(m, 3, Ar H), 9.90 (br s, 1, exchangeable COOH); NMR ($CDCl_3$) for **5e** (55% of mixture) δ 1.63 (d, 3, J = 8 Hz, $=CHCH_3$), 2.85–3.25 (m, 3, C_3 H and C_4 H_2), 4.85 (d, 1, J = 9 Hz, C_2 H), 5.45 (q, 1, J = 8 Hz, $=CHCH_3$), 5.90 (s, 2, OCH_2O), aromatic and carboxylic resonances isochronous with those in **4e**. Anal. Calcd for $C_{14}H_{14}SO_4$: C, 60.35; H, 5.07; S, 11.52. Found: C, 60.06; H, 5.21; S, 11.33.

Attempted Rearrangement of 3b. When **3b** was treated as described above, the blood-red methanolic caustic solution yielded upon concentration a purple solid (mp >360 °C) which left a residue upon ignition and displayed a violet potassium-like flame upon combustion on a platinum wire. It was identified as the salt of **3b**, IR (Nujol) 1635 cm^{-1}. Anal. Calcd for $C_{19}H_{15}SO_3K$: C, 62.96; H, 4.17. Found: C, 62.88; H, 4.19.

Acidification with 20 mL of 10% hydrochloric acid returned **3b** which was identified by melting point, mixture melting point, and infrared spectral comparison with starting material.

The rearrangement was repeated with 2 mmol of **3b** suspended in 25 mL of anhydrous methanol and refluxed for 6 h with 4 mmol of potassium hydroxide as a 10% solution in methanol. After 6 h the blood-red color still remained, and the reaction mixture was allowed to stand for 1 week at room temperature. The red color faded to a pale yellow. Upon concentration in vacuo and chilling in an ice–salt bath, 192 mg (62%) of pale yellow needles (mp 78–81 °C) were obtained whose infrared spectrum, ^1H NMR spectrum, and undepressed mixture melting point with authentic material confirmed the identification of vanillin.

Registry No. **1a**, 61477-86-9; **1c**, 939-09-3; **1d**, 56761-31-0; **2a**, 100-52-7; **2b**, 121-33-5; **2c**, 104-88-1; **2e**, 120-57-0; **3a**, 86239-17-0; **3b**, 86239-18-1; **3b**·K, 86239-27-2; **3c**, 80224-53-9; **3d**, 86239-19-2; **3e**, 86239-20-5; **4d**, 86239-23-8; **4e**, 86239-25-0; **5d**, 86239-24-9; **5e**, 86239-26-1; **6a** (R′ = H), 86239-21-6; **6a** (R′ = CH_3), 67139-62-2; **6c** (R′ = H), 86239-22-7; vanillin, 121-33-5.

Reaction of 3,4-Bis(ethoxycarbonyl)-1,2,5-oxadiazole 2-Oxide with Olefins

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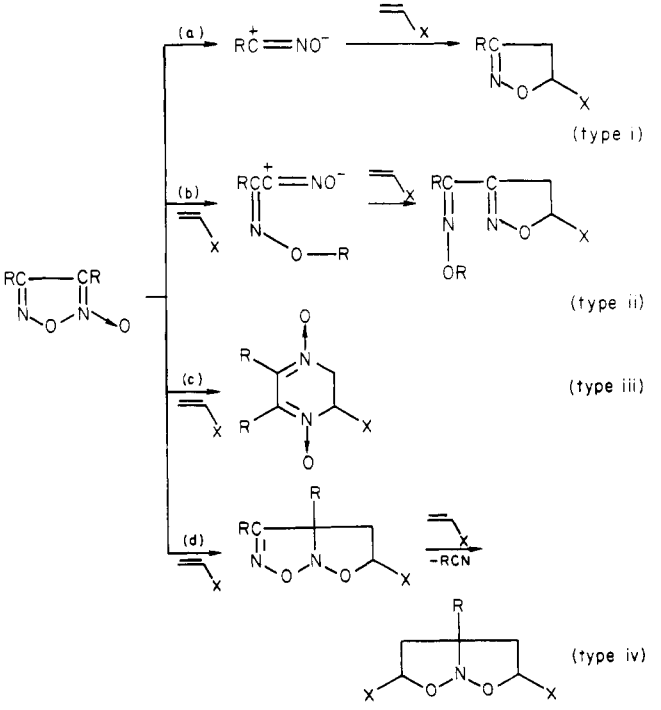
3,4-Bis(ethoxycarbonyl)-1,2,5-oxadiazole 2-oxide (1) has been shown to react with several olefins in a molar ratio of 1:2, giving 5-(ethoxycarbonyl)-1-aza-2,8-dioxabicyclo[3.3.0]octanes (2). Evidence is presented that these products arise from 1,3-dipolar cycloaddition, elimination of ethyl cyanoformate from the initial cycloadducts, and 1,3-dipolar cycloaddition of the resulting isoxazoline *N*-oxides with another mole of olefin.

Extensive studies have been carried out on the syntheses and the reaction of 1,2,5-oxadiazole 2-oxides (furoxans).[1] While it is known that furoxans are relatively stable compounds, three types of reaction with olefins can occur under relatively drastic conditions (Scheme I). Some sterically hindered furoxans[2] are decomposed thermally to 2 mol of nitrile oxides, which undergo 1,3-dipolar cycloaddition with olefins (C–C bond fission of the oxadiazole ring) (type i). Alternatively, N–O bond fission of the oxadiazole ring with concomitant migration of hydrogen[3] or acyl group[4] gives a nitrile oxide (type ii). Also documented is the conversion of benzofuroxan derivatives to olefin [4 + 2]-cycloadducts (type iii).[5]

Furoxans are formally cyclic 1,3-dipolar nitrones, but nitrone-type 1,3-dipolar cycloaddition reactions with olefins

Scheme I



as shown in Scheme I have not been reported so far (type iv).[6] We report here the first example of a nitrone-type reaction involving 3,4-bis(ethoxycarbonyl)-1,2,5-oxadiazole

(1) For reviews, see (a) J. V. R. Kaufman and J. P. Picard, *Chem. Rev.*, **59**, 429 (1959); (b) J. H. Boyer in " Heterocyclic Compounds", R. C. Elderfield, Ed., Wiley, New York, 1961, Vol. 7, pp 499–503; (c) L. C. Behr in "The Chemistry of Heterocyclic Compounds, Five and Six-Membered Compounds with Nitrogen and Oxygen", A. Weissberger, Ed., Interscience, New York, 1962, pp 295–312; (d) A. R. Katritzky and J. M. Lagowski in "Chemistry of the Heterocyclic *N*-Oxides", Academic Press, New York, 1971; (e) A. J. Boulton and P. B. Ghosh, *Adv. Heterocycl. Chem.* **10**, 1 (1969); (f) A. Gasco and A. J. Boulton, *ibid.*, **29**, 251 (1981).

