Mechanistic Impact of Oxime Formation Accompanying 1,3-Dipolar Cycloadditions of Nitrile Oxides

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Benzonitrile oxide (1a) reacts with 1,1,2,2,3,3-hexamethyl-4,5-bis(methylene)cyclopentane (5) to give a mixture of the 1,3-dipolar cycloaddition product 8 and the oxime 9. This reaction is 26 times slower than the corresponding reaction of 1a with 1,2-bis(methylene)cyclopentane (15), which exclusively yields the 2-isoxazoline 19. With the assumption that the oxime 9 is generated by a stepwise process, one can estimate that the barrier for the concerted cycloaddition of 1a with 15 is approximately 2 kcal/mol lower than the barrier for the formation of an intermediate.

A. Introduction

Grünanger's observation[1] that nitrile oxides 1 and arylacetylenes 2 yield the oximes 4 in addition to the normal [3 + 2] cycloadducts 3 has played an important role in the discussion on the mechanism of 1,3-dipolar cycloadditions.[2] While a common intermediate for the formation of 3 and 4 has initially been considered,[3] different pathways for the formation of 3 and 4 have later been suggested[4] (Scheme I).

Examples for the formation of oximes in reactions of nitrile oxides with CC double-bonded dipolarophiles are very rare. Benzonitrile oxide and furan gave 1% of an oxime in addition to the regular cycloadducts,[5] and only in reactions of trifluoroacetonitrile oxide with conjugated olefins, such as styrenes, indenes, and 1,3-dienes, were larger amounts of oximes produced.[6] The latter reaction was interpreted in terms of a competition between a concerted cycloaddition and a two-step substitution through electrophilic attack of the nitrile oxide (Scheme II).

Since the generation of intermediate diradicals or zwitterions from nitrile oxides and dipolarophiles appears to be feasible in view of these results, we have attempted to obtain further knowledge on these intermediates by employing 1,1,2,2,3,3-hexamethyl-4,5-bis(methylene)cyclopentane (5)[7] as a mechanistic probe. As the diene 5 has previously been shown to possess increased 1,4- and reduced 1,2-reactivity,[8] we had speculated that the intermediacy of 7a ↔ 7b might give rise to the formation of the [4 + 3] cycloadduct 6 (Scheme III).
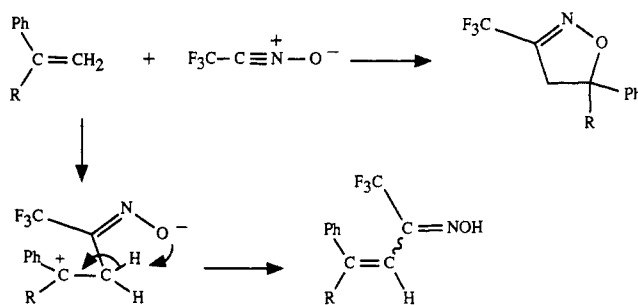
B. Results and Discussion

1. Products from Benzonitrile Oxide and Diene 5.
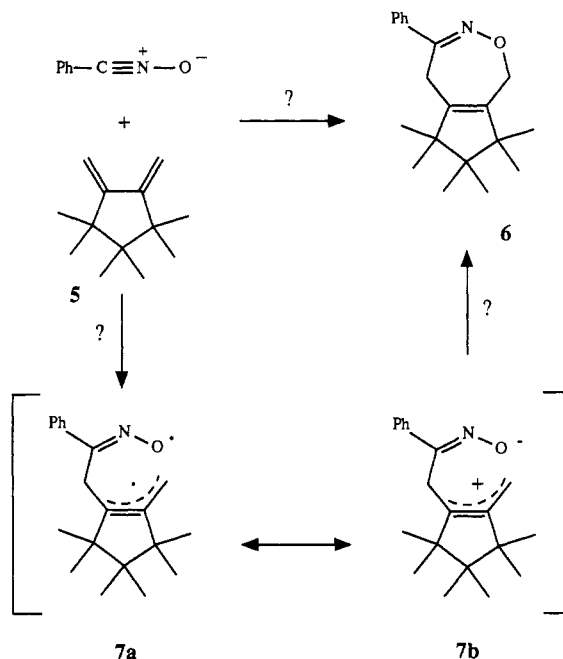
When benzonitrile oxide (1a) was generated from benzo-
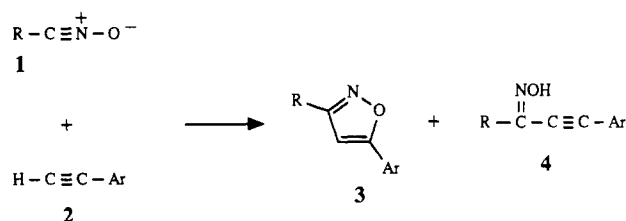
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Scheme I

