1,3-Dipolar Cycloadditions to Bicyclic Olefins. IV. The Influence of Non-neighboring Double Bonds on the Stereoselectivity in 1,3-Dipolar Cycloadditions to Bicyclo[*n*.2.2]alkadienes[1)]

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1,3-Dipoles, such as phenylglyoxylonitrile oxide (**1**), benzonitrile oxide, and phenyl azide, undergo cycloadditions to the more electron-rich double bond of 2,3-bis(methoxycarbonyl)bicyclo[2.2.2]octa-2,5-diene (**5**) to afford only *endo* adducts. The cycloadditions of these 1,3-dipoles to the more electron-rich double bond of 6,7-bis(methoxycarbonyl)bicyclo[3.2.2]nona-6,8-diene (**6**) give only *exo* adducts. Benzonitrile-*N*-phenylimine (**4**) undergoes cycloadditions to both the more electron-rich and the more electron-poor double bonds of **5** or **6**. The reaction of **4** with **5** yields two *endo* adducts, and the reaction of **4** with **6** gives two *exo* adducts. However, the cycloaddition of **1** to 5,6-*endo,endo*-bis(methoxycarbonyl)bicyclo[2.2.2]oct-2-ene affords both the *exo*- and *endo* adducts. The reason for the predominant *endo* cycloadditions toward **5** and *exo* cycloadditions toward **6** is discussed.

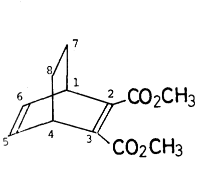
In a previous paper, it was reported that 1,3-dipolar cycloadditions to norbornenes follow the "*exo* rule" of Alder and Stein, but that those to norbornadienes do not follow this rule.[2)] This difference in reactivity has been ascribed to the fact that, in norbornadienes, the homoconjugations are present on their *endo* sides, while in norbornenes such interactions can not be present.[2)] This assumption prompted us to examine the stereochemistry of the 1,3-dipolar cycloadditions to other bicyclic olefins with two carbon-carbon double bonds within each molecule, such as bicyclo[*n*.2.2]alkadienes($n \geqq 2$). Therefore, the 1,3-dipolar cycloadditions of phenylglyoxylonitrile oxide(**1**), benzonitrile oxide(**2**), phenyl azide(**3**), and benzonitrile-*N*-phenylimine(**4**) to 2,3-bis(methoxycarbonyl)bicyclo[2.2.2]octa-2,5-diene(**5**), or 6,7-bis(methoxycarbonyl)bicyclo[3.2.2]nona-6,8-diene (**6**) were carried out. Moreover, for comparison, the 1,3-dipolar cycloaddition of **1** to 5,6-*endo,endo*-bis(methoxycarbonyl)bicyclo[2.2.2]oct-2-ene(**7**), which is a corresponding monoene of **5**, was also carried out. In this paper, it will be emphasized that the interaction between the two carbon-carbon double bonds in **5** or **6** is an important factor controlling the stereochemistry of the additions of 1,3-dipoles to these double bonds.

$C_6H_5\text{-}CO\text{-}\overset{+}{C}{=}N\text{-}\overset{-}{O}$ **1**

$C_6H_5\text{-}\overset{+}{C}{=}N\text{-}\overset{-}{O}$ **2**

$C_6H_5\text{-}\overset{-}{N}\text{-}N{=}\overset{+}{N}$ **3**

$C_6H_5\text{-}\overset{+}{C}{=}N\text{-}\overset{-}{N}\text{-}C_6H_5$ **4**



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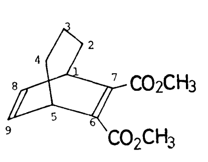

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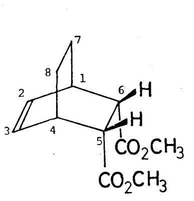

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Results

1,3-Dipolar Cycloadditions. The nitrile oxide, **1**, was easily prepared by the treatment of α-chloro-α-hydroxyiminoacetophenone(**8**) with triethylamine (TEA).[3)] In order to avoid the dimerization of the nitrile oxide, **1**, to 3,4-dibenzoyl-1,2,5-oxadiazole 2-oxide(**9**), the reaction was carried out with low stationary concentrations of **1**. A dilute THF solution of TEA was slowly stirred into a solution of a mixture of **5** and **8** in THF cooled in an ice-bath.[4)] This cycloaddition afforded only one *endo* adduct, 5-benzoyl-8,9-bis(methoxycarbonyl)-2,6-*endo*-3-oxa-4-azatricyclo[5.2.2.0^{2,6}]undeca-4,8-diene(**10**). The cycloaddition of **1** to **6** was carried out by a similar method. In this case, the reaction gave only one *exo* adduct, 5-benzoyl-11,12-bis(methoxycarbonyl)-2,6-*exo*-3-oxa-4-azatricyclo[5.3.2.0^{2,6}]dodeca-4,11-diene(**11**). The monoadducts which were produced by the addition of **1** to the more electron-poor double bonds of **5** and **6** and the bisadducts were not detected at all. These findings show that the nitrile oxide, **1**, acts as an electron-accepting 1,3-dipole toward **5** and **6**.[5)]