(2) (a) J. Ackrell, M. Altaf-ur-Rahman, A. J. Boulton, and R. C. Brown, *J. Chem. Soc., Perkin Trans. 1*, 1587 (1972); (b) A. J. Boulton and S. S. Mathur, *J. Org. Chem.*, **38**, 1054 (1973); (c) A. Dondoni, G. Barbaro, A. Battaglia, and P. Giorgianni, *J. Org. Chem.*, **37**, 3196 (1972); (d) J. A. Chapman, J. Crosby, C. A. Cummings, and R. A. C. Rennie, *J. Chem. Soc., Chem. Commun.*, 240 (1976); (e) J. F. Barnes, M. J. Barrow, M. M. Harding, R. M. Paton, P. L. Ashcroft, J. Crosby, and C. J. Joyce, *J. Chem. Res., Synop.*, 314 (1979); *J. Chem. Res., Miniprint*, 3601 (1979); (f) R. A. Whitney and E. S. Nicholas, *Tetrahedron Lett.*, **22**, 3371 (1981).

(3) (a) J. V. Burakevich, R. S. Butler, and G. T. Volpp, *J. Org. Chem.*, **37**, 593 (1972); (b) A. Gasco, V. Mortarini, R. Calvino, and A. Sarafino, *Tetrahedron Lett.*, 627 (1974).

(4) D. R. Britteli and G. A. Boswell, Jr., *J. Org. Chem.*, **46**, 316 (1981).

(5) (a) J. W. McFarland, *J. Org. Chem.*, **36**, 1842 (1971); (b) P. Devi, J. S. Sandhu, and G. Thyagarajan, *J. Chem. Soc., Chem. Commun.*, 710 (1979).

(6) Recent study[4] indicated that the reaction of dibenzoylfuroxan with phenylacetylene or styrene was classified as a type ii reaction rather than the suggested nitrone-type reaction.[7]

(7) M. Alter-ur-Rahman, A. J. Boulton, and D. Middleton, *Tetrahedron Lett.*, 3469 (1972).

0022-3263/83/1948-3053$01.50/0

Table I. 3,7-Disubstituted 5-(Ethoxycarbonyl)-1-aza-2,8-dioxabicyclo[3.3.0]octanes (2)[a]

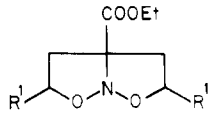
compd	R^1	yield, %	mp (bp), °C	^{1}H NMR ($CDCl_3$), δ
2a	2-naphthoxy	21	135-136	1.3 (t, 3 H, J = 7 Hz), 2.66-3.4 (m, 4 H), 4.33 (q, 2 H, J = 7 Hz), 6.15 (dd, 2 H, J = 3, 6 Hz), 7.0-7.9 (m, 14 H)
2b	n-C_6H_{13}	38	(193-196 (1 mmHg))	0.6-1.1 (m, 6 H), 1.1-2.07 (br, 23 H), 2.07-3.07 (m, 4 H), 4.20 (q, 2 H, J = 7 Hz), 4.2-4.8 (m, 2 H)
2c	n-C_7H_{15}	25	38-39	0.7-1.1 (m, 6 H), 1.1-1.9 (br, 27 H), 2.1-2.7 (m, 4 H), 4.2 (q, 2 H, J = 7 Hz), 4.2-4.7 (m, 2 H)
2d	n-C_8H_{17}	30	52-55	0.7-1.1 (m, 6 H), 1.1-1.9 (br, 31 H), 2.1-2.8 (m, 4 H), 4.2 (q, 2 H, J = 7 Hz), 4.2-4.7 (m, 2 H)
2e	n-$C_{10}H_{21}$	39	65-67	0.7-1.1 (m, 6 H), 1.1-1.7 (br, 39 H), 2.05-2.9 (m, 4 H), 4.2 (q, 2 H, J = 7 Hz), 4.2-4.7 (m, 2 H)
2f	n-$C_{12}H_{25}$	45	72-75	0.7-1.05 (m, 6 H), 1.1-1.9 (br, 47 H), 2.07-2.7 (m, 4 H), 4.2 (q, 2 H, J = 7 Hz), 4.2-4.7 (m, 2 H)
2g	$CH_2C_6H_5$	35	104-105	1.27 (t, 3 H), 1.9-3.3 (m, 8 H), 4.23 (q, 2 H, J = 7 Hz), 4.4-4.9 (m, 2 H), 7.2 (s, 10 H)
2h	$CH_2OC_6H_5$	84	oil	1.27 (t, 3 H), 2.1-3.2 (m, 4 H), 3.9-5.0 (m, 8 H), 6.6-7.3 (m, 10 H)
2i	$CH_2OC_6H_4NO_2$	74	163-165	1.3 (t, 3 H, J = 7 Hz), 2.0-3.3 (m, 4 H), 4.05-4.5 (m, 6 H), 4.5-5.2 (m, 2 H), 6.93 (d, 4 H, J = 9 Hz), 8.1 (d, 4 H, J = 9 Hz)
2j(ex-ex)	C_6H_5	10	104-110[b]	1.3 (t, 3 H, J = 7 Hz), 2.1-3.5 (m, 4 H), 4.27 (q, 2 H, J = 7 Hz), 5.58 (dd, 2 H, J = 9.6, 6.6 Hz), 7.38 (s, 10 H)
2j(ex-en)	C_6H_5	10	104-110[b]	1.33 (t, 3 H, J = 7 Hz), 2.1-3.5 (m, 4 H), 4.30 (q, 2 H, J = 7 Hz), 5.15 (dd, 1 H, J = 10, 6 Hz), 5.7 (dd, 1 H, J = 10, 6 Hz), 7.35 (s, 5 H), 7.38 (s, 5 H)
2k	CO_2CH_3	72	(200-206 (5 mmHg))	1.3 (t, 3 H, J = 7 Hz), 2.5-3.4 (m, 4 H), 3.77 (s, 6 H), 4.23 (q, 2 H, J = 7 Hz), 4.7-5.1 (m, 2 H)

[a] Satisfactory analytical data were obtained for these compounds. [b] The melting point of the mixture of 2j(ex-ex) and 2j(ex-en).