Scheme II

Scheme III

hydroxamoyl chloride and triethylamine in diethyl ether in presence of the diene 5, the [3 + 2] cycloadduct 8 (55%) was formed concomitantly with the oxime 9 (7%), the

Scheme IV
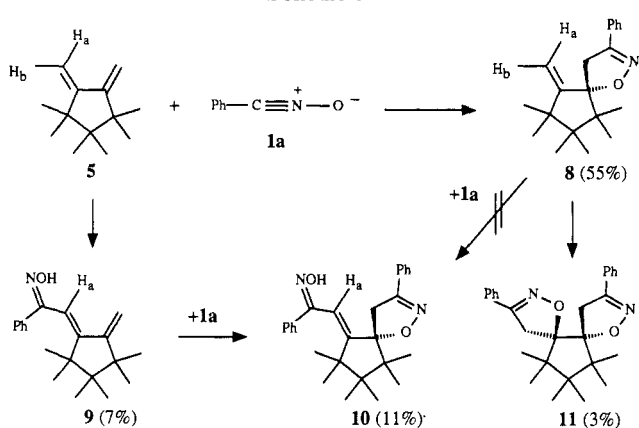
bisadducts **10** (11%) and **11** (3%), and 3,4-diphenylfuroxan, the dimer of **1a**.[9] Evidence for the formation of the cycloadduct **6** and of the stereoisomers of **10** and **11** has not been found.

The *Z* configuration at the trisubstituted CC double bond of **9** is indicated by the fact that the vinylic proton H_a experiences a similar shielding from **9** (δ 6.43) to **10** (δ 6.09) as from **5** (δ 5.30) to **8** (δ 5.04 or 5.07). If **9** and **10** had the opposite configuration at the double bond, the vinylic proton should experience a downfield shift of approximately 0.3 ppm as observed for H_b from **5** (δ 4.75) to **8** (δ 5.04 or 5.07). The bisadduct **11** shows three methyl carbons in the ^{13}C NMR spectrum, indicating C_2 symmetry since for the stereoisomer with C_s symmetry, four signals would be expected. An accidental coincidence of two carbon signals in the stereoisomer of **11** is improbable, since all six methyl signals of **8** are separated from each other by at least 0.7 ppm.

Both **8** and **9** were treated with benzonitrile oxide (**1a**) under the original reaction conditions in order to ascertain that **10** is a sequential product of **9**, not of **8**. While **9** reacted with **1a** instantaneously to give **10**, the reaction of **8** with **1a** gave a low yield of **11** as well as the dimer of **1a**.

The isoxazoline **8** is not affected when treated with triethylamine in hexane (10 h, 25 °C) or trifluoroacetic acid in acetonitrile (10 h, 25 °C). No change in the NMR spectrum was observed when neat **8** was heated at 70 °C for 12 h or when a solution of **8** in toluene was heated at 98 °C for 13 h.

2. Reaction Mechanism. Though the expected [4 + 3] cycloaddition of **1a** with **5** did not take place, another unusual reaction was observed. Compounds **9** and **10** are the first oximes that have been produced from benzonitrile oxide (**1a**) and a nonaromatic CC double-bonded dipolarophile. Therefore, this reaction system appeared to be suited for acquiring more information on the mechanistic significance of oxime formation accompanying the 1,3-dipolar cycloadditions of nitrile oxides.

Influence of Solvent Polarity. In reactions of nitrile oxides with arylacetylenes, the oxime/isoxazole ratio was only slightly affected by a variation of solvent polarity, and the formation of oximes through zwitterionic intermediates has been excluded.[3,4a] The situation has been different for reactions of nitrile oxides with CC double-bonded dipolarophiles. Oxime formation through zwitterionic intermediates has been discussed for the reaction of benzonitrile oxide with furan[5] and postulated for the reactions of tri-
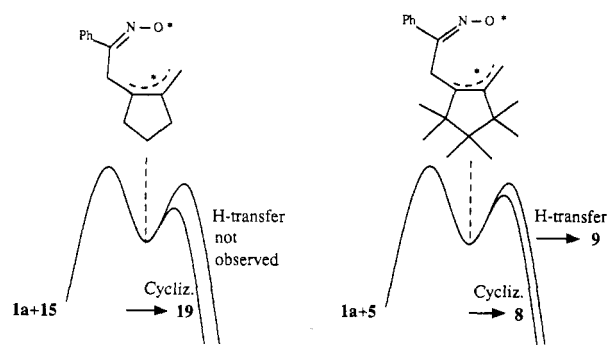

Figure 1. Energy profiles for the reactions of benzonitrile oxide (**1a**) with the dienes **15** and **5** with formation of a common intermediate.
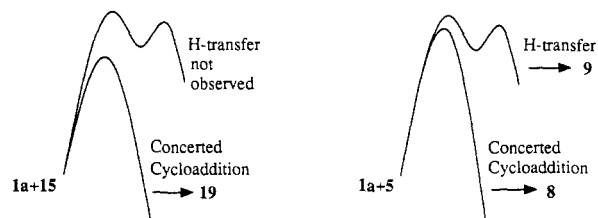

Figure 2. Energy profiles for the reaction of benzonitrile oxide (**1a**) with the dienes **15** and **5** assuming a concerted cycloaddition pathway.

fluoroacetonitrile oxide with conjugated olefins.[6] Therefore, it appeared to be appropriate to study the influence of solvent polarity on the amount of oxime obtained from **1a** and **5**.

