at −78 °C for 4 h. To the mixture was added a solution of compound 14 (5.0 mmol) and $AlCl_3$ (5.0 mmol) in CH_2Cl_2 (15 mL) dropwise. The mixture was stirred at −78 °C for 4 h and allowed to warm to room temperature. The mixture was hydrolyzed with water and extracted three times with ether. The ether phase was washed with brine, dried ($MgSO_4$), and filtered. The filtrate was evaporated and the residue was purified by column chromatography using petroleum ether–ethyl acetate (100:2) as eluent to give 0.87 g of compound **12** (65% yield): $[\alpha]^{20}_D = -2.01$ ($CHCl_3$); IR (neat) 3090, 3070, 3030, 1715, 1140, 1100, 745; ^1H NMR ($CDCl_3$) 1.15 (d, J = 6 Hz, 3 H), 1.0–2.2 (m, 6 H), 3.4 (m, 4 H), 3.9 (tt, J = 5, 11.5 Hz, 1 H), 4.4 (s, 2 H), 7.2 (m, 5 H). Anal. Found: C, 67.02; H, 7.85. Calcd for $C_{15}H_{21}ClO_2$: C, 67.03; H, 7.87.

***cis*-6-Methyl-2-[2-(benzyloxy)ethyl]tetrahydropyran (15).** To a mixture of sodium (0.3 g), *tert*-butyl alcohol (0.5 mL), and ether (10 mL) was added dropwise a solution of compound **12** (0.15 g) in ether (5 mL). The mixture was refluxed for 8 h. The excess sodium was destroyed with methanol and then water (5 mL). The mixture was extracted three times with ether. The ether phase was washed with brine, dried ($MgSO_4$), and filtered. The filtrate was evaporated and the residue was purified with column chromatography using petroleum ether–ethyl acetate (100:2) as eluent to give 0.10 g of compound **15** (76% yield): ^1H NMR ($CDCl_3$) 1.1 (d, J = 6 Hz, 3 H), 1.0–1.8 (m, 8 H), 3.4 (m, 4 H), 4.4 (s, 2 H), 7.2 (m, 5 H); MS 234 (15), 216 (20), 143 (35), 107 (60), 99 (85), 77 (1), 28 (100).

(2*R*,6*R*)-(−)-(*cis*-6-Methyltetrahydropyran-2-yl)acetic Acid (11). Compound **15** (0.10 g) was hydrogenolyzed in ethanol (5 mL) with Pd–C (0.060 g) under hydrogen (2 atm) for 40 h. The catalyst was removed by filtration and the filtrate was evaporated. The residue was dissolved in acetone (5 mL). To the acetone solution was added Jones reagent (3 mL) dropwise. The mixture was stirred at room temperature for 1 h. The excess oxidant was destroyed with 2-propanol (2 mL) and the mixture was extracted with ether. The organic phase was washed with brine twice, dried ($MgSO_4$), and filtered. The filtrate was evaporated and the residue was purified by column chromatography to give 0.052 g of compound **11** (77% yield): $[\alpha]^{21}_D = -5.47°$ ($CHCl_3$) [lit.[20] $[\alpha]^{22}_D = +18.6°$ ($CHCl_3$)]. The spectroscopic data of **11** were in agreement with those reported in the literature.[20]

(20) Keinan, E.; Seth, K. S.; Lamed, R. *J. Am. Chem. Soc.* **1986**, *108*, 3474.

Competing [2 + 3] and [4 + 3] Cycloadditions of *C,N*-Diphenylnitrone with 1,3-Dienes. Evidence for Thermally Nonequilibrated Intermediates†

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C,N-Diphenylnitrone (1) reacts with the 1,3-dienes **2a–f** to give the regular 1,3-dipolar cycloaddition products **3a–f** and **4a–f** as well as several other products (**5–8**), which are explained by the intermediacy of diradicals. The tetrahydrooxazepines **5a–d**, which are obtained in 3–21% yield from **1** and the dienes **2a–d**, are the first [4 + 3] cycloadducts obtained in intermolecular reactions of 1,3-dipoles with 1,3-dienes. Two conformational isomers of **5a** are identified by low-temperature NMR spectroscopy. Thermolyses of the compounds **3a,b**, **4a,b**, and **5a,b** were studied in toluene solution. While **4a** isomerizes into **5a** at 100 °C, the stereoisomeric isoxazolidine **3a** undergoes decomposition under these conditions. For the nonmethylated homologues, the relative stability of the [3 + 2] and [4 + 3] cycloadducts is reversed, and **5b** rearranges into **4b** and traces of **3b**. The stereoselectivity of the **4a,b** ⇌ **5a,b** isomerizations is interpreted by the intermediacy of thermally nonequilibrated diradicals.

Introduction

In agreement with the orbital symmetry rules,[1] 1,3-dipoles and 1,3-dienes usually undergo [$_\pi 4_s$ + $_\pi 2_s$] cycloadditions with formation of five-membered ring compounds,[2] and examples for the generation of seven-membered rings are rare.[3] Two years ago, we described the [4 + 3] cycloaddition of *C,N*-diphenylnitrone (**1**) with 1,1,2,2,3,3-hexamethyl-4,5-dimethylenecyclopentane (**2a**), the first example of an intermolecular [4 + 3] cycloaddition of a 1,3-dipole with a 1,3-diene.[4] This reaction was interpreted by the intermediacy of diradicals, and from a kinetic comparison with "normal" dienes, we had concluded that in reactions of **1** with 1,3-dienes, the stepwise mechanism should generally be accessible. We now report that small amounts of [4 + 3] cycloadducts are also formed from nitrone **1** and other 1,3-dienes, and we discuss the mechanistic impact of these observations.

Reaction Products and Structural Assignments

When diphenylnitrone **1** and the dienes **2a–f** were combined in toluene at 80 °C, the compounds **3–8** were produced (Table I). The ^1H and ^{13}C NMR spectra (Table II and Supplementary Material) reveal the regiochemistry of the [3 + 2] cycloadducts **3** and **4**, which are formed by attack of the benzylic carbon of **1** at the CH_2 termini of the 1,3-dienes. Two regioisomers (**3d**,**4d** and **3d′**,**4d′**) are generated from **2d**, which possesses two nonequivalent CH_2 termini, while in all other cases only one pair of diastereoisomeric [3 + 2] cycloadducts (**3** and **4**) with opposite relative configuration at C-3 and C-5 is formed.

In compounds **3a,b** and **4a,b** the stereochemical assignment was based on NOE difference spectroscopy:

† Dedicated to Professor Ch. Rüchardt on the occasion of his 60th birthday.