The cycloadditions of **2** to **5** and **2** to **6** were carried out by a procedure similar to that described above. In these reactions also, the nitrile oxide, **2**, attacked the more electron-rich double bonds of **5** and **6** to give 8,9-bis(methoxycarbonyl)-5-phenyl-2,6-*endo*-3-oxa-4-azatricyclo[5.2.2.0^{2,6}]undeca-4,9-diene(**12**) and 11,12-bis(methoxycarbonyl)-5-phenyl-2,6-*exo*-3-oxa-4-azatricyclo[5.3.2.0^{2,6}]dodeca-4,11-diene(**13**) respectively. These findings show that **2** also acts as an electron-accepting 1,3-dipole toward **5** and **6**.[5)]

The cycloaddition of the azide, **3**, to **5** was carried out as follows. The benzene solution of a mixture of **3** and **5** was allowed to stand in the dark for two weeks at room temperature. The subsequent usual work-up of the reaction mixture gave only one *endo* adduct, 8,9-bis(methoxycarbonyl)-5-phenyl-2,6-*endo*-3,4,5-triazatricyclo[5.2.2.0^{2,6}]undeca-3,8-diene(**14**). A similar treatment of **3** with **6** afforded one *exo* adduct, 11,12-bis(methoxycarbonyl)-5-phenyl-2,6-*exo*-3,4,5-triazatricyclo[5.3.2.0^{2,6}]dodeca-3,11-diene(**15**). These findings show that the dipole, **3**, acts as an electron-accepting 1,3-dipole toward **5** and **6**.[5)] This is consistent with the fact that the dipole, **3**, acts as an electron-accepting 1,3-dipole toward norbornene and cyclopentene.[5,6)]

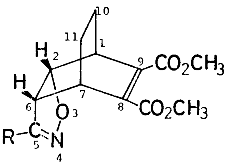
The nitrilimine, **4**, which was prepared from *N*-phenylbenzenecarbohydrazonoyl chloride(**16**)[7)] and TEA in benzene, underwent 1,3-dipolar cycloaddition to **5** to afford a mixture of two monoadducts, 8,9-bis(methoxycarbonyl)-3,5-diphenyl-2,6-*endo*-3,4-diazatricyclo[5.2.2.$0^{2,6}$]undeca-4,8-diene(**17**) and 2-*exo*,6-*exo*-bis(methoxycarbonyl)-3,5-diphenyl-2,6-*endo*-3,4-diazatricyclo[5.2.2.$0^{2,6}$]undeca-4,8-diene(**18**). A similar treatment of **4** with **6** gave two *exo* adducts, 11,12-bis(methoxycarbonyl)-3,5-diphenyl-2,6-*exo*-3,4-diazatricyclo[5.3.2.$0^{2,6}$]dodeca-4,11-diene(**19**) and 2-*endo*, 6-*endo*-bis(methoxycarbonyl)-3,5-diphenyl-2,6-*exo*-3,4-diazatricyclo[5.3.2.$0^{2,6}$]dodeca-4,11-diene(**20**). The cycloadducts, **17** and **19**, are those which were produced by the addition of **4** to the more electron-rich double bonds of **5** and **6**, while the **18** and **20** adducts are those which were produced by the addition of **4** to the more electron-poor double bonds of **5** and **6**. These results indicate that the dipole, **4**, acts both as an electron-accepting 1,3-dipole and as an electron-donating one toward **5** and **6**.[5)]

The cycloaddition of **1** to **7** was carried out by the method described above. This reaction gave a mixture of the *exo*- and *endo* adducts, 5-benzoyl-8-*endo*, 9-*endo*-bis(methoxycarbonyl)-2,6-*exo*-3-oxa-4-azatricyclo[5.2.2.$0^{2,6}$]undec-4-ene(**21**) and 5-benzoyl-8-*endo*, 9-*endo*-bis(methoxycarbonyl)-2,6-*endo*-3-oxa-4-azatricyclo[5.2.2.$0^{2,6}$]undec-4-ene(**22**) in yields of 29% and 6% respectively, with a recovery of 63% of **7**.

Table 1. Yields and product compositions

Olefin	1,3-Dipole	Adduct	Yield[a)] (%)	Composition *exo* (%)	Composition *endo* (%)	Recovery of olefin (%)
5	**1**	**10**	98	0	100	0
6	**1**	**11**	76	100	0	14
5	**2**	**12**	79	0	100	9
6	**2**	**13**	77	100	0	11
5	**3**	**14**	70	0	100	23
6	**3**	**15**	67	100	0	21
5	**4**	**17**	53	0	68	35
		and				
		18		0	32	
6	**4**	**19**	75	81	0	17
		and				
		20		19	0	
7	**1**	**21**	35	83	17	63
		and				
		22				

a) The yields are based on the starting olefins.



