; H, 5.01: N, 15.27%. Calcd for $C_{19}H_{18}N_4O_2S_1$: C, 62.28; H, 4.95; N, 15.29%.

*The Nuclear Overhauser Effects Experiments in the **12**, **13**, **16**, and **17** Adducts.* The NOE in the NMR of these adducts were measured in well-deoxygenated $CDCl_3$ solutions. Table 7 shows the results.

Table 7. NOE experiments in four adducts (**12**, **13**, **16**, and **17**)

Adduct	Signal-irradiated	Proton-affected	Enhancement (%)
12	1-H	10-H	24
		2-H	
		6-H	0
13	7-H	8-H	20
		6-H	5
		2-H	0
16	7-H	8-H	9
		6-H	9
		2-H	0
17	1-H	10-H	24
		2-H	
		6-H	0

*Cycloaddition of **1** to **7**.* *a) At 66 °C*: Into a refluxing solution of **7** (375 mg, 1.5 mmol) and **9** (275 mg, 1.5 mmol) in dry THF (5 cm³) warmed in a water bath, we stirred, drop by drop over a 2-h period, a solution of TEA (200 mg, 2.0 mmol) in dry THF (5 cm³). After an additional 1 h's stirring at the same temperature, the resulting ammonium chloride was removed by filtration. The filtrate showed, on TLC with benzene, their spots. After the removal of the solvent, the residue was chromatographed on silica gel. Elution with benzene gave a small amount of 3,4-dibenzoyl-1,2,5-oxadiazole 2-oxide (**34**) (mp 76—78 °C, (lit,[23] 78—80 °C)), **7** (103 mg, recovery 27%), and **18** (335 mg, 57%), in that order.

Adduct **18**: mp 188—190 °C (colorless cubic crystals from $CHCl_3$–EtOH); IR(KBr) 1648 (C=O), 1562, 1448, 1337, and 1167 cm^{-1}.

Found: C, 63.68; H, 4.98; N, 7.16%. Calcd for $C_{21}H_{20}N_2O_4S_1$: C, 63.61; H, 5.09; N, 7.07%.

b) At 0 °C: The same reaction was carried out under similar conditions, but the reaction temperature was maintained at 0 °C instead of at 66 °C. A similar work-up of

the reaction mixture gave **34**, **7** (272 mg, recovery 72%), and **18** (72 mg, 12%).

Cycloaddition of 2 to 7. *a) At 66* °C: A solution of **7** (375 mg, 1.5 mmol) and **32** (182 mg, 1.5 mmol) in dry THF (5 cm^3) was treated with TEA (200 mg, 2.0 mmol) in dry THF (5 cm^3) as described above. A similar work-up of the reaction mixture produced an oil after the evaporation of THF. The oil showed, on TLC with benzene, three spots—at R_f 0.34 (**7**), R_f 0.25 (3,4-diacetyl-1,2,5-oxadiazole 2-oxide (**35**)), and R_f 0.12 (**19**). The oil was chromatographed on silica gel with benzene to give **7** (145 mg, recovery 39%), an oil of **35** (20 mg), and **19** (218 mg, 45%). The structure of **35** was confirmed by the elemental analysis ($C_6H_6N_2O_4$) and by comparing its IR spectrum with that of the analogous furoxan, **34**.

Adduct **19**: mp 156—158 °C (colorless plates from EtOH); IR (KBr) 1692 (C=O), 1580, 1447, 1347, and 1173 cm^{-1}.

Found: C, 57.35; H, 5.48; N, 8.40%. Calcd for $C_{16}H_{18}N_2O_4S_1$: C, 57.46; H, 5.44; N, 8.38%.

b) At 0 °C: The same recation was carried out under similar conditions, but the reaction temperature was kept at 0 °C. A similar work-up of the reaction mixture gave **7** (295 mg, recoverry 79%), a small amount of **35**, and **19** (51 mg, 10%).

Cycloaddition of 3 to 7. *a) At 66* °C; A solution of **7** (375 mg, 1.5 mmol) and **33** (233 mg, 1.5 mmol) in dry THF (5 cm^3) was treated with TEA (200 mg, 2.0 mmol) in dry THF (5 cm^3) as has been described above. A similar work-up of the reaction mixture gave 3,4-diphenyl-1,2,5-oxadiazole 2-oxide (**36**) (mp 115—116 °C (lit,[29] mp 112 °C)), **7** (194 mg, recovery 52%), and **20** (184 mg, 33%).

Adduct **20**: mp 227—229 °C (colorless cubic crystals from EtOH–$CHCl_3$); IR(KBr) 1453, 1400, 1342, and 1178 cm^{-1}.

Found: C, 64.94; H, 5.41; N, 7.57%. Calcd for $C_{20}H_{20}N_2O_3S_1$: C, 65.19: H, 5.48; N, 7.60%.

b) At 0 °C: The same reaction was carried out under similar conditions, but the reaction temperature was kept at 0 °C. A similar work-up of the reaction mixture gave **36**, **7** (187 mg, recovery 50%), and **20** (185 mg, 33%).