‡ Present address: Institute of Fundamental Chemistry, Technical University of Szczecin, Al. Piastow 42, 71-065 Szczecin, Poland.

(1) Woodward, R. B.; Hoffmann, R. *Angew. Chem.* **1969**, *81*, 797; *Angew. Chem., Int. Ed. Engl.* **1969**, *8*, 781.

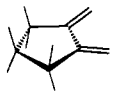
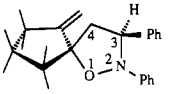
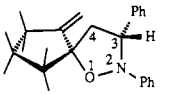
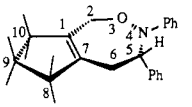
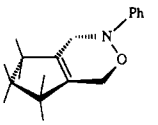
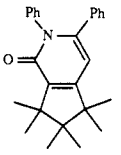
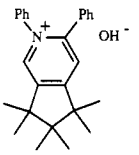
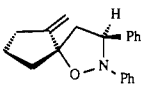
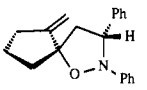
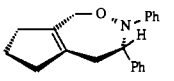
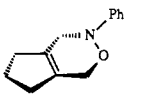
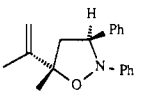
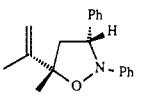
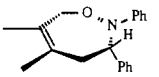
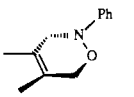
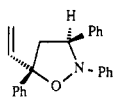
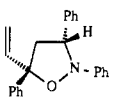
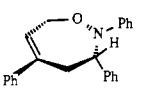
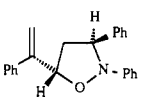
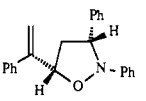
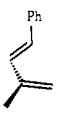
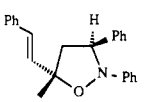
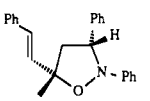
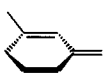
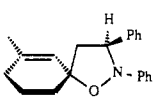
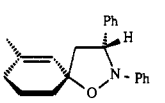
(2) (a) Huisgen, R. *Angew. Chem.* **1963**, *75*, 604, 742; *Angew. Chem., Int. Ed. Engl.* **1963**, *2*, 565, 633. (b) Padwa, A., Ed. *1,3-Dipolar Cycloaddition Chemistry*; Wiley: New York, 1984.

(3) Crabb, J. N.; Storr, R. C. In ref 2b, Vol. II, p 545.

(4) Preliminary communication: Baran, J.; Mayr, H. *J. Am. Chem. Soc.* **1987**, *109*, 6519. Experimental details of this investigation will be reported in this article.

0022-3263/89/1954-5774$01.50/0

Table I. Products Isolated from the Reaction of Diphenylnitrone 1 with the Dienes 2a–f in Toluene at 80 °C

diene	products				
 2a	 **3a** (32%)	 **4a** (5%)	 **5a** (21%)	 **6a** (5%)	
	 **7a** (≈10%)	 **8a** (4%)			
 2b	 **3b** (27%)	 **4b** (19%)	 **5b** (9%)	 **6b** (3%)	
 2c	 **3c** (66%)	 **4c** (24%)	 **5c** (3%)	 **6c** (1%)	
 2d	 **3d** (14%)	 **4d** (4%)	 **5d** (3%)		
	 **3d'** (4%)	 **4d'** (20%)			
 2e	 **3e** (62%)	 **4e** (26%)			
 2f	 **3f** (38%)	 **4f** (33%)			

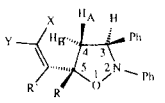
While in compounds **3a** and **3b** the low-field protons at C-4 (trans to 3-Ph)[5] show NOEs with a vinylic proton, in the stereoisomers **4a** and **4b**, an NOE between the high field 4-H (cis to 3-Ph)[5] and a vinyl proton is observed (Table II). In accord with this assignment, an NOE between 3-H and a vinyl proton could be detected in compound **3b**, and an NOE between the high-field 4-H (cis to 3-Ph) and one of the methyl groups was found in **3a**.[6] The configurational assignments of compounds **3c–f** and **4c–f**, which are based on a comparison of chemical shifts, are not reliable and should be considered tentative.

The tetrahydrooxazepines **5a–d** are identified by their ^{13}C NMR spectra with triplets at δ 74–80 and 31–40 (Table III). Their 200-MHz ^1H NMR spectra, taken at 25 °C, show several broad signals which sharpen when the temperature is raised (60 °C). The existence of two conformers with a slow rate of interconversion, which is indicated by this observation, was corroborated for **5a** by low-temperature 300-MHz ^1H NMR spectra taken at −70 °C.

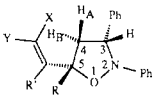
Under these conditions, two conformers (ratio 12:7) are observed, which show characteristic differences in their vicinal coupling constants $J_{5,6}$. In the minor conformer, one of the coupling constants is 11.9 Hz, indicating the anti-periplanar arrangement of two hydrogens. The ge-

(5) Sustmann, R.; Huisgen, R.; Huber, H. *Chem. Ber.* **1967**, *100*, 1802.
(6) The formula drawings of **3a** and **3b** in Scheme I of ref 4 have to be exchanged.

Table II. ^{1}H NMR Chemical Shifts (δ) of the Isoxazolidines 3a–f and 4a–f ($CDCl_3$, TMS)[a]



3a-f

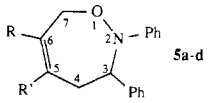


4a-f

	3								4							
	3-H	4-H_A	4-H_B	$J_{3,4A}$	$J_{3,4B}$	J_{AB}	vinyl-H		3-H	4-H_A	4-H_B	$J_{3,4A}$	$J_{3,4B}$	$J_{A,B}$	vinyl-H	
a	4.83	2.49	2.76	9.9	7.6	12.7	5.03	4.98	4.24	2.91	2.35	9.8	7.8	13.1	5.28	5.11
b	4.68	2.39	2.92	7.5	8.7	12.4	5.11	5.04	4.75	2.71	2.50	7.1	10.1	12.2	5.39	5.20
c	4.52	2.31	2.97	9.5	7.5	12.4	5.07	4.82	4.65	2.71	2.52	8.3	8.7	12.2	5.10	4.91
d	4.74	2.79	3.24	8.9	7.8	12.3	5.19	5.16	4.51	3.20	2.85	7.7	8.7	12.3	5.21	5.25
							6.14								6.27	
d′	4.54	m (2.44–2.77)		8.5	6.0		5.53	5.44	4.83	3.00	2.29	7.9	7.9	12.1	5.46	5.59
e	4.71	2.44	2.92	9.5	7.3	12.1	6.56	6.28	4.74	2.80	2.52	8.1	8.7	12.1	6.47	6.72
f	4.72	2.28	2.73	8.1	8.5	12.3	5.36		4.80	2.67	2.33	7.4	9.9	12.2	5.39	

[a] Assignment of **3a,b** and **4a,b** based on NOE experiments; configurational assignments of compounds **3,4c–f** are tentative (see text).