When **1a** and **5** were combined in different solvents, the ratio **8**/(**9** + **10**) was 4.0 in hexane, 2.1 in CCl$_4$, 2.7 in ether, and 2.1 in acetonitrile. The small amount of **11** was not quantitatively detectable under the conditions of these experiments. The lack of correlation between the isoxazoline/oxime ratio and solvent polarity excludes the possibility that **8** and **9** are generated via transition states of widely varying polarity. Therefore, **9** cannot be formed through zwitterionic intermediate **7b** if a concerted pathway for the formation of **8** is assumed.

Comparison of 5 with Other Dienes. In accordance with previous results,[4b,10] only the 2-isoxazoline **16** was found when **1a** was combined with styrene (**12**). Analogously, the dienes **13–15** exclusively gave [3 + 2] cycloadducts with **1a** (Scheme V). While **14** and **15** selectively yielded the compounds **18** and **19**, respectively, compound **17**, which was obtained from **1a** and **13**, was accompanied by small amounts (<10%) of a regioisomer. Formation of **16–19** via cyclization of initially produced oximes during workup can be excluded, since oximes have not been detected in the crude reaction products by NMR spectroscopy.
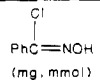
The selective formation of **19** from **1a** and **15** indicates that the methyl groups in **5** are responsible for the formation of the oxime **9** in addition to **8**. Two possibilities to explain the different behavior of **5** and **15** are shown in Figures 1 and 2.

(a) Nitrile oxide **1a** yields intermediates with both **5** and **15**. While the intermediate formed from **1a** and **15** undergoes exclusive cyclization with formation of **19**, the corresponding cyclization to give **8** is sterically hindered, and hydrogen transfer with formation of the oxime **9** can compete. Since **20** was found to undergo the Diels–Alder reaction with **5** even 4 times faster than with **15**,[11] one can
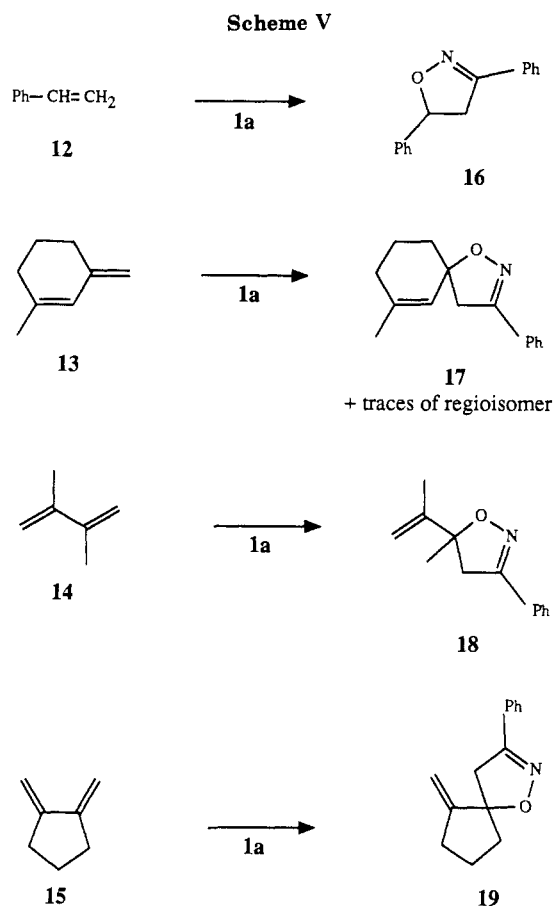
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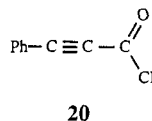(10) von Auwers, K.; Müller, H. *J. Prakt. Chem.* **1933**, *137*, 102.