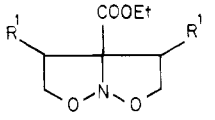
2-oxide (1, diethyl furoxandicarboxylate) and the mechanistic features of this reaction.

Results and Discussion

The reactions of 1 with various olefins (1:2 molar ratio) were carried out in refluxing xylene for 24 h. 3,7-Disubstituted 5-(ethoxycarbonyl)-1-aza-2,8-dioxabicyclo[3.3.0]-octanes (2) were isolated from the reaction mixture of 1 and several monosubstituted olefins (see type iv in Scheme I and Table I). The structure of the cycloadducts were assigned on the basis of spectral and analytical data and comparison to NMR spectral data of analogous compounds appearing in the literature.[8] Although three regioisomers (2-4) are possible, only one product was obtained. The



2a-k



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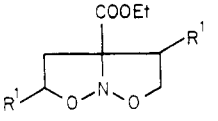
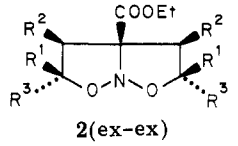
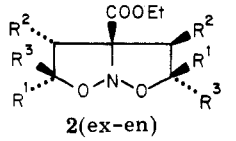


4

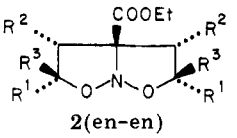
structure of the 3,7-disubstituted regioisomer (2) seems to accord best with the observed chemical shifts of 3- and 7-methine protons. Any of three exo and endo stereoisomers [2(ex-ex), 2(ex-en), and 2(en-en), (R^2, R^3 = H)] are



2(ex-ex)

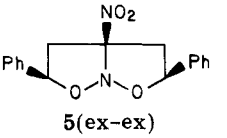


2(ex-en)

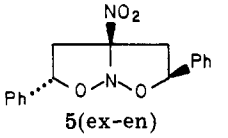


2(en-en)

proposed for the structure of the 1:2 cycloadducts. Although the precise stereochemistry of all the cycloadducts could not be assigned on the basis of their NMR spectra, the product from 1 and styrene was deduced to be a mixture (ca. 1:1 molar ratio) of 2j(ex-ex) and 2j(ex-en) by comparison of their spectra with those of the corresponding nitro compounds [5(ex-ex) and 5(ex-en)], which have been



5(ex-ex)



5(ex-en)

thoroughly studied.[8] The NMR spectrum of 2j(ex-ex) shows both phenyl protons at the same chemical shift value and all the ring protons of the bicyclic system as a single ABX pattern. In the exo-endo isomer the protons of the bicyclic system appear as two ABX patterns.

Similar cycloadducts (2m-2v) were also obtained from the reaction of 1 with polysubstituted olefins (Table II). The reaction of 1 with 1,1-disubstituted olefins gave 3,3,7,7-tetrasubstituted cycloadducts (2m-2p). Both an exo-exo isomer 2n(ex-ex) and an exo-endo isomer 2n-(ex-en) were isolated in 20% and 35% yield, respectively, from the reaction of 1 and *p*-(isopropenyloxy)nitrobenzene. Maleimides treated with 1 gave exo-endo ring-fused isomers 2r-2t. On the other hand, exo-exo isomer 2q was the only isolable product from the reaction mixture of 1 and norbornene. The products from the reaction of 1 with acenaphthylene are a mixture of two stereoisomers, 2u-(ex-ex) and 2u(ex-en), in 12% and 61% yields, respectively. Each isomer was isolated and characterized separately by NMR. An abnormal upfield shift of methyl protons [δ 0.37 and 0.43 for 2u(ex-ex) and 2u(ex-en), respectively] and methylene protons [δ 3.50 and 3.60 for 2u(ex-ex) and 2u(ex-en), respectively] was noted for the carbethoxy ethyl protons. These upfield shifts can be ascribed to the shielding effect of the exo naphthalene ring, and consequently the 2u(ex-ex) isomer is more shielded than exo-endo isomer.

(8) V. M. Shitkin, V. A. Korenevskii, V. G. Osipov, M. V. Kashutina, S. L. Ioffe, I. E. Chlenov, and V. A. Tartakovskii, *Zh. Org. Khim.*, 8, 864 (1972).

Table II. Polysubstituted 5-(Ethoxycarbonyl)-1-aza-2,8-dioxabicyclo[3.3.0]octanes (2)[a]