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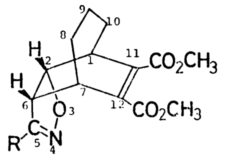
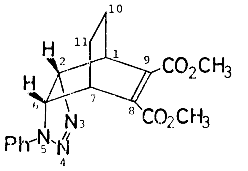
12, R = C_6H_5



11, R = C_6H_5CO
13, R = C_6H_5



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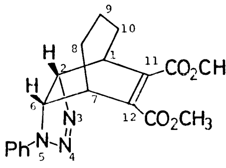

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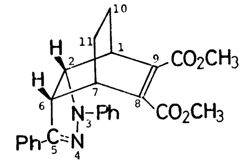

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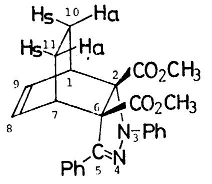

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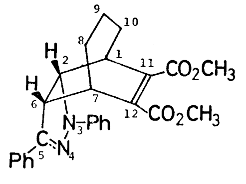

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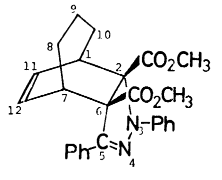

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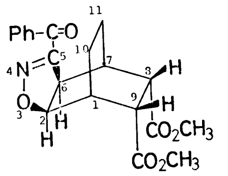

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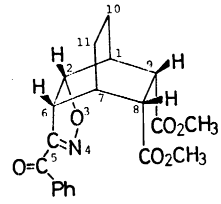

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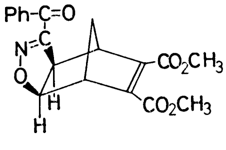

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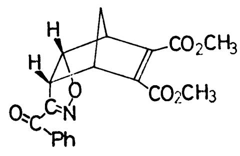

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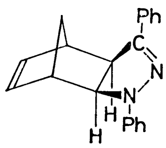

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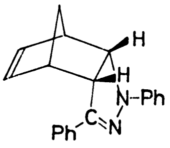

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The yields of the adducts and the product compositions are summarized in Table 1.

Analyses of NMR Spectra of Adducts. The *exo*- or *endo* assignment of each adduct was based on the NMR data(Table 2). The configurations of all the adducts except for **18** and **20** could be determined from the chemical shifts of their methoxycarbonyl groups. As is shown in Table 2, for the **10**—**15** and **22** adducts, one of the two methoxycarbonyl groups of each adduct appeared in a field higher by 0.21—0.48 ppm than the other. Moreover, the low-field methoxycarbonyl groups have chemical shifts of about δ 3.7—3.8 ppm which resemble the chemical shifts of mehtoxycarbonyl goups of the referential compounds (**5**, **6**, and dimethyl maleate (**23**)). For the **17** and **19** adducts the two methoxycarbonyl groups of each adduct appeared in fields higher by about 0.3—0.4 ppm than those of

Table 2. Chemical shifts of methoxycarbonyl groups and vinyl protons in adducts and referential compounds[a,b]

Compound	CO_2CH_3		$\Delta\delta$[c]	Vinyl protons
10	3.44	3.78	0.34	
12	3.38	3.74	0.36	
14	3.38	3.75	0.37	
17	3.33	3.45	0.42[d]	
11	3.50	3.75	0.25	
13	3.49	3.74	0.25	
15	3.50	3.71	0.21	
19	3.44	3.54	0.32[e]	
21	3.63	3.67	0.04	
22	3.16	3.62	0.48	
23	3.81	3.81	0.00	
24	3.78[f]	3.81[f]	0.03	
25	3.33[f]	3.78[f]	0.45	
5	3.73	3.73	0.00	6.34
6	3.75	3.75	0.00	6.27
7	3.58[g]	3.58[g]	0.00	6.33[g]
18	3.58	3.68	0.10	5.93[h]
20	3.62	3.69	0.07	5.80[h]
26				6.25[i]
27				6.25[f]
28				5.89[f]

a) The spectra were recorded at 60 MHz. b) Expressed in δ ppm units, with TMS as the internal standard, in $CDCl_3$ solutions. c) The difference in chemical shift between the high-field methoxycarbonyl and the low-field methoxycarbonyl protons. d) The difference between the chemical-shift value (3.81) of the methoxycarbonyl of dimethyl maleate and the average of the values, 3.33 and 3.45. e) The difference between the chemical-shift value (3.81) of the methoxycarbonyl of dimethyl maleate and the average of the values, 3.44 and 3.54. f) Ref. 2. g) K. Tori, Y. Takano, and K. Kitakonoki, *Chem. Ber.*, **97**, 2798 (1964). h) The value at the center of the ABq. i) K. Tori, Y. Hata, R. Muneyuki, Y. Takano, T. Tsuji, and H. Tanida, *Can. J. Chem.*, **42**, 926 (1964).

the referential compound, **23**. The molecular models of the adducts reveal that the high field methoxycarbonyl groups lie in the shielding cones of benzene rings attached on the heterocyclic moieties of the adducts. On the other hand, the **21** adduct exhibited the chemical shifts of the two methoxycarbonyl groups at δ 3.63 and 3.67 ppm, whose values were normal. This indicated that the adduct has the *exo* configuration. Such an assignment has also been carried out for the *exo*- and *endo* adducts, **24** and **25**, formed by the cycloaddition of **1** to 2,3-bis(methoxycarbonyl)-norbornadiene.[2] The configurations of the **18** and **20** adducts were determined as follows. The vinyl protons of these adducts appeared as AB quartets of doublets in fields higher by about 0.3—0.4 ppm than those of the referential compounds, **5**, **6**, **7**, and bicyclo[2.2.2]-oct-2-ene(**26**). These up-field shifts are probably due to the diamagnetic anisotoropy effects of the carbon-nitogen double bonds.[8] This finding indicates that the vinyl protons of these adducts are placed above the carbon-nitrogen double bonds of the heterocyclic moieties. The structures of **18** and **20** are consistent with this finding. Such an assignment has also been carried out for the *exo*- and *endo* adducts, **27** and **28**, formed by the cycloaddition of **4** to norbornadiene.[2]

Discussion

This kind of 1,3-dipolar cycloaddition has been shown to be a kinetically controlled reaction.[1,2,9] Hence, all the adducts obtained here are kinetically controlled products.