Table I. Competition Experiments for Determining Relative Reactivities of 5, 12, 13, and 15 toward Benzonitrile Oxide (1a)

dipolarophiles (mg, mmol)	Cl PhC=NOH (mg, mmol)	NEt₃ (mg, mmol)	product ratio (molar)	rel addtn rates[a]
5 (91.6, 0.513), 13 (56.4, 0.521)	14.9, 0.096	10.9, 0.108	8:17 = 1:4.36	$k(5){:}k(13)$ = 1:3.49 (NMR)
13 (56.3, 0.520), 12 (52.6, 0.505)	15.1, 0.097	10.9, 0.108	17:16 = 1:2.53	$k(13){:}k(12)$ = 1:2.73 (NMR)
5 (89.2, 0.500), 12 (51.9, 0.498)	15.8, 0.102	10.9, 0.108	8:16 = 1:11.7	$k(5){:}k(12)$ = 1:9.89 (NMR)
			8:16 = 1:12.0	$k(5){:}k(12)$ = 1:10.1 (GC)
12 (45.5, 0.437), 15 (41.5, 0.441)	13.6, 0.087	10.9, 0.108	16:19 = 1:2.63	$k(12){:}k(15)$ = 1:2.73 (GC)

[a] Calculated according to ref 18 with the assumption that 8 and 9 are formed in 77:23 ratio (see above); the formation of the 2:1 products 10 and 11 is negligible under these conditions.
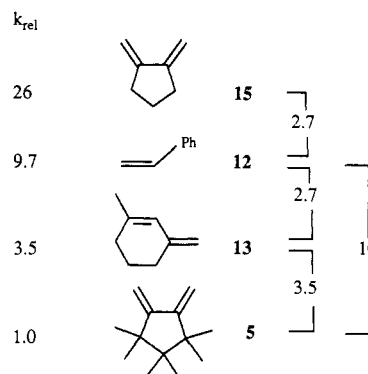
Scheme V

+ traces of regioisomer

Figure 3. Relative reactivities toward benzonitrile oxide (1a).

Competition experiments in CCl_4 revealed that benzonitrile oxide (1a) reacts 26 times faster with 15 than with 5, in accord with the energy profiles described in Figure 2. It should be mentioned, however, that our kinetic data do not exclude the improbable hypothesis of reversible formation of intermediates from 1a and 5 or 15 and successive rate-determining cyclization or hydrogen transfer. Though explanation b (Figure 2) offers a satisfactory explanation for the different reaction rates of 5 and 15 as well as for the different product composition, a blend of explanations a and b is also conceivable. A change of mechanism, i.e., concerted reaction of 15 and stepwise reaction of 5, even appears to be quite attractive, since with this assumption all products obtained from 1a and 5 could be rationalized by the intermediacy of diradicals.

On the basis of Figure 2 (right) the barrier for the formation of the intermediate 7 can be calculated to be 0.3 kcal/mol higher than the barrier for the concerted formation of 8. This number is an upper limit, however, since 8 may also arise from cyclization of 7 (Figure 1, right). The small reactivity difference between 15 and 5 indicates that the reaction of 1a with 15 (which is regarded as a "normal" diene) does not profit highly from concertedness (energy of concert[12] ≈ 2 kcal/mol).

C. Conclusion

If an intermediate diradical (7) accounts for the formation of the oxime 9, closely similar activation energies for the concerted and stepwise 1,3-dipolar cycloadditions of benzonitrile oxide (1a) with 1,3-dienes can be derived. Though 7 is a reasonable intermediate to explain the formation of 9, a concerted process for oxime formation cannot rigorously be excluded, particularly since 6, an expected cyclization product of the tentative intermediate 7 could not be detected (cf. ref 8b). If a mechanism for oxime formation can be found, which avoids the inter-

assume that the approach of a phenyl-substituted sp-hybridized carbon to one of the diene termini is not hindered by the methyl groups. The barrier for the formation of an intermediate from 5 can therefore be expected to be of equal height, if not lower than in the case of 15 (Figure 1).

20

(b) The isoxazolines 8 and 19 are formed by concerted cycloadditions. Since the concerted reaction of 1a with 5 is retarded by steric hindrance, the formation of the oxime 9 can compete (Figure 2).

Whereas the product-determining step succeeds the rate-determining step in a (Figure 1), product determination occurs in the rate-determining step in explanation b (Figure 2). A kinetic comparison of 5 and 15 should, therefore, allow differentiation of these possibilities (Figure 3, Table I).

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mediacy of **7**, the above estimates for the energy of concert of the 1,3-dipolar cycloaddition had to be augmented correspondingly.

Experimental Section

General. IR spectra were recorded on a Shimadzu IR-435 spectrometer. NMR spectra were taken on a Varian XL 200 spectrometer using tetramethylsilane as internal standard. Mass spectra were recorded on a 70-250E VG spectrometer and the microanalyses were carried out by Ilse Beetz, Microanalytisches Laboratorium, D-8640 Kronach. Melting points are uncorrected. GC analyses were run on a Shimadzu GC 9A gas chromatograph equipped with FID.