compd	R^1	R^2	R^3	yield, %	mp, (bp), °C	^{1}H NMR,[b] δ
2m	$CH_2OC_6H_5$	H	CH_3	62	oil	1.1-1.7 (m, 9 H), 2.1-3.3 (m, 4 H), 3.7-4.65 (m, 6 H), 6.6-7.5 (m, 10 H)
2n(ex-ex)	$CH_2OC_6H_4NO_2$-*p*	H	CH_3	20	160-162	1.2 (t, 3 H, *J* = 7 Hz), 1.7 (s, 6 H), 2.37 (d, 2 H, *J* = 13 Hz), 3.1 (d, 2 H, *J* = 13 Hz), 4.07 (s, 4 H), 4.22 (q, 2 H, *J* = 7 Hz), 6.98 (d, 2 H, *J* = 10 Hz), 8.18 (d, 4 H, *J* = 10 Hz)
2n(ex-en)	$CH_2OC_6H_4NO_2$-*p*	H	CH_3	35	132-135	1.3 (t, 3 H, *J* = 7 Hz), 1.55 (s, 3 H), 1.60 (s, 3 H), 2.47 (d, 1 H, *J* = 13 Hz), 2.58 (d, 1 H, *J* = 13 Hz), 2.95 (d, 1 H, *J* = 13 Hz), 3.02 (d, 1 H, *J* = 13 Hz), 4.08 (s, 2 H), 4.22 (s, 2 H), 4.27 (q, 2 H, *J* = 7 Hz), 6.99 (d, 4 H, *J* = Hz), 8.18 (d, 4 H, *J* = 9 Hz)
2p	CO_2CH_3	H	CH_3	54	(160-165 (1 mmHg))	1.1-1.7 (m, 9 H), 2.2-3.6 (m, 4 H), 3.73 (s, 6 H), 4.0-4.5 (m, 4 H)
2q(ex-ex)	-C_5H_8-		H	21	107-108	0.70-1.87 (m, 12 H), 1.35 (t, 3 H, *J* = 7 Hz), 2.2-2.67 (m, 6 H), 4.33 (q, 2 H, *J* = 7 Hz), 4.43 (d, 2 H, *J* = 7 Hz)
2r(ex-en)	-CON(Ph)CO-		H	55	268	1.17 (t, 3 H, *J* = 7 Hz), 4.2 (q, 2 H, *J* = 7 Hz), 4.55 (d, 1 H, *J* = 8 Hz), 4.65 (d, 1 H, *J* = 8 Hz), 5.15 (d, 1 H, *J* = 8 Hz), 5.82 (d, 1 H, *J* = 8 Hz), 7.1-7.8 (m, 10 H)
2s(ex-en)	-CON(Et)CO-		H	85	184-185	0.85-1.4 (m, 9 H), 3.4 (q, 4 H, *J* = 7 Hz), 4.15 (q, 2 H, *J* = 7 Hz), 4.25 (d, 1 H, *J* = 8 Hz), 4.35 (d, 1 H, *J* = 8 Hz), 4.72 (d, 1 H, *J* = 8 Hz), 5.5 (d, 1 H, *J* = 8 Hz)
2t(ex-en)	-CON(Ph)CO-		CH_3	20	257-259	1.13 (t, 3 H, *J* = 7 Hz), 1.42 (s, 3 H), 1.65 (s, 3 H), 4.23 (q, 2 H, *J* = 7 Hz), 4.35 (s, 1 H), 4.45 (s, 1 H), 7.2-7.8 (m, 10 H)
2u(ex-ex)	-$C_{10}H_6$-		H	12	228-234	0.37 (t, 3 H, *J* = 7 Hz), 3.5 (q, 2 H, *J* = 7 Hz), 5.08 (d, 2 H, *J* = 7 Hz), 6.55 (d, 2 H, *J* = 7 Hz), 7.2-8.0 (m, 12 H)
2u(ex-en)	-$C_{10}H_6$-		H	61	254-257	0.43 (t, 3 H, *J* = 7 Hz), 3.63 (q, 2 H, *J* = 7 Hz), 4.1 (d, 1 H, *J* = 7 Hz), 5.22 (d, 1 H, *J* = 7 Hz), 5.97 (d, 1 H, *J* = 7 Hz), 6.05 (d, 1 H, *J* = 7 Hz), 7.1-8.0 (m, 12 H)
2v	H	CH_3	CO_2Et	46	(140-145 (1 mmHg))	1.1-1.67 (m, 15 H), 3.3-5.15 (m, 10 H)

[a] Satisfactory analytical data were obtained for these compounds. [b] **2r-t** were dissolved in Me_2SO-d_6; the others were dissolved in $CDCl_3$.

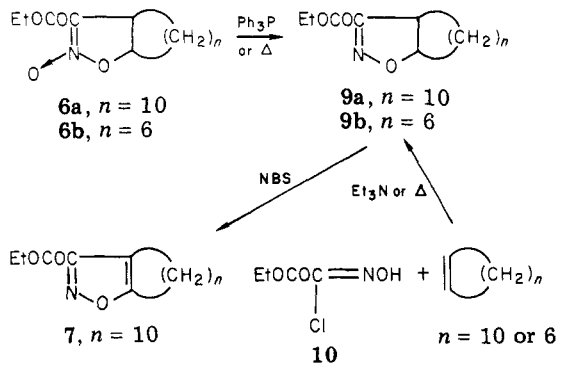
Table III. 1,3-Dipolar Cycloadducts[a] from the Reaction of 6 and Olefins

compd	*n*	R^1	R^2	R^3	yield, %	mp, °C	^{1}H NMR,[b] δ
11a	10	$CH_2OC_6H_4NO_2$-*p*	H	H	42	144-145	1.10-2.1 (br, 23 H), 2.17-3.03 (m, 3 H), 3.83-4.53 (m, 5 H), 4.67-5.23 (m, 1 H), 6.98 (d, 2 H, *J* = 9 Hz), 8.18 (d, 2 H, *J* = 9 Hz)
11b	10	CN	H	H	15	118-119	1.15-1.90 (br, 23 H), 2.4-3.4 (m, 3 H), 3.9-4.6 (m, 3 H), 5.05 (dd, 1 H, *J* = 5, 8 Hz)
11c	10	*n*-$C_{12}H_{25}$	H	H	12	57-59	0.7-1.8 (br, 48 H), 2.2-2.5 (m, 2 H), 2.7-3.3 (m, 1 H), 3.9-4.5 (m, 3 H)
11d	10	-CON(Ph)CO-		H	37	170-171	0.8-2.0 (br, 23 H), 2.8-3.5 (m, 1 H), 3.7-4.5 (m, 1 H), 4.26 (q, 2 H, *J* = 7 Hz), 4.3 (d, 1 H, *J* = 8 Hz), 5.5 (d, 1 H, *J* = 8 Hz), 7.0-7.7 (m, 5 H)
11e	10	CO_2CH_3	H	CH_3	10	105-106	1.15-1.83 (br, 23 H), 1.54 (s, 3 H), 2.4-2.9 (m, 1 H), 2.7 (d, 1 H, *J* = 13 Hz), 3.15 (d, 1 H, *J* = 13 Hz), 3.77 (s, 3 H), 3.8-4.1 (m, 1 H), 4.3 (q, 2 H, *J* = 7 Hz)
11f	10	$CO_2C_6H_4NO_2$-*p*	H	H	9	90-91	1.1-1.97 (br, 23 H), 2.53-3.3 (m, 3 H), 3.97-4.63 (m, 3 H), 4.95-5.3 (m, 1 H), 7.38 (d, 2 H, *J* = 9 Hz), 8.3 (d, 2 H, *J* = 9 Hz)
11g	6	$CH_2OC_6H_4NO_2$-*p*	H	H	13	163-165	0.9-2.1 (br, 12 H), 1.3 (t, 3 H, *J* = 7 Hz), 2.4-3.15 (m, 3 H), 4.19 (d, 2 H, *J* = 5 Hz), 4.25 (q, 2 H, *J* = 7 Hz), 4.5-5.3 (m, 2 H), 6.9 (d, 2 H, *J* = 9 Hz), 8.13 (d, 2 H, *J* = 9 Hz)