About Steric Hindrance. Two 7,8-*syn*-hydrogen atoms are present on the *exo* side of **5**, but such hydrogen atoms are absent on the *endo* side. A similar difference in steric hindrance is present between the *exo*- and *endo* sides of **6**. For this reason, it might appear that the steric hindrance is a factor which brings about the highly stereoselective cycloadditions of 1,3-dipoles toward the dienes, **5** and **6**.

From the fact that the cycloaddition of **1** to **7** gave both the *exo*- and *endo* adducts, however, we doubt the above explanation based on the steric hindrance theory. The molecular models of **5** and **7** show that the difference in steric crowding between the *exo*- and *endo* sides of **5** is smaller than that in steric crowding between the *exo* and *endo* sides of **7**. This implies that the *endo*/*exo* product ratio for the cycloaddition of **1** to **5** must become closer to unity than that for the cycloaddition of **1** to **7**, provided that the preferred direction of reaction is controlled only by the steric hindrance. As Table 1 shows, however, the *endo*/*exo* product ratio for the cycloaddition of **1** to **5** is infinity, while that for the cycloaddition of **1** to **7** is 0.21. This finding shows that the direction of the attack of the 1,3-dipole, **1**, on the double bond of **5** can not be determined only by the steric hindrance. For the same reason, the predominant *exo* cycloaddition of **1** to **6** can not be explained by the steric hindrance alone. For all the other cycloadditions carried out here as well, these findings suggest that the steric hindrance is not a main factor controlling the stereochemistry of these reactions.

The Interaction of the Two Carbon-Carbon Double Bonds.

a) For bicyclo[2.2.2]octa-2,5-diene and bicyclo-[3.2.2]nona-6,8-diene, the presence of a homoconjugation between the two non-neighboring carbon-carbon double bonds has been found by investigating the photoelectron spectroscopy of these dienes.[10]

b) The relative rate ratios of the cycloadditions of **4** to cyclohexene, cyclopentene, 1-heptene, dimethyl maleate, and dimethyl fumarate can be derived from the data of Eckell *et al.*[5c] (Table 3). Table 3 suggests that the dipole, **4**, undergoes cycloadditions to the more electron-poor double bonds of the dienes, **5** and **6**, rather than to the more electron-rich double bonds. In practice, however, the 1,3-dipolar cycloadditions occured preferentially on the more electron-rich double bonds of **5** and **6** (Table 4). This attack on the reverse site must be ascribed to the interaction between the two non-neighboring carbon-carbon

Table 3. Relative rates of the addition of **4**[a)]

Compound	Relative rates
Cyclohexene	1
Cyclopentene	8.7
1-Heptene	9.1
Dimethy maleatc	530
Dimethy fumalate	19, 100

a) Derived from Ref. 5c.

Table 4. The attacking site of **4** on **5** and **6**

Diene	Electron-rich double bond (%)	Electron-poor double bond (%)
5	68	32
6	81	19

double bonds of **5** or **6**, as will be described below.

A Tentative Explanation of the Highly Stereoselective Cycloadditions. *a) The LU-Controlled Reactions of 1,3-Dipoles with the Dienes, 5 and 6*: As has described above, the 1,3-dipoles **1**—**4**, act as electron-accepting dipoles toward the more electron-rich double bonds of **5** and **6**. In Houk's terminology, these cycloadditions are called LU-controlled reactions.[5b)] In these cases, the interaction of the dipole LUMO(lowest unoccupied molecular orbital) with the dipolarophile HOMO (highest occupied molecular orbital) is greatest.[5b)] The predominant *endo* cycloadditions toward **5** and *exo* cycloadditions toward **6** can be reasonably explained by the orbital mixing rule.[11)] This rule treats the extension of an orbital at an interacting center in a certain direction. Now, we shall consider the orbital extension of the HOMO of the more electron-rich double bond (C_5–C_6) of **5** to the *exo*- and *endo* sides. The rehybridization originates from the mixing of the C_5–C_6 σ orbital in the C_5–C_6 π orbital(HOMO) under the influence of the C_2–C_3 π orbital(HOMO). The C_5–C_6 double bond interacts with the C_2–C_3 double bond on the *endo* side, as has been described above. The three orbitals and their energy relation are shown in Fig. 1.[12)] From the orbital mixing rule, it can be predicted that the HOMO of the C_5–C_6 double bond extends more to the *endo* side than to the *exo* side (Fig. 1.). Consequently, the 1,3-dipoles, **1**—**4**, attack predominantly from the *endo* side. In the same treatment, the HOMO of the C_8–C_9 double bond of **6** can be predicted to extend more greatly to the *exo* side than to the *endo* side. This explains the predominant *exo* cycloaddition to the C_8–C_9 double bond of **6**. Such a treatment has also been carried out for the HOMO of norbornene.[11a)]