Treatment of 4 with 7. A solution of **7** (375 mg, 1.5 mmol) and **4** (180 mg, 1.5 mmol) in dry benzene was allowed to stand in the dark for one week at room temperature. Then, the solution showed, on TLC with benzene, only two spots—at R_f 0.80 (**4**) and R_f 0.47 (**7**).

Cycloadditon of 5 to 8. A solution of **8** (2.22 g, 16.3 mmol) and **5** (1.60 g, 8.2 mmol) in dry toluene (4 cm^3) was heated under reflux for 24 h. The solvent was then removed under reduced pressure to give a solid which consisted of **5** and a mixture of **21** and **22**. It was column chromatographed on silica gel. Elition with benzene gave 2.25 g (83%) of a mixture of **21** and **22**. The NMR spectrum of the mixture showed that the **21**/**22** product ratio was *ca.* 1/1. The 1:1 mixture of **21** and **22**: mp 108—116 °C (from hexane); IR (KBr) 1600, 1500, and 1285 cm^{-1}; NMR ($CDCl_3$ δ=6.8—7.5 (20H, m), 4.61 (2H, t, J=8.0 Hz, 4′-H of **21** and 4′-H of **22**), 2.24 and 2.88 (2H, ABq of d, J=14.0 and 8.0 Hz, 5′-CH_2 of **21** or **22**), 2.20 and 2.86 (2H, ABq of d J=11.0 and 8.0 Hz, 5′-CH_2 of **21** and **22**), and 1.0—2.6 (20H, m).

Found: C, 82.69; H, 7.52; N, 4.81%. Calcd for $C_{21}H_{23}N_1O_1$: C, 82.58; H, 7.59; N, 4.59%.

Hydrogenolysis of a Mixture of 21 and 22. To a solution of a mixture of **21** and **22** (305 mg, 1.0 mmol) in ethyl acetate (10 cm^3), 5% paradium-on-carbon catalyst (300 mg) was added. The solution was then shaken with hydrogen for 3 days at room temperature in a low-pressure apparatus. After the removal of the catalyst by filtration, the solvent was evaporated under reduced pressure to afford an oil. The oil showed, on TLC with hexane–ether (6:4), two spots—at R_f 0.36 (**26**) and R_f 0.23 (aniline). The oil was chromatographed on silica gel. Elution with hexane–ether (6:4) gave pure **26** (171 mg, 79%).

Product **26**: oil; IR (naet) 3380 (OH), 1605, 1500, and 1475 cm^{-1}; NMR ($CDCl_3$) δ=7.21 (5H, m) and 1.1—2.9 (15H, m); 2-phenethyl-2-*exo*-norbornyl phenylcarbamate: mp 116—117 °C (from hexane).

Found: C, 78.99; H, 7.50; N, 4.23%. Calcd for $C_{22}H_{25}N_1O_2$: C, 78.77; H, 7.51; N, 4.18%.

*Preparation of 2-Phenethyl-2-*endo*-norbornanol (27).* This compound was prepared by a procedure similar to that described in the literature.[8] Phenethyl bromide (14.8 g, 0.08 mol) dissolved in dry ethyl ether (25 cm^3) was stirred, drop by drop, into a suspension of magnesium turnings (1.82 g, 0.075 mol) in dry ether (50 cm^3) containing a small amount of I_2. The resulting solution was treated dropwise with 2-norbornanone (5.50 g, 0.05 mol) in dry ether (25 cm^3). After this addition was complete (45 min), the reaction mixture was stirred for 1 h, after which it was hydrolyzed with a saturated aq solution of ammonium chloride and extracted with ether (3×50 cm^3). The ether layer was separated, dried over $MgSO_4$, and evaporated to yield a colorless oil (**27**): bp 132—134 °C/1.2 Torr; IR(neat) 3360 (OH), 1605, 1500, and 1455 cm^{-1}; NMR ($CDCl_3$) δ=7.21 (5H, s) and 1.0—2.9 (15H, m); 2-phenethyl-2-*endo*-norbornyl phenylcarbamate: mp 160—162 °C (from benzene–hexane).

Found: C, 78.92; H, 7.32; N, 4.23%. Calcd for $C_{22}H_{25}N_1O_2$: C, 78.77; H, 7.51; N, 4.18%.

References

1) Presented at the 36th National Meeting of the Chemical Society of Japan, Higashi-Osaka, Japan, April 1977, Abstracts II, 3S 11.

2) Preceding paper: H. Taniguchi, T. Ikeda, and E. Imoto, *Bull. Chem. Soc. Jpn.*, **51**, 1495 (1978).

3) a) K. Alder and G. Stein, *Justus Liebigs Ann. Chem.*, **485**, 211, 223 (1931); b) K. Alder and G. Stein, *ibid.*, **501**, 1 (1933); c) K. Alder and G. Stein, *ibid.*, **515**, 165, 185 (1935); d) K. Alder, H-J. Ache, and F. H. Flock, *Chem. Ber.*, **93**, 1888 (1960).

4) H. Taniguchi, T. Ikeda, Y. Yoshida, and E. Imoto, *Bull. Chem. Soc. Jpn.*, **50**, 2694 (1977), and the references cited therein.