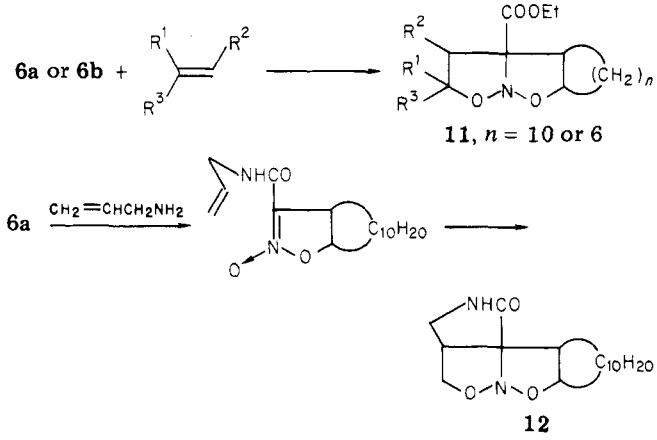
[a] Satisfactory analytical data were obtained for these compounds. [b] **11d** in Me_2SO-d_6; the others in $CDCl_3$.

Interestingly, the reaction of **1** with cyclododecene (a mixture of cis and trans isomers, ca. 2:1) gave a 1:1 molar cycloadduct (**6a**), 3-(ethoxycarbonyl)-4,5-decamethylene-Δ^2-isoxazoline *N*-oxide, in 42% yield. Besides **6a**, small amounts of 3-(ethoxycarbonyl)-4,5-decamethyleneisoxazole (**7**) and ethyl oxamate (**8**) were obtained from the reaction mixture. On the other hand, the same reaction of pure *cis*-cyclododecene gave **6a** in only 5% yield at best. Consequently, the structure of **6a** was tentatively assigned as a trans isomer.[9] Deoxygenation of **6a** with triphenylphosphine proceeded smoothly to the isoxazoline (**9a**), which exhibited identical spectral and physical properties with an authentic specimen prepared from the reaction of ethyl chloro(hydroxyimino)acetate (**10**) with cyclododecene

(9) Trans alkenes are generally more reaction toward 1,3-dipoles; G. Bianchi, C. De Micheli, and R. Gandolfi in "The Chemistry of Double-bonded Functional Groups, Part I", S. Patai, Ed., Wiley New York, 1977, pp 398.



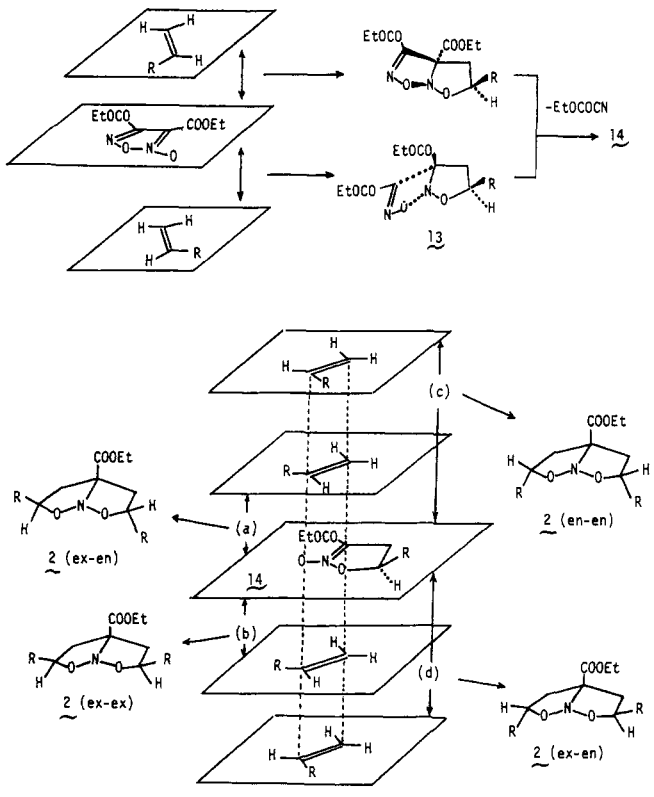
(cis–trans mixture) in the presence of triethylamine at room temperature or the thermal 1,3-dipolar cycloaddition of **10** with cyclododecene (mixture). The assignment of the nitrone structure of **6a** was further supported by the 1,3-dipolar cycloaddition of **6a** with several dipolarophiles in refluxing xylene, giving cycloadducts **11** (Table III).



The reaction of **6a** with allylamine gave a fused-ring product (**12**). Aminolysis of the ester **6a** followed by cycloaddition gave **12**. Several attempts to isolate such 1:1 cycloadducts as **6a** with other olefine failed. We could not isolate pure 3-(ethoxycarbonyl)-4,5-hexamethylene-Δ^2-isoxazoline 2-oxide (**6b**) from the reaction mixture of **1** and (**Z**)-cyclooctene. An attempt to isolate **6b** by vacuum distilation led to decomposition with the evolution of a white gas, giving the deoxygenated product 3-(ethoxycarbonyl)-4,5-hexamethylene-Δ^2-isoxazoline (**9b**) in 39% yield. Compound **9b** exhibited identical spectral and physical properties with an authentic specimen prepared from the reaction of **10** with (*Z*)-cyclooctene.[10] 5-(Ethoxycarbonyl)-3,4-hexamethylene-7-[(*p*-nitrophenoxy)methyl]-1-aza-2,8-dioxabicyclo[3.3.0]octane (**11g**) was obtained by the subsequent treatment of the reaction mixture of **1** and (*Z*)-cyclooctene with an equimolar amount of *p*-nitrophenyl allyl ether in refluxing xylene for 24 h.