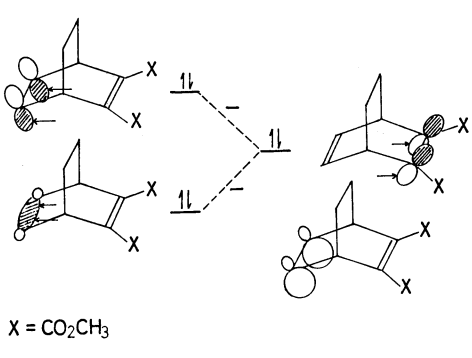

Fig. 1. Origin and direction of nonequivalent HOMO extension of **5**,

b) *The HO-Controlled Reaction of the Nitrilimine, 4, with 5 and 6*: The 1,3-dipole, **4**, acts as an electron-donating dipole toward the more electron-poor double bonds of **5** and **6**, as has been described above. In Houk's terminology, these cycloadditions are called HO-controlled reactions.[5b)] In these cases, the interaction of the dipole HOMO with the dipolarophile LUMO is greatest.[5b)] Hence, we shall consider the orbital extension of the LUMO of the more electron-poor double bond(C_2–C_3) of **5** using the orbital mixing rule in order to explain the predominant endo cycloaddition of **4** to this double bond. In this case, the interaction among the three orbitals, the C_2–C_3 σ^* orbital, the C_2–C_3 π^* orbital(LUMO), and the C_5–$C_6\pi^*$ orbital(LUMO), is taken account of on the *endo* side. The three orbitals and their energy relation are shown in Fig. 2.[14)] The orbital mixing rule predicts that the LUMO of the C_2–C_3 double bond will extend more to the *endo* side than to the *exo* side (Fig. 2.). Consequently, the dipole, **4** attacks predominantly from the *endo* side. In the same treatment, the LUMO of the C_6–C_7 double bond of **6** is predicted to extend more to the *exo* side than to the *endo* side. This reasonably explains the predominant *exo* cycloaddition of **4** to the C_6–C_7 double bond of **6**.

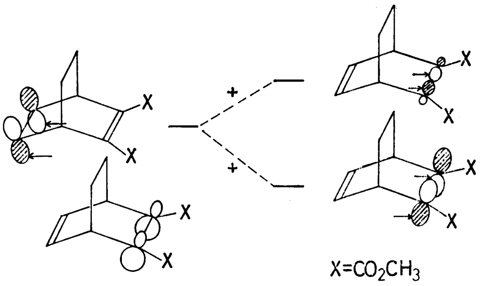

Fig. 2. Origin and direction of nonequivalent LUMO extension of **5**.

Experimental

Materials. The precursors of 1,3-dipoles (**8**,[3)] **16**,[15)] and *N*-hydroxybenzenecarboximidoyl chloride (**29**)[16)]) and the azide, **3**,[17)] were prepared by methods described in the literature. The dienes, **5**[18)] and **6**,[19)] and the monoene, **7**,[20)] were also prepared by the methods described in the literature.

Cycloaddition of 1 to 5. Into a stirred solution of **5** (1.10 g, 5.0 mmol) and **8**(0.92 g, 5.0 mmol) in dry THF (15 cm^3) cooled in an ice bath, a solution of triethylamine (TEA) (0.65 g, 6.5 mmol) in dry THF (10 cm^3) was added, drop by drop, over a period of 1 h. After an additional stirring for 1 h at the same temperature, the resulting triethylammonium chloride was removed by filtration. The TLC of the filtrate showed only one spot (elution with benzene–ether(9:1)). After the evaporation of the solvent, the yellowish residue was washed with several drops of 95%

EtOH. The solid was separated by filtration and dried under reduced pressure to give 1.79 g(98%) of the adduct, **10**. It was recrystallized from 95% EtOH to afford colorless needles: Mp 97—98 °C; IR(KBr) 1733(ester C=O), 1710(ester C=O), 1650(C=O), 1440 and 1280 cm^{-1}; NMR ($CDCl_3$) δ=1.56(4H, m, CH_2CH_2), 3.44(3H, s, 8-CO_2CH_3), 3.58(1H, m), 3.76(1H, m), 3.78(3H, s, 9-CO_2CH_3), 3.95 (1H, dd, J=10 and 4 Hz, 6-H), 4.98(1H, dd J=10 and 4 Hz, 2-H), and 7.3—8.3 ppm (5H, m).

Found: C, 65.03; H, 5.10; N, 3.56%. Calcd for $C_{20}H_{19}N_1O_6$: C, 65.03; H, 5.19; N, 3.79%.

*Cycloaddition of **1** to **6**.* A solution of **6**(710 mg, 3.0 mmol) and **8**(551 mg, 3.0 mmol) in dry THF(15cm^3) was treated with TEA(370 mg, 3.7 mmol) in dry THF(10 cm^3) as has been described above. A similar work-up of the reaction mixture and evaporation of the solvent produced a yellowish viscous oil. This oil showed, on TLC with benzene–ether(95 : 5), two marked spots, at R_f 0.45(**6**) and at R_f 0.32(**11**). The oil was chromatographed on silica gel (200—300 mesh). Elution with benzene–ether(95 : 5) gave **6**(96 mg, recovery 14%) and a white solid of **11**(877 mg, 76%). The solid was recrystallized from MeOH to afford colorless leaves: Mp 98—99 °C; IR(KBr) 1735(ester C=O), 1715(ester C=O), 1660(C=O), 1440, 1275, and 1260 cm^{-1}; NMR($CDCl_3$) δ=1.74(6H, s, $(CH_2)_3$), 3.27(1H, m), *ca.* 3.5(1H, m), 3.50(3H, s, 12-CO_2CH_3), 3.75(3H, s, 11-CO_2CH_3), 4.18(1H, dd, J=10.5 and 1.5 Hz, 6-H), 5.18(1H, dd, J=10.5 and 2.5 Hz, 2-H), and 7.1—8.2 ppm(5H, m).