Substrates. Benzonitrile oxide (**1a**) was generated in situ from benzohydroxamoyl chloride[14] and triethylamine as described in ref 4b. The dipolarophiles **12** and **14** are commercially available, and **5** was prepared as described previously.[7] Diene **13** has previously been prepared with a second isomer from 3-methyl-2-cyclohexen-1-one and methylmagnesium iodide and successive dehydration.[15] We obtained pure **13** in 56% yield from 3-methyl-2-cyclohexen-1-one (Aldrich), methyltriphenyl-phosphonium bromide, and sodium amide (Instant Ylide, Fluka) in THF following the general procedure by Schlosser.[16] 1,2-Bis(methylene)cyclopentane (**15**) was prepared in 12% overall yield from cyclopentanone by using the five-step synthesis described in ref 17.

Benzonitrile Oxide (1a) and Diene 5. A solution of triethylamine (3.35 mL, 2.43 g, 24 mmol) in 50 mL of dry ether was added dropwise at ambient temperature to a stirred solution of **5** (1.68 g, 9.42 mmol) and benzohydroxamoyl chloride (3.40 g, 21.8 mmol) in 50 mL of dry ether. Stirring was continued for 12 h, and triethylammonium hydrochloride was removed by filtration and washed with a few milliliters of dry ether. The combined filtrates were concentrated under reduced pressure and finally kept at 0.01 mbar/20 °C for 1 h to give 4.72 g of a crude product. Separation by MPLC (RP 18, CH_3OH) gave six fractions (increasing retention times): 3,4-diphenyl-1,2,5-oxadiazole 2-oxide (dimer of benzonitrile oxide)[9] (1.04 g), **10** (442 mg, 11.3%), **9** (186 mg, 6.6%), **8** (1.53 g, 54.6%), **11** (114 mg, 2.9%), and traces of nonidentified products, probably formed by attack of **1a** at the nitrogen of the monoadducts.

6,6,7,7,8,8-Hexamethyl-9-methylene-3-phenyl-1,2-oxazaspiro[4.4]non-2-ene (8): mp 124–125 °C (hexane); IR (KBr) 2986, 2943, 2911, 2866, 1598, 1447, 1383, 1376, 1363, 907, 895, 827, 761, 692, 667, 542 cm^{-1}; ^{1}H NMR (CDCl$_3$) δ 0.91 (s, 6 H), 0.97 (s, 3 H), 1.13 (s, 3 H), 1.14 (s, 3 H), 1.18 (s, 3 H), AB system with ν_A = 3.22, ν_B = 3.34, and J_{AB} = 17.2 Hz (2 H), 5.04 (s, 1 H), 5.07 (s, 1 H), 7.40–7.44 (m, 3 H), 7.70–7.75 (m, 2 H); ^{13}C NMR (CDCl$_3$) δ 18.25 (q), 22.22 (q), 23.75 (q), 24.70 (q), 29.99 (q), 30.73 (q), 39.28 (t), 44.68 (s), 46.32 (s), 48.07 (s), 99.03 (s), 107.51 (t), 126.44 (d), 128.66 (d), 129.75 (d), 129.97 (s), 155.74 (s), 165.24 (s); mass spectrum (70 eV), m/z (relative intensity) 297 (M$^+$, 44), 282 (26), 214 (28), 213 (42), 212 (42), 198 (31), 164 (23), 163 (27), 149 (100), 137 (38), 121 (27), 110 (62), 95 (26), 84 (49), 77 (30), 69 (24), 68 (21), 67 (45), 57 (21), 55 (24), 43 (37), 41 (52). Anal. Calcd for C$_{20}$H$_{27}$NO (297.4): C, 80.76; H, 9.15; N, 4.71. Found: C, 80.89; H, 9.33; N, 4.95.

1-[2-(Hydroxyimino)-2-phenylethylidene]-2,2,3,3,4,4-hexamethyl-5-methylenecyclopentane (9): mp 135–137 °C (methanol); IR (KBr) 3209, 2977, 2944, 2909, 2870, 1491, 1473, 1456, 1405, 1393, 1377, 1367, 1296, 1142, 1082, 948, 887, 793, 761 cm^{-1}; ^{1}H NMR (CDCl$_3$) δ 0.77 (s, 6 H), 0.92 (s, 6 H), 1.13 (s, 6 H), 4.94 (s, 1 H), 5.58 (s, 1 H), 6.43 (s, 1 H), 7.34–7.38 (m, 3 H), 7.65–7.70 (m, 2 H); ^{13}C NMR (CDCl$_3$) δ 20.74 (q), 24.23 (q), 28.64 (q), 45.10 (s), 46.73 (s), 47.58 (s), 105.03 (t), 109.51 (d), 126.94 (d), 128.31 (d), 129.32 (d), 136.45 (s), 155.64 (s), 156.70 (s), 159.71 (s);

mass spectrum (70 eV), m/z (relative intensity) 297 (M$^+$, 4), 296 (8), 282 (12), 196 (11), 160 (42), 136 (20), 118 (100), 77 (17), 43 (42), 41 (14). Anal. Calcd for C$_{20}$H$_{27}$NO (297.4): C, 80.76; H, 9.15; N, 4.71. Found: C, 80.56; H, 9.12; N, 5.16.