The reaction of **1** with olefins described here did not proceed at appreciable rate up to 130 °C, while **1** by itself is stable in refluxing xylene for 30 h. A stoichiometric amount of ethyl cyanoformate (bp 113–116 °C) was isolated from the volatile fraction of the reaction mixture of **1** and olefins. Cycloadducts **2** and **11** were obtained by using electron-rich, -poor, or conjugated olefins as described above. From these results, the mechanism of these reactions may be as follows: (i) diethyl furoxandicarboxylate as a cyclic nitrone reacts with olefins to give 1,3-dipolar cycloadducts, (ii) elimination of ethyl cyanoformate occurs from the cycloadducts by a retro-1,3-dipolar cycloaddition to give 3-(ethoxycarbonyl)-Δ^2-isoxazoline *N*-oxides, (iii) 1,3-dipolar cycloaddition reaction of these isoxazoline *N*-oxides with another mole of olefin gives **2** (Scheme II). Either of two possible approaches by the olefin toward **1** would give the same product (**14**) by further collapse of the intermediate (**13**). It has been reported that nitrones bearing *N*-alkoxy and *C*-ethoxycarbonyl groups generally give regioisomers such as **13** predominantly due to avoidance of pseudo-1,3-diaxial interactions.[11] In the final step of the reaction, only two of the four possible approaches would be likely due to steric interactions. Among the two probable approaches (a and b), b is the more favorable one because of the absence of steric repulsion between the substituent (R) on the isoxazoline *N*-oxide ring and the approaching olefin present in the transition state (a). Therefore, the exo–exo isomer would be expected to predominate from the reaction of **1** with dipolarophiles (1-alkenes, allyl derivatives, and norbornene) in which there are no significant secondary orbital interactions. On the other hand, an exclusive formation of exo–endo isomers as obtained from the reaction of **1** with maleimides is rationalized on the basis of a secondary orbital interaction[12] between the lobes of the nitrogen atom of the dipole (**14**) and the carbon atom of the amide group of the maleimide. Between the two possible endo transition states (c and d) that are stabilized by a secondary orbital interaction, the endo–anti transition state (d) is more favored than c because of a steric interaction. Therefore, the exo–endo isomers are formed exclusively from the reaction of **1** with maleimides. Such favorable stabilization in an endo–anti transition state (d) seems to

Scheme II[a]



[a] (a) Exo,syn transition state; (b) exo,anti transition state; (c) endo,syn transition state; (d) endo,anti transition state.

(10) L. Gajsler, R. M. Paton, J. H. Hall, and D. J. Harper, *J. Polym. Sci., Polym. Lett. Ed.*, 18, 635 (1980).

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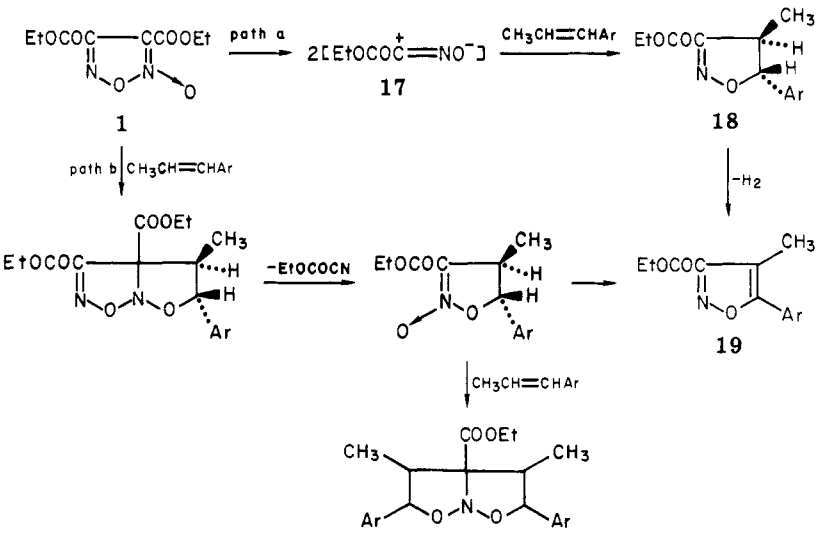
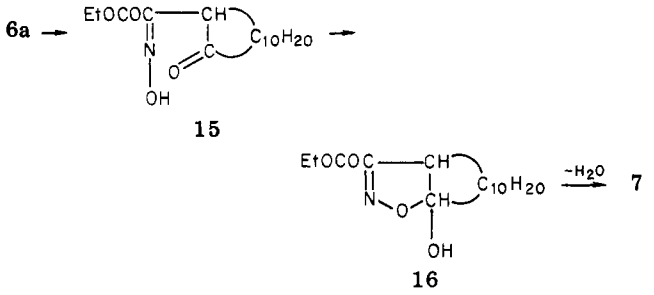
(12) (a) R. Gree and R. Carrie, *Tetrahedron Lett.*, 2987 (1972); (b) Y. Iwakura, K. Uno, S. Hong, and T. Hongu, *Bull. Chem. Soc. Jpn.*, **45**, 192 (1972).

Scheme III



operate in the reaction of 1 with other electron-poor dipolarophiles,[11,13] e.g., methyl methacrylate and methyl acrylate, to give the exo-endo adducts. A similar secondary orbital interaction between the nitrogen atom of the nitrones and aryl groups is also known.[14] The formation of the mixture of exo–exo and exo–endo isomers in the reaction of 1 with styrene or acenaphthylene can be accounted for in terms of relatively weak secondary orbital interactions. On the other hand, 1:1 cycloadducts such as 6 do not undergo subsequent cycloadditions with olefins bearing bulky substituents because of steric hindrance. Consequently, the reaction of 1 with cyclododecene or cyclooctene gave 1:1 cycloadducts 6. The formation of 7 could be explained in the following manner. Isomerization of **6a** to an oxime (**15**) and subsequent cyclization would



give 3-(ethoxycarbonyl)-4,5-decamethylene-5-hydroxy-Δ^2-isoxazoline (**16**) and then dehydration of **16** would give **7**. The transformation of isoxazoline *N*-oxides to isoxazoles via ketoximes like **15** is known under basic conditions.[15,16] Water, formed from **16**, would be trapped by ethyl cyanoformate, giving **8**. One example[17] of the reaction of 1 with an olefin (anethole) has been reported, in which it was suggested that 3-(ethoxycarbonyl)-4-methyl-5-(*p*-methoxyphenyl)isoxazole (**19**), isolated in only 0.5% yield, comes from stepwise reactions via an (ethoxycarbonyl)nitrile oxide (**17**) (see path a in Scheme III). We reinvestigated this reaction and could isolate ethyl cyanoformate in 43% yield along with a trace amount of **19** from the reaction mixture. Attempts to isolate the intermediate (**18**) (or similar intermediates in our reactions) failed, although it is known isoxazolines such as **18** are stable under the reaction conditions. Thus, doubt can be cast on the formation of nitrile oxide **17** from 1, and we propose as more reasonable mechanism (path b in Scheme III) via intermediates similar to **15** and **16**.