Found: C, 65.75; H, 5.51; N, 3.55%. Calcd for $C_{21}H_{21}N_1O_6$: C, 65.78; H, 5.52; N, 3.65%.

*Cycloaddition of **2** to **5**.* A solution of **5**(1110 mg, 5.0 mmol) and **29**(778 mg, 5.0mmol) in dry THF(15 cm^3) was treated with TEA(610 mg, 6.0 mmol) in dry THF(10 cm^3) by a procedure like that described above. A similar work-up of the reaction mixture and evaporation of the solvent gave a yellowish viscous oil. On TLC with benzene–ether (95:5), the oil showed three spots, at R_f 0.75(3,4-diphenyl-1,2,5-oxadiazole 2-oxide (**30**)), R_f 0.40(**5**), and R_f 0.13(**12**). The oil was column chromatographed on silica gel with benzene–ether (95:5) to give a white solid of **30**(37 mg, mp 115—116 °C (lit,[21] mp 112 °C)), **5**(116 mg, recovery 10%), and a solid of **12**(1331 mg, 78%).

Adduct **12** : Mp 148—149 °C(colorless cubic crystals from MeOH); IR(KBr) 1705(ester C=O), 1433, and 1290 cm^{-1} ; NMR($CDCl_3$) δ=1.46 and 1.62(4H, ABq, J=12 Hz, CH_2CH_2), 3.38(3H, s, 8-CO_2CH_3), *ca.* 3.5(1H, m), 3.65(1H, m), 3.74(3H, s, 9-CO_2CH_3), 3.88(1H, dd, J=10 and 3 Hz, 6-H), 4.93(1H, dd, J=10 and 4.0 Hz, 2-H), and 7.2—7.8 ppm(5H, m).

Found: C, 66.91; H, 5.50; N, 4.15% Calcd for $C_{19}H_{19}N_1O_5$: C, 66.85; H, 5.61; N, 4.10%.

*Cycloaddition of **2** to **6**.* A solution of **6**(710 mg, 3.0 mmol) and **29**(476 mg, 3.0 mmol) in dry THF(15 cm^3) was treated with TEA(370 mg, 3.7 mmol) in dry THF(10 cm^3) as has been described above. A similar work-up of the reaction mixture and evaporation of the solvent afforded a yellowish viscous oil, which showed three spots on TLC with benzene–ehyl acetate(95:5). It was column chromatographed on silica gel. Elution with benzene–ethyl acetate (95:5) gave **30**(24 mg), **6**(78 mg, recovery 11%),and a solid of **13**(819 mg, 77%).

Adduct **13** : Mp 129—130 °C(colorless cubic crystals from MeOH–H_2O); IR(KBr) 1720(ester C=O), 1440, and 1295 cm^{-1}; NMR($CDCl_3$) δ=1.71(6H, s, $CH_2CH_2CH_2$), 3.11(1H, m), 3.38(1H, m), 3.49(3H, s, 12-CO_2CH_3), 3.74 (3H, s, 11-CO_2CH_3), 4.12(1H, dd, J=10.5 and 1.5 Hz, 6-H), 5.26(1H, dd, J=10.5 and 2.5 Hz, 2-H), and 7.2—7.8 ppm (5H, m).

Found: C, 67.37; H, 5.89; N, 3.98%. Calcd for $C_{20}H_{21}N_1O_5$: C, 67.59; H, 5.96; N, 3.94%.

*Cycloaddition of **3** to **5**.* A mixture of **5**(560 mg, 2.5 mmol) and **3**(298 mg, 2.5 mmol) was dissolved in dry benzene (5 cm^3). After the solution had then been allowed to stand in the dark for two weeks at room temperature, it showed two spots(**5** and **14**) on TLC with benzene–ethyl acetate(8:2). After the removal of the solvent, the residue was column chromatographed on alumina. Elution with benzene–ehtyl acetate(8:2) gave **5**(129 mg, recovery 23%). Further elution with the same solvent afforded **14** (600 mg, 70%), which was subsequently recrystallized from MeOH to give colorless prisms: Mp 151—152 °C; IR(KBr) 1715(ester C=O), 1605, 1493, 1440, and 1300 cm^{-1}; NMR($CDCl_3$) δ=1.47 and 1.68(4H, ABq, J=11 Hz, CH_2CH_2), 3.38(3H, s, 8-CO_2CH_3), 3.75(3H, s, 9-CO_2 CH_3), 3.6—3.9(2H, m), 4.10(1H, dd, J=11.5 and 3.5 Hz, 6-H), 4.86(1H, dd, J=11.5 and 3.5 Hz, 2-H), and 6.7—7.6 ppm(5H, m).