Table III. ^{13}C NMR Chemical Shifts of the Tetrahydrooxazepines 5a–d ($CDCl_3$)



5a-d

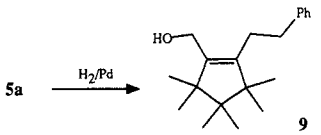
	C-3	C-4	C-5,6	C-7
5a	71.4	31.5	135.8, 138.7	74.6
5b	69.9	33.2	133.1, 134.1	75.9
5c	70.6	40.3	124.3, 125.7	79.7
5d	70.3	38.4	*a*	75.7

[a] Assignment uncertain.

ometry of this conformer can be assumed to resemble structure **5a′**, which was calculated by the MMX program[7] to be the most stable conformer of **5a** (2 kcal/mol more stable than **5a″**). While the 11.9-Hz coupling is precisely that expected for the calculated dihedral angle of 179°, the second vicinal coupling constant (5.7 Hz) is larger than that estimated for the calculated dihedral angle of 64°.

In the major conformer, vicinal coupling constants of 5.8 and 1.9 Hz were observed, in accord with a geometry resembling **5a″**, the second minimum obtained by the MMX calculations. The origin of the large $\Delta\delta$ value for the two geminal 6-hydrogens is not clear. With the assumption that **5a′** and **5a″** are also the two conformers predominantly populated at 60 °C, the two absorptions of the 6-protons in the major isomer can be assigned. Only if the δ 3.40 absorption is assigned to the upper hydrogen and the δ 1.96 signal to the lower hydrogen can the position of the averaged signals at 60 °C (δ 2.39 and 3.03) be explained (Figure 1).

Additional structural evidence for **5a** is the catalytic hydrogenation of **5a**, which gave **9**.



The dihydrooxazines **6a–c** possess characteristic broad singlets at δ 3.7 ± 0.1 and 4.4 ± 0.1 in their ^{1}H NMR spectra, and two of them (**6a,c**) have independently been synthesized from nitrosobenzene and **2a** or **2c**, respectively. Structural evidence for the α-pyridone **7a** comes from its IR absorptions at 1654 and 1649 cm^{-1} and the absence of

(7) MMX version by K. E. Gilbert and J. J. Gajewski based on MM2 (Allinger, QCPE 395) and MMP1 Pi (Allinger, QCPE 318) modified by K. Steliou.

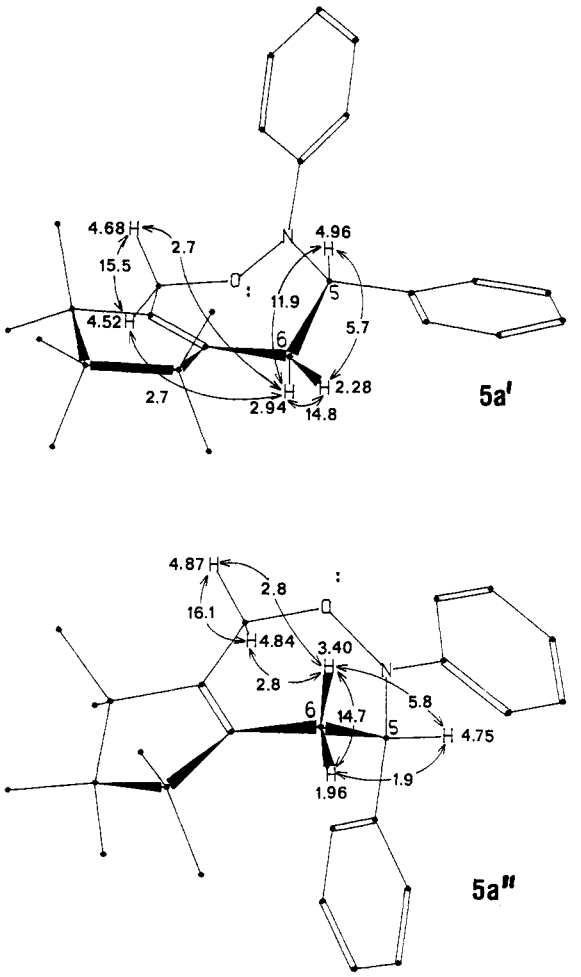


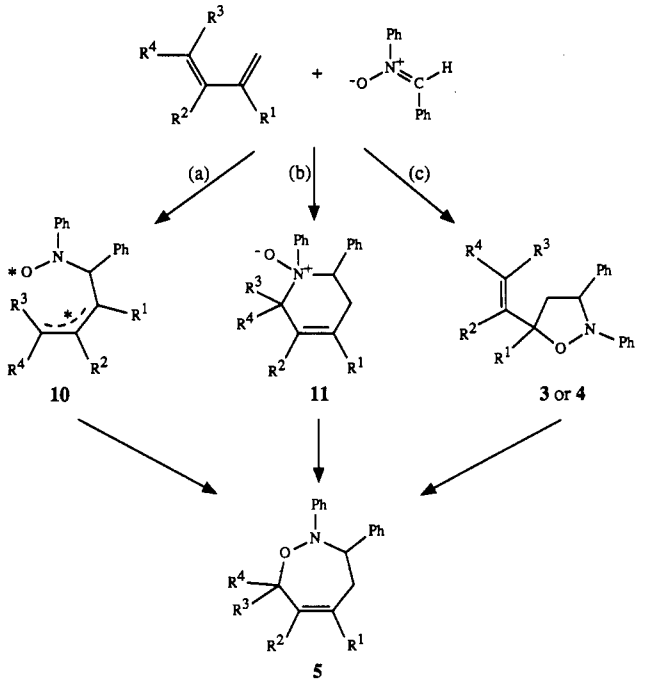
Figure 1. Calculated conformations (MMX)[7] of **5a** and ^{1}H NMR chemical shifts (δ) and coupling constants (hertz) observed at −70 °C in CH_2Cl_2 (300 MHz).

^{1}H NMR absorptions at δ 6.5–7, which are characteristic for the aniline derivatives **3–6**. In accord with the suggested structures **7a** and **8a**, compound **7a** was converted into **8a** by treatment with $LiAlH_4$.