6-[2-(Hydroxyimino)-2-phenylethylidene]-7,7,8,8,9,9-hexamethyl-3-phenyl-1,2-oxazaspiro[4.4]non-2-ene (10): mp 192–194 °C dec (ethanol); IR (KBr) 3190, 3051, 2964, 1592, 1493, 1479, 1446, 1401, 1380, 1373, 1358, 1320, 1303, 1147, 1124, 1087, 1072, 1008, 992, 945, 920, 911, 879, 854, 827, 802, 780, 763, 754, 692, 665 cm^{-1}; ^{1}H NMR (CDCl$_3$) δ 0.88 (s, 3 H), 0.91 (s, 3 H), 1.02 (s, 3 H), 1.04 (s, 3 H), 1.05 (s, 3 H), 1.08 (s, 3 H), AB system with ν_A = 3.43, ν_B = 3.53, and J_{AB} = 17.6 Hz (2 H), 6.09 (s, 1 H), 7.32–7.37 (m, 3 H), 7.40–7.45 (m, 3 H), 7.61–7.66 (m, 2 H), 7.73–7.78 (m, 2 H); ^{13}C NMR (CDCl$_3$) δ 19.39 (q), 22.04 (q), 23.46 (q), 23.93 (q), 27.10 (q), 27.95 (q), 40.92 (t), 45.25 (s), 47.01 (s), 47.64 (s), 99.77 (s), 114.96 (d), 126.54 (d), 126.68 (d), 128.37 (d), 128.72 (d), 129.40 (d), 129.79 (s), 129.91 (d), 135.86 (s), 155.69 (s), 155.75 (s), 160.40 (s); mass spectrum (70 eV), m/z (relative intensity) 416 (M$^+$, 8), 399 (100), 315 (38), 296 (37), 282 (25), 230 (35), 229 (57), 212 (31), 196 (30), 188 (39), 187 (97), 186 (26), 184 (25), 146 (71), 144 (31), 105 (18), 104 (37), 103 (21), 77 (40), 41 (37). Anal. Calcd for C$_{27}$H$_{32}$N$_2$O$_2$ (416.6): C, 77.85; H, 7.74; N, 6.72. Found: C, 77.44; H, 7.77; N, 6.66.

11,11,12,12,13,13-Hexamethyl-3,9-diphenyl-1,7-dioxa-2,8-diazadispiro[4.0.4.3]trideca-2,8-diene (11): mp 286–287 °C (methanol); IR (KBr) 3099, 3047, 2948, 2913, 1599, 1462, 1445, 1425, 1400, 1357, 1258, 1125, 1103, 1050, 1021, 911, 860, 811, 758, 690, 674, 664, 538 cm^{-1}; ^{1}H NMR (CDCl$_3$) δ 1.01 (s, 6 H), 1.06 (s, 6 H), 1.14 (s, 6 H), AB system with ν_A = 3.30, ν_B = 3.37, and J_{AB} = 18.6 Hz (4 H), 7.30–7.33 (m, 6 H), 7.56–7.61 (m, 4 H); ^{13}C NMR (CDCl$_3$) δ 22.63 (q), 24.23 (q), 25.41 (q), 37.56 (t), 47.56 (s), 48.25 (s), 102.76 (s), 126.53 (d), 128.57 (d), 129.15 (s), 129.95 (d), 156.72 (s); mass spectrum (70 eV) m/z (relative intensity) 416 (M$^+$, 6), 230 (50), 229 (89), 228 (68), 187 (71), 159 (33), 146 (46), 144 (81), 117 (100), 104 (28), 103 (20), 84 (46), 83 (18), 77 (35), 69 (41), 67 (12), 57 (15), 55 (20), 43 (14), 41 (41). Anal. Calcd for C$_{27}$H$_{32}$N$_2$O$_2$ (416.6): C, 77.85; H, 7.74; N, 6.72. Found: C, 77.65; H, 7.81; N, 7.29.