Found: C, 63.49; H, 5.50; N, 12.30%. $C_{18}H_{19}N_3O_4$: C, 63.33; H, 5.61; N, 12.31%.

*Cycloaddition of **3** to **6**.* A solution of **6**(708 mg, 3.0 mmol) and **3**(357 mg, 3.0 mmol) in dry benzene(3 cm^3) was allowed to stand in the dark for one week at room temperature. Then, the solution showed three spots (**3**, **6**, and **15**) on TLC with benzene–ethyl acetate(9:1). The solvent was evaporated under reduced pressure to give a residue, which was column chromatographed on alumina with benzene–ethyl acetate(9:1) to afford a trace amount of **3**, **6**(148 mg, recovery 21%), and **15**(713 mg, 67%).

Adduct **15**: Mp 137—139 °C(colorless leaves from MeOH); IR(KBr) 1710(ester C=O), 1600, 1490, 1433, and 1287 cm^{-1}; NMR($CDCl_3$) δ=1.73(6H, s, $CH_2CH_2CH_2$), 3.38 (1H, m), 3.50(3H, s, 12-CO_2CH_3), *ca.* 3.7(1H, m), 3.71(3H, s, 11-CO_2CH_3), 4.37(1H, dd, J=12 and 1.5 Hz, 6-H), 5.01(1H, dd, J=12 and 2 Hz, 2-H), and 6.8—7.6 ppm (5H, m).

Found: C, 64.26; H, 6.06; N, 11.81%. Calcd for $C_{19}H_{21}N_3O_4$: C, 64.21; H, 5.96; N, 11.83%.

*Cycloaddition of **4** to **5**.* A mixture of **5**(558 mg, 2.5 mmol) and **16**(576 mg, 2.5mmol) was dissolved in dry benzene(10 cm^3). Into the solution, TEA(940 mg, 9.3 mmol) was then added all at once, after which the solution was allowed to stand in the dark for two weeks at room temperature. The resulting ammonium chloride was removed by filtration. The filtrate showed, on TLC with benzene, four spots, at R_f 0.65(**16**), R_f 0.25(**18**), R_f 0.16(**5**), and R_f 0.09(**17**). A large amount of the solvent was removed under reduced pressure. Then, the concentrated solution was chromatographed on silica gel. Subsequent elution with benzene afforded a solid of **16**(229 mg, recovery 40%), a solid of **18**(174 mg, 17%), **5**(193 mg, recovery 35%), and a yellow solid of **17**(379 mg, 36%) in that order.

Adduct **17**: Mp 169—170 °C(yellow sticks from EtOH); IR(KBr) 1717(ester C=O), 1600, 1500, and 1300 cm^{-1}; NMR($CDCl_3$) δ=1.49 and 1.69(4H, ABq, J=10 Hz, CH_2CH_2), 3.33(3H, s, CO_2CH_3), 3.45(3H, s, CO_2CH_3), 3.55 (1H, m), 3.89(1H, dd, J=12 and 2.5 Hz, 6-H), 3.90(1H, m), 4.45(1H, dd, J=12 and 2.5 Hz, 2-H), and 6.6—7.8 ppm(10H, m).

Found: C, 72.22; H, 5.97; N, 6.97%. Calcd for $C_{25}H_{24}N_2O_4$: C, 72.10; H, 5.81; N, 6.73%.

Adduct **18**: Mp 217—219 °C(colorless cubic crystals from hexane–benzene); IR(KBr) 1742(ester C=O), 1737(ester C=O), 1600, 1593, 1500, 1262 cm^{-1}; NMR($CDCl_3$) δ=

1.12(2H, d, J=8 Hz, 10-*syn* H and 11-*syn* H), 2.35(2H, d, J=8H, 10-*anti* H and 11-*anti* H), 3.58(3H, s, CO_2CH_3), 3.68(3H, s, CO_2CH_3), 3.5—3.7(2H, m), 5.86 and 6.01(2H, ABq of d, $J_{8,9}$=8 Hz and $J_{7,8}$=$J_{1,9}$=6.5 Hz, 8-H and 9-H), and 6.8—7.9 ppm(10, m).

Found: C, 71.94; H, 5.65; N, 6.68%. Calcd for $C_{25}H_{24}N_2O_4$: C, 72.10; H, 5.81; N, 6.73%.

Cycloaddition of 4 to 6. A mixture of **5**(710 mg, 3.0 mmol), **16**(692 mg, 3.0 mmol), and TEA(1130 mg, 11.2 mmol) was dissolved in dry benzene(10 cm^3). The solution was then allowed to stand for 24 h, and the resulting triethylammonium chloride was removed by filtration. On TLC with benzene, the filtrate showed four spots, at R_f 0.79(**16**), R_f 0.36(**20**), R_f 0.25(**6**), and R_f 0.20(**19**). After the removal of the solvent, the residue was chromatographed on silica gel. Elution with benzene gave a trace of **16**, a solid of **20**(176 mg, 14%), **6**(123 mg, recovery 17%), and a yellow solid of **19** (792 mg, 61%), in that order.