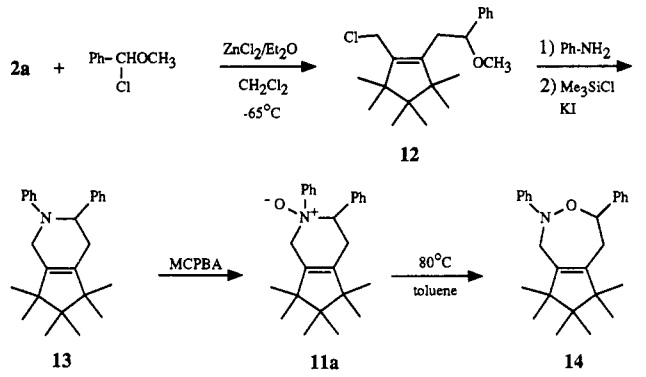
Reaction Mechanism

In contrast to compounds **3** and **4**, which may be formed by an orbital symmetry allowed [$_\pi4_s$ + $_\pi2_s$] process,[1] a concerted pathway for the formation of **5a–d** ($_\pi4_s$ + $_\pi4_s$) is orbital symmetry forbidden,[1] and a stepwise process has to be assumed (Scheme I).

Scheme I



Scheme II



Apart from the biradicaloid or zwitterionic species **10** (Scheme Ia), compounds **11** (Scheme Ib) or **3** and **4** (Scheme Ic) have to be considered as potential intermediates in a stepwise process. Pathway b involves a Diels–Alder reaction with the C=N double bond of **1** acting as the dienophile[8] and a subsequent Meisenheimer rearrangement.[9] According to pathway c, a regular 1,3-dipolar cycloaddition of **1** with **2** (→**3**,**4**) is succeeded by a 1,3-sigmatropic rearrangement.

1. Mechanism b Is Improbable. To examine the potential intermediacy of amine oxides, compound **11a** has been synthesized by the sequence shown in Scheme II. Zinc chloride/ether[10] catalyzed reaction of **2a** with α-methoxybenzyl chloride gave the 1,4-addition product **12**, which was converted into the tetrahydropyridine derivative **13** by combination with aniline and successive treatment with Me_3SiCl/KI.[11] Oxidation of **13** with *m*-chloroperbenzoic acid yields the amine oxide **11a**, the stereochemistry of which has not been determined. When **11a** was heated in toluene at 80 °C, Meisenheimer rearrangement with benzyl migration gave compound **14** (59%), and evidence for the alternative allyl migration with formation of compound **5a** has not been obtained.

This observation does not rigorously exclude the operation of mechanism b, however, since the potential Diels–Alder adduct formed from **1** and **2a** may have a stereochemistry different from the amine oxide obtained by oxidation of **13**. Meisenheimer rearrangements, however, have been proven to proceed through radical intermediates,[9b,c] and one can assume that the relative location of the two phenyl groups in **11a** has little influence on the site of C–N cleavage. The formation of **14** from **11a**, therefore, is a strong though not unequivocal argument against mechanism b.

Table IV. Influence of Solvent Polarity on the Cycloadduct Ratio Obtained from 1 and 2a at 80 °C[a]

solvent	3a:4a:5a	solvent	3a:4a:5a
benzene	68:3:30	acetonitrile	62:6:32
benzene	63:3:34	ethanol	63:4:33
toluene	63:7:30	ethanol	57:4:39
DMSO	53:7:40		

[a] Content of other products not obtainable by the HPLC method used for this analysis.

2. Mechanism c Can Be Excluded. If 1,3-sigmatropic rearrangements of the isoxazolidines **3** or **4** would account for the formation of the [4 + 3] cycloadducts **5**, isolated samples of **3** and **4** should rearrange into **5** under the conditions of the cycloaddition reaction. Compounds **3a,b** and **4a,b** were found to be stable in toluene at 80 °C (temperature of the cycloaddition reactions), and the isoxazolidines **3c,d** and **4c,d′** proved to be stable even at 100 °C (**3d′** and **4d** not examined). Therefore, the isoxazolidines **3** and **4** cannot be precursors of the tetrahydrooxazepines **5** under the conditions of the cycloadditions. This conclusion is corroborated by the observation that the ratios of compounds **3**,**4** and **5** (**6**,**7** and **8** not detectable under the HPLC conditions employed) remained constant during the course of the reaction of **1** with **2a** and **2b**, respectively (see below).

3. Intermediate 10 Does Not Have Zwitterionic Character. As a consequence of the experiments described in sections 1 and 2, we explain the formation of the [4 + 3] cycloadducts **5** by the intermediacy of **10** (Scheme Ia), which may a priori be formulated as a biradical or as a zwitterion, though both may be considered to be extremes on a continuous scale. When the reaction of **1** with **2a** was carried out in different solvents, the ratio **3a**:**4a**:**5a** did not change significantly (Table IV), and the total yields of the cycloadducts remained similar. This observation and the failure to detect products that arise from reaction of **10** with the solvent ethanol argue against the zwitterionic character of the intermediate.[13]

4. Kinetics of the Cycloadditions and Thermolyses of the Cycloadducts: The Intermediate Diradicals Are Not Thermally Equilibrated. Second-order rate constants k_2(**2a**) = 1.1 × 10^{-5} M^{-1} s^{-1}, k_2(**2b**) = 3.3 × 10^{-4} M^{-1} s^{-1}, and k_2(**2f**) = 4.4 × 10^{-5} M^{-1} s^{-1} were determined for the reactions of diphenylnitrone **1** with the dipolaro-

(8) Nitrones have previously been postulated to undergo this type of cycloaddition with tetraphenylcyclopentadienone: Brown, C. W.; Marsden, K.; Rogers, M. A. T.; Tylor, C. M. B.; Wright, R. *Proc. Chem. Soc.* **1960**, 254.

(9) (a) Review: Johnstone, R. A. W. In *Mechanisms of Molecular Migrations*; Thyagarajan, B. S., Ed.; Wiley: New York, 1969; Vol. II, p 249. (b) Schöllkopf, U.; Ludwig, U.; Patsch, M.; Franken, W. *Liebigs Ann. Chem.* **1967**, *703*, 77. (c) Lorand, J. P.; Grant, R. W.; Samuel, P. A.; O'Connell, E. M.; Zaro, J.; Pilotte, J.; Wallace, R. W. *J. Org. Chem.* **1973**, *38*, 1813, and references cited therein.

(10) Mayr, H.; Striepe, W. *J. Org. Chem.* **1985**, *50*, 2995.

(11) Morita, T.; Okamoto, Y.; Sakurai, H. *Synthesis* **1981**, 32.

(12) Estimated from k_2 at 100 °C assuming $\Delta S^{\ddagger}$ = −28 cal mol^{-1} K^{-1}: Huisgen, R.; Seidl, H.; Brüning, I. *Chem. Ber.* **1969**, *102*, 1102.