7-Methyl-3-phenyl-1,2-oxazaspiro[4.5]deca-2,6-diene (17) was obtained from 1-methyl-3-methylenecyclohexene (**13**)[15] (269 mg, 2.49 mmol), benzohydroxamoyl chloride (109 mg, 0.701 mmol) and triethylamine (200 μL, 145 mg, 1.43 mmol) in 8 mL of ether, following the procedure described above. After isolation of 54% of crystalline **17**, evaporation of the mother liquors afforded additional 45% of **17**, contaminated by traces of its regioisomer, which have not been purified. **17**: mp 55–56 °C (methanol); IR (KBr) 3041, 2920, 2882, 2857, 2812, 1591, 1564, 1495, 1443, 1433, 1374, 1359, 1073, 1004, 962, 954, 928, 905, 868, 850, 787, 753, 706, 692, 676, 549 cm^{-1}; ^{1}H NMR (CDCl$_3$) δ 1.60–1.72 (m, 2 H), 1.75 (br s, 3 H), 1.89–2.10 (m, 4 H), AB system with ν_A = 3.08, ν_B = 3.20, and J_{AB} = 16.6 Hz (2 H), 5.51 (br s, 1 H), 7.37–7.43 (m, 3 H), 7.64–7.70 (m, 2 H); ^{13}C NMR (CDCl$_3$) δ 19.93 (q), 23.78 (q), 29.73 (t), 34.59 (t), 46.37 (t), 85.14 (s), 123.39 (d), 126.45 (d), 128.64 (d), 129.75 (d), 130.33 (s), 141.14 (s), 156.29 (s); mass spectrum (70 eV), m/z (relative intensity) 227 (M$^+$, 41), 212 (38), 210 (20), 205 (16), 117 (16), 108 (100), 106 (23), 93 (59), 91 (23), 79 (24), 77 (24). Anal. Calcd for C$_{15}$H$_{17}$NO (227.3): C, 79.26; H, 7.54; N, 6.16. Found: C, 79.59; H, 7.60; N, 6.00.

5-Methyl-5-(1-methylvinyl)-3-phenyl-2-isoxazoline (18) was obtained in 95% yield from 2,3-dimethyl-1,3-butadiene (**14**) (620 mg, 7.55 mmol), benzohydroxamoyl chloride (64.7 mg, 0.416 mmol), and triethylamine (80 μL, 58 mg, 0.57 mmol) in 1 mL of dry ether: viscous oil; IR (neat 2953, 1259, 1087, 1016, 859 cm^{-1}; ^{1}H NMR (CDCl$_3$) δ 1.57 (s, 3 H), 1.85 (br s, 3 H), AB system with ν_A = 3.11, ν_B = 3.35, and J_{AB} = 16.8 Hz (2 H), 4.90 (br s, 1 H), 5.12 (br s, 1 H), 7.37–7.41 (m, 3 H), 7.63–7.68 (m, 2 H); ^{13}C NMR (CDCl$_3$) δ 18.73 (q), 25.35 (q), 45.39 (t), 88.75 (s), 111.02 (t), 126.47 (d), 128.65 (d), 129.85 (d), 130.02 (s), 146.42 (s), 155.81 (s); mass spectrum (70 eV), m/z (relative intensity) 201 (M$^+$, 50), 186 (34), 171 (31), 118 (63), 117 (18), 91 (19), 82 (26), 77 (60), 69 (100), 67 (54), 51 (21), 43 (56); high resolution mass spectrum, m/z calcd for C$_{13}$H$_{15}$NO 201.11536, found 201.11518.

Benzonitrile Oxide (1a) and 1,2-Bis(methylene)cyclopentane (15). Benzohydroxamoyl chloride (106 mg, 0.681 mmol), compound **15** (270 mg, 2.87 mmol), and triethylamine (120 μL, 87.1 mg, 0.861 mmol) were combined in 5 mL of diethyl ether as

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(16) Schlosser, M.; Schaub, B. *Chimia* **1982**, *36*, 396.

(17) van Straten, J. W.; van Norden, J. J.; van Schaik, T. A. M.; Franke, G. T.; de Wolf, W. H.; Bickelhaupt, F. *Recl. Trav. Chim. Pays-Bas* **1978**, *97*, 105.

described before to give 160 mg of crude 19, which was purified by MPLC (RP 18, CH_3OH/H_2O = 9:1). Yield: 119 mg (82%) of 19 and traces (20 mg) of a bisadduct, which has not been purified.

6-Methylene-3-phenyl-1,2-oxazaspiro[4.4]non-2-ene (19): mp 42–43 °C (pentane); IR (neat) 2946, 1444, 1357, 915, 757, 690 cm^{-1}; ^1H NMR (CDCl$_3$) δ 1.63–2.72 (m, 8 H), AB system with ν_A = 3.27, ν_B = 3.44, and J_{AB} = 17.0 Hz (2 H), 5.13 (mc, 1 H), 5.21 (mc, 1 H), 7.37–7.42 (m, 3 H), 7.66–7.71 (m, 2 H); ^{13}C NMR (CDCl$_3$) δ 22.12 (t), 31.10 (t), 40.01 (t), 45.14 (t), 92.78 (s), 108.50 (t), 126.52 (d), 128.66 (d), 129.86 (d), 129.98 (s), 153.43 (s), 155.91 (s); mass spectrum (70 eV), m/z (relative intensity) 213 (M$^+$, 36), 212 (18), 196 (8), 185 (8), 184 (8), 117 (100), 104 (9), 103 (7), 95 (9), 94 (21), 93 (8), 91 (11), 79 (34), 77 (34); high resolution mass spectrum, m/z calcd for $C_{14}H_{15}NO$ 213.11536, found 213, 11519. Anal. Calcd for $C_{14}H_{15}NO$ (213.3): C, 78.84; H, 7.09; N, 6.57. Found: C, 78.84; H, 6.95; N, 6.35.