Adduct **19**: Mp 181—183 °C(yellow sticks from ethyl acetate–EtOH); IR(KBr) 1713(ester C=O), 1593, 1492, and 1285 cm^{-1}; NMR($CDCl_3$) δ=1.78(6H, s, $CH_2CH_2CH_2$), 3.30 (1H, m), 3.44(3H, s, CO_2CH_3), 3.54(3H, s, CO_2CH_3), *ca.* 3.6(1H, m), 4.18(1H, dd, J=12 and 1.5 Hz, 6-H), 4.68(1H, dd, J=12 and 2 Hz, 2-H), and 6.7—8.0 ppm(10H, m).

Found: C, 72.60; H, 6.06; N, 6.44%. Calcd for $C_{26}H_{26}N_2O_4$: C, 72.54; H, 6.09; N, 6.51%.

Adduct **20**: Mp 198—200 °C(colorless needles from EtOH); IR(KBr) 1740(ester C=O), 1720(ester C=O), 1595, 1587, 1500, 1492, and 1255 cm^{-1}; NMR($CDCl_3$) δ=1.1—2.5(6H, m, $CH_2CH_2CH_2$), 3.0—4.0(2H, m), 3.62(3H, s, CO_2CH_3), 3.69(3H, s, CO_2CH_3), 5.71 and 5.90(2H, ABq of d, $J_{11,12}$= 8 Hz and $J_{1,11}$=$J_{7,12}$=6.5 Hz, 11-H and 12-H), and 6.7—8.0 ppm(10H, m).

Found: C, 72.35; H, 6.03; N, 6.39%. Calcd for $C_{26}H_{26}N_2O_4$: C, 72.54; H, 6.09; N, 6.51%.

Cycloaddition of 1 to 7. Into a solution of **7**(1120 mg, 5.0 mmol) and **8**(920 mg, 5.0 mmol) in dry THF(15 cm^3) cooled in an ice bath, a solution of TEA(620 mg, 6.1 mmol) in dry THF (10 cm^3) was stirred, drop by drop, over a period of 1 h. 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 hexane–acetone (7 : 3), four spots, at R_f 0.47(**7**), R_f 0.41(**9**), R_f 0.35(**21**), and R_f 0.32(**22**). The solvents was evaporated under reduced pressure to give a residue. It was column-chromatographed on silica gel. Elution with hexane–acetone(31:12) gave **7** (705 mg, recovery 63%), 405 mg of **9**(mp, 76—78 °C(lit$^{3)}$ 78—80 °C), a white solid of **21**(540 mg, 29%), and a white solid of **22**(110 mg, 6%) in that order.

Adduct **21**: Mp 113—114 °C(colorless plates from EtOH); IR(KBr) 1750(ester C=O) and 1660 cm^{-1}(C=O); NMR($CDCl_3$) δ=1.4—1.6(4H, m, CH_2CH_2), 2.50(1H, m), 2.77(1H, m), 3.00—3.15(2H, m, 8-H and 9-H), 3.63(3H, s, CO_2CH_3), 3.67(3H, s, CO_2CH_3), 3.88(1H, dd, J=12 and 3.5 Hz, 6-H), 5.27(1H, dd, J=12 and 3.5 Hz, 2-H), and 7.3—8.2 ppm(5H, m).

Found: C, 64.57; H, 5.76; N, 3.58%. Calcd for $C_{20}H_{21}N_1O_6$: C, 64.68; H, 5.70; N, 3.77%.

Adduct **22**: Mp 104—108 °C(dec); IR(KBr) 1750(ester C=O), 1725(ester C=O), and 1660 cm^{-1}(C=O); NMR($CDCl_3$) δ=1.3—2.0(4H, m, CH_2CH_2), 2.35—2.55(2H, m), 3.03(2H, broad, 8-H and 9-H), 3.16(3H, s, 8-CO_2CH_3), 3.62(3H, s, 9-CO_2CH_3), 4.30(1H, dd, J=12 and 4.0 Hz, 6-H), 5.28(1H, dd, J=12 and 4.0 Hz, 2-H), and 7.4—8.2 ppm(5H, m).

Found: C, 64.94; H, 5.85; N, 3.82%. Calcd for $C_{20}H_{21}N_1O_6$: 64.68; H, 5.70; N, 3.77%.

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4) Since Compound **8** is very soluble in THF(solubility, 1250 mg/cm^3 at 25 °C), the hydrogen-bonded complex between **8** and **5** (or **6**) can not be formed in THF.$^{1)}$

5) According to the calculations of Houk *et al.* for various 1,3-dipoles, the nitrile oxides, **1** and **2**, acts as electron-accepting 1,3-dipoles toward a variety of dipolarophiles. Phenyl azide also acts as an electron-accepting 1,3-dipole toward the electron-rich double bonds. The nitrilimine, **4**, varies its electron-accepting or donating character according to the kind of dipolarophile. a) K. N. Houk, J. Sims, R. E. Duke, Jr., R. W. Strozier, and J. K. George, *J. Am. Chem. Soc.*, **95**, 7287 (1973); b) K. N. Houk, J. Sims, C. R. Watts, and L. J. Luskus, *ibid.*, **95**, 7301 (1973); c) A. Eckell, R. Huisgen, R. Sustmann, G. Wallbillich, D. Grashey, and E. Spindler, *Chem. Ber.*, **100**, 2192 (1967).

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7) Since Compound **16** is sufficiently soluble in benzene (solubility, 91 mg/cm^3), the compound may not associate with **5** (or **6**) in benzene.$^{1)}$

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