In conclusion, some mechanistic considerations for the reaction of furoxan (1) should be noted. The observed reactivity with both electron-rich and -poor alkenes is consistent with a relatively low LUMO and high HOMO in the 1,3-dipole and Sustmann type II behavior.[18] The carbethoxy group has little tendency to migrate and must stabilize the furoxan nucleus from cycloreversion to nitrile oxide. It seems reasonable to expect that other furoxans bearing substituents which exhibit the same properties as carbethoxy will undergo the reactions mentioned in this paper.

Experimental Section

Measurements. All the melting and boiling points are uncorrected. the IR spectra were determined on a Hitachi 215 infrared spectrophotometer. The ^{1}H NMR spectra were measured on Varian T-60A instrument with Me_4Si as an internal standard. All the new products gave correct elemental analyses (±0.4% for C, H, N).

Materials. Diethyl furoxandicarboxylate (1),[19] allyl *p*-nitrophenyl ether and its derivatives,[20] *cis*-cyclododecene,[21] and ethyl chloro(hydroxyimino)acetate (**10**)[22] were prepared according to the methods described in the literature. Naphthyl vinyl ether (mp 31–33 °C (lit.[23] mp 33–35 °C)) was prepared in 90% yield from the reaction of 1-bromo-2-naphthoxyethane and potassium *tert*-butoxide. The other chemicals were of commercial origin and were used without further purification.

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Reaction of Diethyl Furoxandicarboxylate (1) with Olefins. General Procedure. A mixture of 1 (15 mmol, 3.45 g) and olefin (30 mmol) was refluxed in xylene (20 mL) for 24 h. Evaporation of the solvent and other low-boiling products from the reaction mixture in a rotary evaporator gave the crude products. Compounds **2a,c–g,i,n,q–t,u** were crystalline while the others were oils, which were chromatographed (silica gel) with chloroform. Compounds **2h,j,m** were thus obtained crystalline. Oily residues obtained for the others were distilled in vacuo (**2b,k,q,v**). Compound **2a** was recrystallized from ethanol–ethyl acetate (2:1), **2r** was recrystallized from ethanol–acetone (3:1), and **2s** was recrystallized from ethanol–benzene (2:1); the other crystalline cycloadducts were recrystallized from ethanol. Fractional distillation of the volatile solvent and products gave a fraction, bp 113–116 °C in 95% yield, that was shown to be ethyl cyanoformate (lit.[24] bp 115–116 °C). In some cases (e.g., methyl acrylate), the reactions were carried out in a sealed tube at 140 °C to avoid loss of the dipolarophile.

Reaction of 1 with Cyclododecene. The reaction was carried out by the general procedure. Crystalline **6a** was obtained in 42% yield: mp 125–126 °C (from ethanol); IR (Nujol) 1735 (COO) and 1600 cm^{-1} (C=N); ^1H NMR ($CDCl_3$) δ 0.80–2.30 (br, 23 H), 3.17–3.67 (m, 1 H), 4.30 (q, 2 H, J = 7 Hz), 4.33–4.87 (br, 1 H).

Anal. Calcd for $C_{16}H_{27}NO_4$: C, 64.62; H, 9.15; N, 4.71. Found: C, 64.56; H, 9.20; N, 4.68.

The distillation of the filtrate of **6a** gave a trace amount of ethyl oxamate (mp 115–117 °C (lit.[25] 114–115 °C)) and 0.6 g (14%) of 3-(ethoxycarbonyl)-4,5-decamethyleneisoxazole (**7**): bp 150–155 °C (2 mmHg); IR (neat) 1740 cm^{-1} (COO); ^1H NMR ($CDCl_3$) δ 0.8–2.1 (m, 21 H), 2.1–2.9 (m, 2 H), 4.32 (d q, 2 H, J = 5, 7 Hz).

Anal. Calcd for $C_{16}H_{25}NO_3$: C, 68.78; H, 9.02; N, 5.01. Found: C, 68.70; H, 9.07; N, 5.08.

Reaction of 1 with Cyclooctene. The reaction was carried out by the general procedure. 3-(Ethoxycarbonyl)-4,5-hexamethylene-Δ^2-isoxazoline (**9b**) was obtained in 39% yield: bp 135–140 °C (1 mmHg); IR (neat) 1730 cm^{-1} (COO); ^1H NMR ($CDCl_3$) δ 0.9–2.3 (m, 15 H), 3.06–3.5 (m, 1 H), 4.32 (q, 2 H, J = 7 Hz), 4.3–4.8 (m, 1 H).

Anal. Calcd for $C_{12}H_{19}NO_3$: C, 63.97; H, 8.50; N, 6.22. Found: C, 63.88; H, 8.54; N, 6.30.

Reaction of 6a with Olefins. An equimolar amount of **6a** (3.37 mmol, 1.0 g) and olefin was heated to reflux in xylene (30 mL) for 24 h. After evaporation of the solvent from the reaction mixture, the residue was chromatographed (silica gel) with chloroform to give cycloadduct **11** in the yields shown in Table III. Compounds **11** were recrystallized from ethanol.

Deoxygenation Reaction of 6a with Triphenylphosphine. A mixture of **6a** (2.0 g, 6.73 mmol) and triphenylphosphine (1.76 g, 6.7 mmol) was heated to 200 °C for 1 h. The reaction mixture was chromatographed (silica gel) with chloroform to give 3-(ethoxycarbonyl)-4,5-decamethylene-Δ^2-isoxazoline (**9a**) in 20% yield: mp 72–73 °C (from ethanol): IR (Nujol) 1730 cm^{-1} (COO); ^1H NMR ($CDCl_3$) δ 0.83–2.33 (m, 23 H), 3.10–3.57 (m, 1 H), 4.37 (q, 2 H, J = 7 Hz), 4.57–5.00 (m, 1 H).