Solvent Dependence of the Product Ratio from 1a and 5. The reaction was carried out with equimolar amounts of 1a and 5 at ambient temperature in different solvents as described for ether (see above).[19] The crude product mixture was analyzed by ^1H NMR using the singlets at δ 5.04 and 5.07 for 8, the singlets at δ 5.58 and 6.43 for 9, and the singlet at δ 6.09 for 10. The small

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(18) Ingold, C. K.; Shaw, F. R. *J. Chem. Soc.* **1949,** 575.

(19) The deviation of the 8:9:10 product ratio (ether) from that reported above is due to the use of 1a and 5 in a 1:1 ratio (2:1 in the previous experiment), which reduces the probability of the sequential reaction of 1a with 9 to give 10.

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amounts of 11 have been neglected.

solvent	8:9:10	8:(9+10)
hexane	8:1:1	4.0
CCl$_4$	5.8:1.7:1	2.1
Et$_2$O	10.1:2.7:1	2.7
CH$_3$CN	6.0:1.8:1	2.1

Relative Reactivities of Dipolarophiles toward Benzonitrile Oxide (1a). A mixture of two dipolarophiles and benzohydroxamoyl chloride were dissolved in 4 mL of CCl$_4$. Triethylamine was added, and the mixture was stirred at 20.5 °C for 8 h. The mixture was filtered to remove triethylammonium hydrochloride, and the filtrate was concentrated under reduced pressure to give a mixture of products, which was analyzed by ^1H NMR or GC.

The ^1H NMR analyses were based on the relative intensities of the following signals: 8, δ 5.04 and 5.07 (2 s, 2 H); 16, δ 5.70, (dd, 1 H); 17, δ 5.51, (s, 1 H).

The GC separation was carried out on a 50-m SE 30 fused-silica capillary column (id 0.2 mm) at 270 °C. Compounds 8, 16, and 19 had retention times of 7.66, 5.87, and 4.72 min, respectively. For the evaluation of the product ratios, area factors of 0.5934 (8), 1.000 (16), and 0.6448 (19) were used.

Stepwise [4 + 2]- and [4 + 4]-Cyclodimerizations of 1,1,2,2,3,3-Hexamethyl-4,5-bis(methylene)cyclopentane

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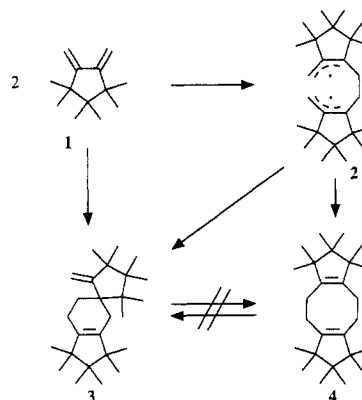
The thermal dimerization of the title compound 1 yields the [4 + 2]-cyclodimer 3 and the [4 + 4]-cyclodimer 4 in a ratio of approximately 3.5:1. Comparison of activation enthalpies ($\Delta H^\ddagger$(3) = 80.1 kJ/mol, $\Delta H^\ddagger$(4) = 76.6 kJ/mol) and activation entropies ($\Delta S^\ddagger$(3) = -143.1 J/mol K, $\Delta S^\ddagger$(4) = -163.3 J/mol K) indicates both cycloadditions proceed by analogous mechanisms. A study of the pressure dependence (0.5–9.3 kbar) yields activation volumes in the same order of magnitude for both dimerizations ($\Delta V_0^\ddagger$ = -(15 to 16) cm^3/mol), indicative of two parallel stepwise processes. A selective cyclodimerization of 1 to give the [4 + 2]-cyclodimer 3 is achieved by acid catalysis.

Dimerizations of 1,3-dienes have attracted great attention in the mechanistic discussion of Diels–Alder reactions[1] since the regular [4 + 2]-cyclodimers are often accompanied by certain amounts of 1,2-divinylcyclobutanes and 1,5-cyclooctadienes.[1–3] The question of whether the diradical pathway, which accounts for the formation of the four- and eight-membered ring compounds, also represents the dominant route to the Diels–Alder products has been intensively studied, and evidence for concerted and stepwise Diels–Alder reactions has been presented.[1] Since in most cases the studies have been carried out with acyclic dienes, the analysis of the results is complicated by the conformational freedom of the dienes.

A conformationally rigid diene fragment with sterically shielded 2- and 3-positions is incorporated in the bis(methylene)cyclopentane 1.[4] Since this compound has

Scheme I

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been found to give a higher amount of 1,4-adducts than other dienes in several cycloadditions,[5] it appeared to be