(13) For trapping of zwitterionic intermediates with alcohols see: Huisgen, R. *Acc. Chem. Res.* **1977**, *10*, 199.

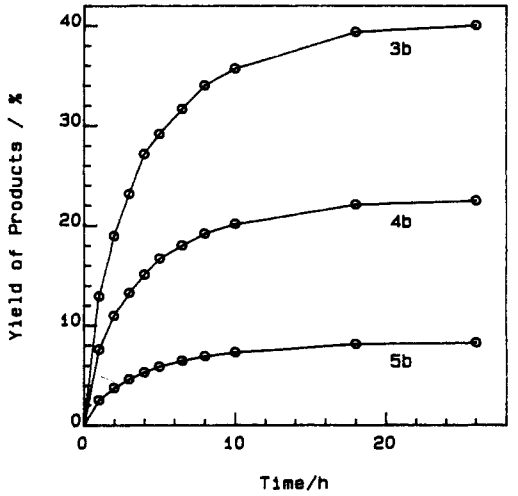


Figure 2. Formation of the cycloadducts **3b–5b** from **1** and **2b** in toluene at 80 °C.

philes **2a,b,f** (toluene, 80 °C) when the disappearance of the nitrone was monitored by HPLC. These rate constants are of the same order of magnitude as that previously determined for the reaction of **1** with ethyl crotonate (1.4×10^{-4} M^{-1} s^{-1}).[12] Evaluation of the kinetic experiments (Figure 2) furthermore showed that the ratio of the various cycloadducts remained constant during the course of the reactions.

At somewhat higher temperature (100 °C), rearrangements and/or decompositions of some of the cycloadducts take place, as shown in Table V. While more than half of the [3 + 2] cycloadduct **3a** was decomposed at 100 °C within 60 h to give nonidentified (polymeric?) compounds with just a small amount of **5a**, the stereoisomeric isoxazolidine **4a** was almost completely rearranged into **5a** under these conditions. In a control experiment, the [4 + 3] cycloadduct **5a** was shown to be rather stable under these conditions, and only traces of **3a** could be detected along with **5a**.

In the nonmethylated series **3b–5b** the relative stability of the [3 + 2] and [3 + 4] cycloadducts is opposite to that in the methylated series **3a–5a**. When **5b** was heated at 100 °C, rearrangement to the isoxazolidines **3b** and **4b** took place, but the isoxazolidine **4b**, which was produced in lower yield during the cycloaddition, was now generated with high preference (Table V). This experiment indicates that the barrier between **4b** and **5b** is lower than the barrier between **3b** and **5b**, in accord with the observation that thermolysis of **4b** yields a higher percentage of **5b** than themolysis of **3b** (microscopic reversibility!). In conclusion, the same stereochemical preference, **4** ⇌ **5** equilibration being faster than the **3** ⇌ **5** equilibration, is found in the methylated (**3a–5a**) as in the nonmethylated series (**3b–5b**).

How can these rearrangements be explained? Cycloreversion and renewed cycloaddition cannot account for the findings. In this case, the composition of the rearranged products should be independent of the nature of the precursor. Since the rate of the cycloaddition of **1** with **2a** at 100 °C ($k_2 = 6.0 \times 10^{-5}$ L mol^{-1} s^{-1}) is known, we can even exclude the possibility that noticeable fractions of the rearranged products reported in Table V are formed via a cycloreversion–cycloaddition sequence, because the second-order reactions of **1** with **2** become very slow at the low concentrations of **1** and **2**, which might be present in the reaction mixtures.[14]

(14) HPLC analysis shows [1] < 10^{-7} mol/L in all samples.

Table V. Thermolysis of the Cycloadducts 3a–5a and 3b–5b in Toluene at 100 °C

reaction time/h	content of 3	4	5	3 + 4 + 5	k_1/s^{-1}
	Thermolysis of **3a** (6 mmol/L)				
0	100			100	5×10^{-6} [a]
6	85.4		1.2	86.6	
21	67.5		3.6	71.1	
36	55.4		4.9	60.2	
60	40.2		5.6	45.8	
	Thermolysis of **4a** (7 mmol/L)				
0		100		100	1.0×10^{-5}
6		76.0	21.8	97.8	
21		43.9	56.2	100.1	
36		26.3	72.4	98.7	
60		11.9	88.1	100.0	
	Thermolysis of **5a** (6.5 mmol/L)				
0			100	100	
6	0.6		99.3	99.9	
21	0.7		98.4	99.1	
36	0.7		97.2	97.9	
60	0.7		94.3	95.0	
	Thermolysis of **3b** (7.5 mmol/L)				
0	100			100	
10	89.2	0.9	0.4	90.5	
31	84.3	2.3	1.1	87.7	
46	83.0	3.5	1.3	87.8	
71	73.9	5.2	1.8	80.9	
	Thermolysis of **4b** (8 mmol/L)				
0		100		100	
10	0.1	95.6	2.4	98.1	
31	0.8	81.1	5.3	87.2	
46	1.3	78.7	6.4	86.4	
71	2.2	73.6	7.5	83.3	
	Thermolysis of **5b** (8 mmol/L)				
0			100	100	6.8×10^{-6}
10	1.5	33.2	76.1	110.8	
31	3.7	56.2	44.7	104.6	
46	5.0	63.3	31.9	100.2	
71	6.6	73.9	19.9	100.4	

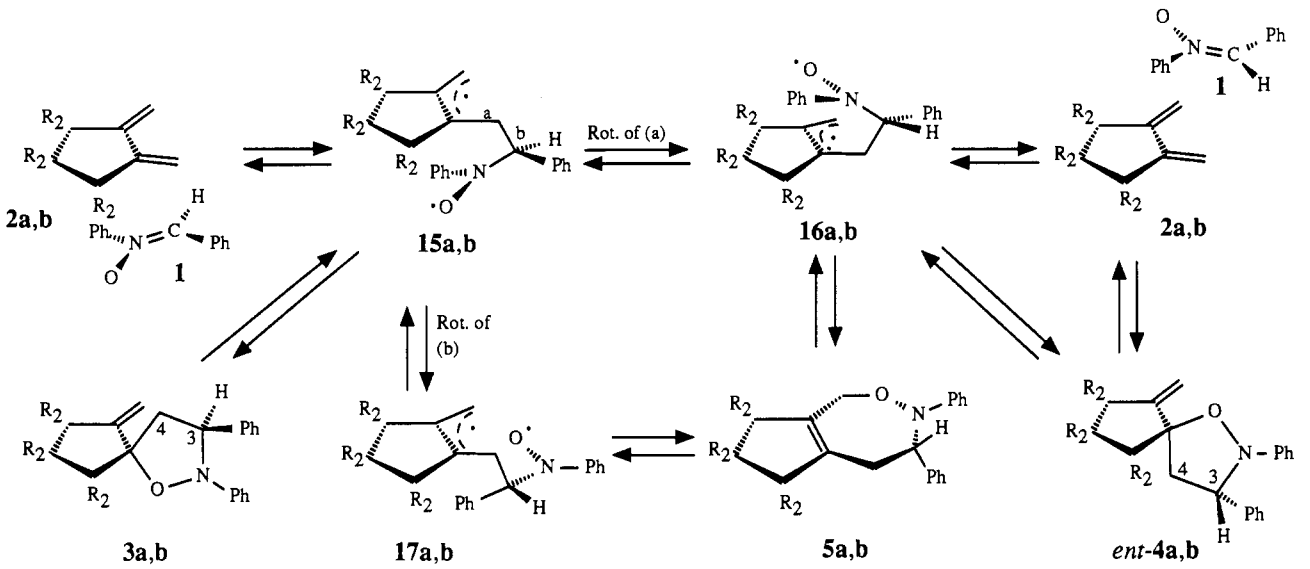
[a] Approximate value, which is not well reproducible and may vary by a factor of 2.