5) A. G. Anastassiou and H. Kasmai, *J. Chem. Soc., Chem. Commum.*, **1975**, 201.

6) F. A. L. Anet, and A. J. R. Bourn, *J. Am. Chem. Soc.*, **87**, 5250 (1965).

7) a) P. Scheiner, *Tetrahedron*, **24**, 349 (1967); b) R. Huisgen, L. Moebius, G. Mueller, J. Stangle, G. Szeimes, and J. M. Vernon, *Chem. Ber.*, **98**, 3992 (1965); c) D. Barraclough, J. S. Oakland, and F. Scheinmann, *J. Chem. Soc., Perkin Trans. 1*, **1972**, 1500.

8) E. M. Burgess, H. R. Penton, Jr., and E. A. Taylor, *J. Org. Chem.*, **38**, 26 (1973).

9) a) H. Taniguchi, Y. Yoshida, and E. Imoto, *Bull. Chem. Soc. Jpn.*, **50**, 3335 (1977); b) H. Taniguchi and E. Imoto, *Bull. Chem. Soc. Jpn.*, in press.

10) In LU-controlled reactions, the interaction of the dipole LUMO (lowest unoccupied molecular oribital) with the dipolarphile HOMO (highest occupied molecular orbital is greatest: K. N. Houk, J. Sims, C. R. Watts, and L. J. Luskus, *J. Am. Chem. Soc.*, **95**, 7301 (1973).

11) a) S. Inagaki, H. Fujimoto, and K. Fukui, *J. Am. Chem. Soc.*, **98**, 4054 (1976); b) K. Fukui, "Kagaku Hanno To Denshi No Kido," Maruzen, Tokyo (1976), Chaps. 3 and 4; c) K. Fukui, *Kagaku To Kogyo*, **29**, 666 (1976).

12) As has been described above, in the 2-azabicyclo-[3.2.1]octa-3,6-diene system the exsistence of homoconjugation has been found by NMR and UV spectroscopy.[5] From the structure of **6**, however, it may be considered that this homoconjugation on the endo side is weaker than that of norbornadiene,[4] so the interaction between the HOMO of the carbon-carbon double bond on the exo side in this system would surpass the homoconjugation on the endo side.

13) H. Taniguchi, K. Umano, and E. Imoto, unpublished data.

14) D. H. McDaniel and H. C. Brown, *J. Org. Chem.*, **23**, 420 (1958).

15) This can be deduced from the orbital mixing rule.[11] According to this rule, the resonance integrals as well as the orbital energies are important factors in the second-order pertubed orbital (see Ref. 11).

16) R. S. McDaniel and A. C. Oehlschlager, *Can. J. Chem.*, **48**, 345 (1970).

17) It has been reported that the vinyl protons (6-H and 7-H) of the diene, **6**, appear at δ 5.15—5.5 and 6.15 respectively.[18] However, that these assignments are incorrect has been found by a re-examination of its NMR spectrum (a double-resonance technique was used).

18) A. C. Oehlschlarger and L. H. Zalkow, *J. Org. Chem.*, **30**, 4205 (1965).

19) In the NMR spectrum of **31** in THF, the 6-H which corresponds to the 7-H of the olefin, **6**, appears in a field higher by 0.53 ppm than the 7-H which corresponds to the 6-H of the olefin, **6**.[20]

20) S. Winstein, M. Ogliaruso, M. Sakai, and J. M. Nicholson, *J. Am. Chem. Soc.*, **89**, 3656 (1967).

21) K. N. Houk, J. Sims, R. E. Duke, Jr., R. W. Strozier, and J. K. George, *J. Am. Chem. Soc.*, **95**, 7287 (1973).

22) In the reactions of 1,3-dipoles with the **7** and **8** olefins the cycloaddition of the reverse orientation did not occur. This may result from both the polarized carbon-carbon double bonds in these olefins, described above, and the steric hindrance (in the cycloadditions to **7**, the steric hindrance between the *N*-phenylsulfonyl group in **7** and the substituents in 1,3-dipoles, and in the cycloaddition of **5** to **8**, the steric hindrance between the methano-bridge in **8** and the phenyl group attached to the carbon atom in **5**).

23) Y. Otsuji, Y. Tsujii, A. Yoshida, and E. Imoto, *Bull. Chem. Soc. Jpn.*, **44**, 223 (1971).

24) Y. Otsuji, H. Nishikawa, and E. Imoto, the 30th National Meeting of the Chemical Society of Japan, Higashi-Osaka, April 1974, Abstracts III, p. 1302.

25) P. Pajahopalan, B. G. Advani, and C. N. Talaty, *Org. Synth.*, Coll. Vol. V, 505 (1973).

26) R. O. Lindsay and C. F. H. Allen, *Org. Synth.*, Coll. Vol. III, 710 (1955).

27) S. R. Sandler and W. Karo, "Organic Functional Group Preparations III," Academic Press, New York (1972), p. 307.

28) H. C. Brown and K-T. Liu, *J. Am. Chem. Soc.*, **97**, 600 (1975).

29) A. Werner and H. Buss, *Chem. Ber.*, **27**, 2197 (1894).