Anal. Calcd for $C_{16}H_{27}NO_3$: C, 68.29; H, 9.67; N, 4.98. Found: C, 68.24; H, 9.82; N, 4.97.

This deoxygenation was not affected by treatment with Zn–AcOH, Zn–HCl, or phosphorus compounds such as $P(OEt)_3$, PCl_3, or PCl_5.[1c]

Preparation of Authentic Specimens of 9. Method A. To a mixture of cyclododecene (or cyclooctene) (8.54 mmol), triethylamine (2.0 g, 19.8 mmol), and benzene (20 mL) was added a benzene solution (20 mL) of ethyl chloro(hydroxyimino)acetate (**10**, 1.3 g, 8.58 mmol) at room temperature and the mixture was stirred for 20 h at room temperature. After the solution was washed with water several times and then dried over anhydrous sodium sulfate, the solvent was evaporated to give a pale yellow oil. The oil was chromatographed (silica gel) with chloroform to give **9a** (or **9b**) in 18% (or 20%) yield.

Method B. A mixture of cyclododecene (cis–trans mixture) (7.0 g, 42.1 mmol) and **10** (3.0 g, 19.8 mmol) was heated to reflux in toluene (50 mL) for 80 h. After the distillation of the solvent at atmospheric pressure, the oily residue was distilled in vacuo to give a fraction at 175–185 °C (2 mmHg) weighing 4.5 g (81%), mp 72–73 °C (from ethanol), which shows the same spectral and physical properties as **9a**. An authentic specimen of **9b** was prepared similarly from the reaction of **10** and cyclooctene in 72% yield: bp 130–135 °C (2 mmHg).

Preparation of an Authentic Specimen of 7. Bromination of **9a**, followed by dehydrobromination of **7** was carried out according to the method described in the literature.[26] An authentic specimen of **7** was obtained in 30% yield; bp 170–175 °C (4 mmHg).

Reaction of 1 with Anethole. A mixture of 1 (3.45 g, 15 mmol) and anethole (4.45 g, 30 mmol) was heated for 24 h at 150 °C in a Claisen distilling flask under nitrogen. Distillation of the mixture gave a fraction, bp 113–116 °C, weighing 0.43 g (32%), which was found to be ethyl cyanoformate. A total of 0.64 g of **1** and 1.2 g of anethole were recovered by further distillation of the residue in vacuo. The residue was chromatographed (silica gel) with chloroform to give **19** in 2% yield. **19** was recrystallized from ethanol, mp 94–96 °C (lit.[17] mp 89–90 °C).

Reaction of 6a with Allylamine. An ethanol solution (50 mL) of **6a** (1.4 g, 4.7mmol) and allylamine (1.0 g, 17.5 mmol) was refluxed for 24 h. Evaporation of the solvent and the excess amount of allylamine yielded a white crystal, which was recrystallized from ethanol to give **12** in 29% yield (0.42 g): mp 195–197 °C; IR (Nujol) 3200 and 3100 (NH), 1695 cm^{-1} (CON); ^1H NMR (Me_2SO-d_6) δ 1.0–2.17 (m, 20 H), 2.7–3.5 (m, 4 H), 3.5–4.37 (m, 3 H), 8.0 (d, 1 H, J = 7 Hz).

Anal. Calcd for $C_{17}H_{28}N_2O_3$: C, 66.20; H, 9.15; N, 9.08. Found: C, 66.07; H, 9.27; N, 9.17.

Registry No. **1**, 18417-40-8; **2a**, 86497-62-3; **2b**, 86497-63-4; **2c**, 86497-64-5; **2d**, 86497-65-6; **2e**, 86497-66-7; **2f**, 86497-67-8; **2g**, 86497-68-9; **2h**, 86497-69-0; **2i**, 86497-70-3; **2j** (ex–ex), 86497-71-4; **2j** (ex–en), 86541-65-3; **2k**, 86497-72-5; **2m**, 86497-73-6; **2n** (ex–ex), 86497-74-7; **2n** (ex–en), 86541-66-4; **2p**, 86497-75-8; **2q**, 86507-92-8; **2r** (ex–en), 86497-76-9; **2s** (ex–en), 86497-77-0; **2t** (ex–en), 86497-78-1; **2u** (ex–ex), 86497-79-2; **2u** (ex-en), 86541-67-5; **2v**, 86497-80-5; *trans*-**6a**, 86497-89-4; **7**, 86497-90-7; *trans*-**9a**, 86497-91-8; **9b**, 75625-08-0; **10**, 14337-43-0; **11a**, 86497-81-6; **11b**, 86497-82-7; **11c**, 86497-83-8; **11d**, 86497-84-9; **11e**, 86497-85-0; **11f**, 86497-86-1; **11g**, 86497-87-2; **12**, 86497-92-9; **19** (Ar = *p*-$MeOC_6H_4$), 51291-35-1; 2-naphthyl vinyl ether, 7309-03-7; 1-octene, 111-66-0; 1-nonene, 124-11-8; 1-decene, 872-05-9; 1-dodecene, 112-41-4; 1-tetradecene, 1120-36-1; 2-propenylbenzene, 300-57-2; (2-propenyloxy)benzene, 1746-13-0; 4-(2-propenyloxy)-1-nitrobenzene, 1568-66-7; styrene, 100-42-5; methyl acrylate, 96-33-3; [(2-methyl-2-propenyl)oxy]benzene, 5820-22-4; 4-[(2-methyl-2-propenyl)oxy]-1-nitrobenzene, 86497-88-3; methyl methacrylate, 80-62-6; norbornene, 498-66-8; *N*-phenylmaleimide, 941-69-5; *N*-ethylmaleimide, 128-53-0; acenaphthylene, 208-96-8; ethyl crotonate, 10544-63-5; 1-bromo-2-(2-naphthoxy)ethane, 13247-80-8; *cis*-cyclododecene, 1129-89-1; *trans*-cyclododecene, 1486-75-5; cyclooctene, 931-88-4; anethole, 104-46-1; allylamine, 107-11-9.

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