Concerted 1,3-sigmatropic shifts might be an alternative explanation for the rearrangements **3,4** ⇌ **5**, and one could argue that steric factors are favoring the transition state of the **4** ⇌ **5** rearrangement over that of the **3** ⇌ **5** rearrangement. With this hypothesis, the isomerizations **3b** ⇌ **4b** had to be explained by two successive 1,3 shifts. This assumption is contradicted by the observation that during the thermolysis of **3b**, the concentrations of **4b** and of **5b** are growing uniformly (Table V), not in the way expected for series first-order reactions.[15] Though this observation does not rigorously exclude a concerted process for the **4a** → **5a** rearrangement, the close similarity of the disappearance rates of **3a** and **4a** indicates that the transition state of the **4a** → **5a** rearrangement does not or just slightly profits from concertedness. Therefore all reactions will be rationalized by the intermediacy of diradicals (Occam's razor[16]).

How can the different behavior of **3** and **4** be explained? Since the ratio of the products formed in the thermolysis reactions depends on the nature of the precursor, the intermediate diradicals cannot be thermally equilibrated. Starting from both diastereoisomers **3** and *ent*-**4**,[17] the

(15) Moore, J. W.; Pearson, R. G. *Kinetics and Mechanism*, 3rd ed.; Wiley: New York, 1981; p 290.
(16) Entia non sunt multiplicanda praeter necessitatem (explanations should not be made more complicated than necessary).

Scheme III



cleavage of the C–O bond can be assumed to be coupled with a rotation of the planar nitroxide fragment[18] giving the diradicals **15** or **16** with anti alignment of the two phenyl groups (Scheme III). In **16**, the nitroxide oxygen is close to the CH_2 terminus of the allylic radical, and cyclization to yield the seven-membered ring compound **5** via a boatlike transition state requires only small geometric reorganizations. The conformer **15**, on the other hand, can cyclize only to a seven-membered ring, after rotation around bond a or b has taken place. These rotations are obviously slow, so that side reactions are taking place: The isoxazolidine **3a** undergoes decomposition faster than rearrangement to **5a**. Because of the manifold of elementary steps, the coupling of which is not precisely known (i.e., bond-breaking or -forming reactions and rotations may not be independent processes), it is impossible to derive a complete set of rate constants from our experiments. A rationalization of the experimental findings can be obtained from the qualitative energy profiles shown in Figure 3, which is simplified by omission of the chair-shaped diradical **17a,b**.

It is assumed that the combination of the cycloaddends **1** and **2a,b** gives two types of diradicals (**15**, **16**) which undergo cyclization faster than mutual interconversion. The different barriers for the cycloadditions of **2a** and **2b**, which result from the kinetic experiments reported above, have been neglected in the qualitative picture in Figure 3. The preferred way of cyclization of the diradical **16** is controlled by steric effects. While the nonmethylated diradical **16b** gives the isoxazolidine **4b** preferentially (**4b**:**5b** = 19:9), the formation of the spiro compound **4a** from **16a** is sterically hindered, and cyclization to yield the seven-membered ring is preferred (**4a**:**5a** = 5:21). The different strain in the methylated and nonmethylated isoxazolidines **4a** and **4b** accounts for the opposite direction of the **4** ⇌ **5** rearrangements in both series, and the high barrier between **16** and **15** is responsible for the stereoselectivity of these rearrangements. As discussed above, the height of the barrier between **15** and **16** also explains that the stereoisomers **3a** and **3b** undergo decomposition faster than rearrangement.

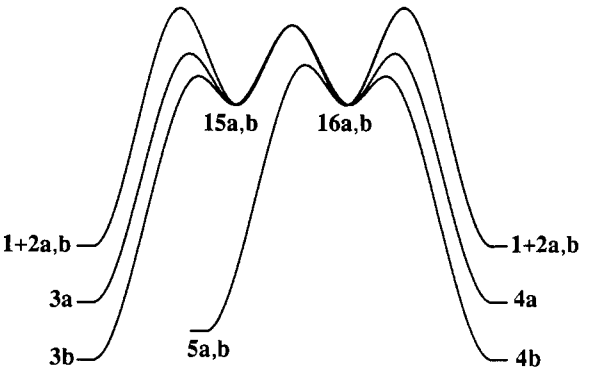
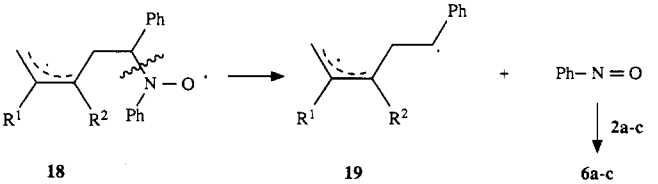


Figure 3. Schematic energy profiles for the cycloadditions of diphenylnitrone **1** with the dimethylenecyclopentanes **2a,b** and the thermolytic behavior of the cycloadducts **3a,b**–**5a,b** (side reactions not included).

5. Rationalization of Further Reaction Products on the Basis of Intermediate Diradicals. Compounds **6a–c**, which are formed in 1–5% yield during the reactions of **1** with **2a–c**, can be assumed to arise via Diels–Alder reaction of these dienes with nitrosobenzene. Though diphenylnitrone **1** has been reported to give some nitrosobenzene when heated in benzene at 250 °C,[19] we do not have evidence for thermal decomposition of **1** at 80 °C, and we suggest that fragmentation of the diradical **18** is responsible for the formation of nitrosobenzene. We have not been able, however, to support this hypothesis by isolating products derived from **19**.



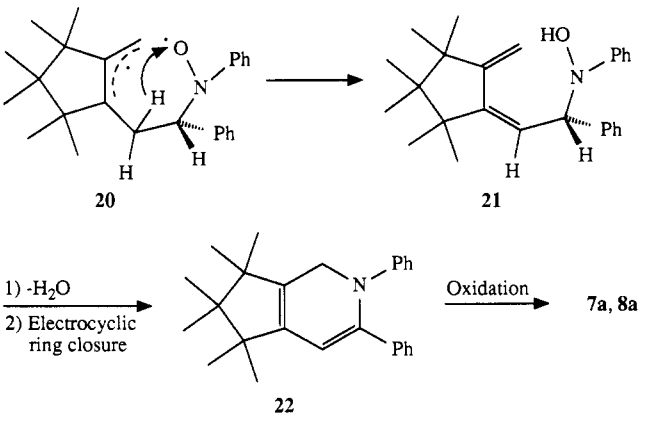
The hydroxylamine **21** (Scheme IV), which is considered to be a precursor of compounds **7a** and **8a**, may be formed

(17) Since all experiments in this investigation have been carried out with racemic material, all discussions refer to both enantiomers. As cyclization of the depicted isomer of diradical **16** (Scheme III) yields the enantiomers of the isoxazolidines **4a,b** drawn in Table I, the relationship between the two drawings is specified by the prefix *ent*; cf.: Quinkert, G.; Stark, H. *Angew. Chem.* **1983**, *95*, 651; *Angew. Chem., Int. Ed. Engl.* **1983**, *22*, 637.

(18) Geometry of nitroxides: Aurich, H. G. in Patai, S. Ed. *The Chemistry of Amino, Nitroso and Nitro Compounds and Their Derivatives*; Wiley: New York, 1982; Chapter 14 and Suppl. F, Chapter 5 (1989).

(19) Staudinger, H.; Miescher, K. *Helv. Chim. Acta* **1919**, *2*, 554.

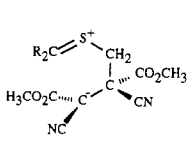
Scheme IV

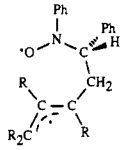


via intramolecular hydrogen transfer in the diradical **20**, a conformer closely resembling **17a**. Dehydration and electrocyclic ring closure yields the dihydropyridine **22**, which may be oxidized to give **7a** or **8a**, the absolute and relative yield of which changes from run to run. The initial hydrogen transfer, which resembles that observed during nitrile oxide cycloadditions[20] offers a straightforward explanation for the formation of **7a** and **8a**. We do not have evidence for the operation of that mechanism, however, and we cannot exclude the amine oxide **11a** being the precursor of these two compounds.

Conclusion

Though most mechanistic criteria point to the concertedness of 1,3-dipolar cycloadditions,[21] arguments for their stepwise progress have been presented.[22] Huisgen studied reactions of the highly nucleophilic thiocarbonyl ylides with electron-deficient alkenes and obtained evidence for intermediates with prevailing zwitterionic character (**23**).[23] The stabilization of positive charge at one end and of negative charge at the other end of **23** makes the stepwise process more attractive than the concerted mechanism.

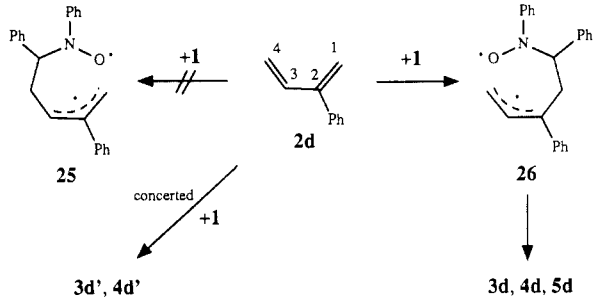

23


24

This investigation has shown that intermediates with prevailing diradicaloid character are encountered in reactions of diphenylnitrone **1** with 1,3-dienes. Now, the operation of the stepwise mechanism is triggered by the creation of a nitroxide radical at one terminus and of an allylic radical at the other terminus of the intermediate.

In spite of the stabilization of this intermediate, the diradical mechanism does not seem to be operating exclusively in the reactions of **1** with 1,3-dienes. If the diradical mechanism were strongly preferred, 2-phenylbutadiene **2d** should only be attacked at C-1 (→**3d**, **4d**, **5d**), since the 3-phenylallyl radical **26** (Scheme V) can be expected to be considerably better stabilized than the 2-phenylallyl radical **25**, the potential precursor of **3d'** and **4d'**. Searching for reasons for why the reaction at the monosubstituted double bond of **2d** is favored, one encounters the concerted process which may profit from the more favorable steric situation at this site. In accord with this assumption, a [4 + 3] cycloadduct arising from cyclization of **25** could not be detected (i.e., <0.5%).

Scheme V



We, therefore, conclude that the reactions of nitrone **1** with 1,3-dienes represent borderline cases, in which concerted and diradical processes possess closely similar barriers. Since the stabilization energy of the allyl radical is approximately 16 kcal/mol,[24] the concerted mechanism can be expected to be favored in reactions of nitrones with normal alkenes, as derived from recent ab initio calculations.[25]

Experimental Section

General Techniques. 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 and $CDCl_3$ as the solvent. 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. The preparative MPLC separations were carried out on 30 × 2.5 cm columns filled with LiChroprep (RP-18, 15–20-μm particles) using a Knauer HPLC pump 64, a VIVI-Valco motor valve for automatic injection, a Hitachi-Merck 655A-22 UV detector, and a Lincoln Isco Foxy fraction collector. The automatic separation system was controlled by a Schneider PC using a program developed by R. Polat (Diplomarbeit, FH Lübeck, 1987). Analytical HPLC has been carried out on 250 × 4.6 mm steel columns with Nucleosil 100, 5-μm particles RP-18, using a LDC Milton-Roy chromatography system with the UV detector spectro Monitor D.

Substrates. Diphenylnitrone **1** was prepared from benzaldehyde and *N*-phenylhydroxylamine.[26] 1,1,2,2,3,3-Hexamethyl-4,5-dimethylenecyclopentane (**2a**) was synthesized in six steps (36%) from acetyl chloride, 2-methyl-2-butene, and 2,3-dimethyl-2-butene.[27] 1,2-Dimethylenecyclopentane (**2b**)[28] was obtained from cyclopentanone in 12% overall yield by Mannich reaction, Wittig olefination, and Hoffmann elimination following the general procedure in ref 29. 2-Phenylbutadiene (**2d**) was prepared by Prins reaction from α-methylstyrene and successive dehydration.[30] 1-Phenyl-3-methyl-1,3-butadiene (**2e**)[31] was synthesized from 4-phenyl-3-buten-2-one via Wittig reaction using

(20) (a) Morrocchi, S.; Ricca, A.; Zanarotti, A.; Bianchi, G.; Gandolfi, R.; Grünanger, P. *Tetrahedron Lett.* **1969**, 3329 (b) Baran, J.; Mayr, H. *J. Org. Chem.* **1989**, *54*, 5012.
(21) Huisgen, R. in ref 2b, Vol. I, Chapter 1.
(22) Firestone, R. A. *Tetrahedron* **1977**, *33*, 3009.
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Instant Ylide by Fluka.[32] The same procedure gave 1-methyl-3-methylenecyclohexene (**2f**)[33] from 3-methyl-2-cyclohexen-1-one, methyl-triphenylphosphonium bromide, and sodium amide.

1. Diphenylnitrone 1 and Diene 2a. Nitrone 1 (2.94 g, 14.9 mmol), diene **2a** (2.13 g, 11.9 mmol), and toluene (6 mL) were heated at 80 °C for 67 h (stoppered flask, N_2 atmosphere). The crude material was separated by MPLC (RP 18, methanol) without prior removal of the solvent to give (ordered by increasing elution volumes) **8a** (0.19 g, 4%), 1 (0.91 g), **7a** (0.50 g, contaminated by several unknown compounds, some of which gave **7a** when exposed to air), **6a** and **2a** (0.27 g, 5:4 molar ratio ≅ 5% of **6a**), **3a** and **4a** (2.02 g, 45%), and **5a** (0.92 g, 21%).

Compound **6a** was separated from **2a** by extracting it from an ethereal solution with 5% aqueous HCl. Addition of NaOH and extraction with ether gave a solution of **6a**, which was dried over $MgSO_4$ and evaporated to give pure **6a**. During purification of **7a** by thin-layer chromatography on silica gel plates with CH_2Cl_2, some of the unknown precursors were converted into **7a**. Compound **3a** (1.44 g, 32%) was separated from **4a** (0.24 g, 5%) by MPLC (RP 18, $CH_3OH:H_2O$ = 9:1). Melting points: **3a**, 101.5–102 °C (EtOH); **4a**, 118–119 °C (EtOH); **5a**, 39–41 °C (CH_3OH); **6a**, 58–59 °C (CH_3OH); **7a**, 195–197 °C (CH_3OH); **8a** (mixed crystals with CCl_4, decomposition), 264–266 °C ($CHCl_3/CCl_4$), from which an analytical sample of the perchlorate of **8a** was obtained.

The total yield obtained in this cycloaddition is slightly higher than described previously.[4] The percentage of the isolated oxidation products **7a** and **8a** strongly depends on the reaction conditions and is variable in contrast to the yields of the cycloadducts **3a**, **4a** and **5a**.

Catalytic Hydrogenation of 5a. Charcoal loaded with 10% Pd (64 mg) was added to a solution of **5a** (190 mg, 0.506 mmol) in methanol (25 mL) and stirred in a hydrogen atmosphere (1.03 bar) for 37 h. The mixture was filtered, and the residue was washed with 15 mL of warm methanol. Evaporation of the solvent and Kugelrohr distillation (180 °C/0.6 mbar) gave 88 mg (61%) of **9** (colorless liquid).

Independent Synthesis of 6a. Compound **2a** (0.89 g, 5.0 mmol) and nitrosobenzene (0.55 g, 5.1 mmol) were dissolved in toluene (1 mL) and heated for 5 h in a N_2 atmosphere. Toluene was removed under reduced pressure, and the residue was filtered over silica gel with CH_2Cl_2 as the eluent to give **6a** (1.34 g, 94%) as a spectroscopically pure oil. Colorless air-sensitive crystals with mp 58–59 °C were obtained by crystallization from methanol.

Reduction of the Pyridone 7a. A solution of **7a** (11 mg, 0.030 mmol) in 2 mL of THF was added to a suspension of $LiAlH_4$ (9 mg, 0.24 mmol) in 1 mL of THF and heated under reflux for 7 h. After this cooled, 0.2 mL of H_2O and 5 mL of ether were added. The organic layer was separated and evaporated to give a residue which showed the ^1H NMR signals of **8a** and of a second, unidentified compound. A precipitate formed when CCl_4 (1 mL) was added. The suspension was placed into an ultrasonic bath for 1 min and filtered to give 5.5 mg of colorless crystals (mixed crystals of **8a** with CCl_4), which were identified by their ^1H NMR spectrum.

2. Diphenylnitrone 1 and Diene 2b. Nitrone 1 (986 mg, 5.00 mmol), diene **2b** (512 mg, 5.44 mmol), and toluene (1.5 mL) were heated in a stoppered flask at 80 °C for 7 h (N_2 atmosphere). Toluene was then evaporated under reduced pressure, and the residue was separated by MPLC (RP 18, methanol) to give unreacted 1 (50 mg, 5%), unidentified products (10 mg), compounds **3b**, **4b**, **6b** (870 mg), **5b** (130 mg, 9%), and another fraction of unidentified compounds (40 mg). Separation of the 870 mg fraction by MPLC (RP 18, methanol/water = 90/10) gave **4b** (280 mg, 19%), **3b** (400 mg, 27%) and an impure sample of **6b** (30 mg, 3%). Compounds **3b**, **4b**, and **5b** gave colorless crystals from methanol with melting points 64.5–65 °C (**3b**), 113–114 °C (**4b**), and 78.5–79 °C (**5b**).

3. Diphenylnitrone 1 and 2,3-Dimethylbutadiene (2c). Nitrone 1 (2.48 g, 12.6 mmol), diene **2c** (5.67 g, 69.0 mmol), and toluene (3.0 mL) were heated in a nitrogen atmosphere (stoppered flask) at 80 °C for 28 h. After evaporation of the excess diene **2c** and of toluene, 10 mL of methanol was added to give 1.86 g (53%) of a 9:1 mixture of **3c** and **4c**. Recrystallization from methanol afforded pure **3c** with mp 76–77 °C. Chromatographic separation (MPLC, RP-18, CH_3OH) of the mother liquors yielded compounds **4c** (mp 64–65 °C, methanol), **5c** (mp 53–55 °C, methanol), and **6c**; total yield **3c** (66%), **4c** (24%), **5c** (2.6%), **6c** (0.6%).

Since **6c** was not obtained in pure form from this mixture, it was independently synthesized from nitrosobenzene (5.0 mmol) and **2c** (32.9 mmol) without a solvent. The exothermic reaction afforded **6c** (80%) which was recrystallized from methanol; mp 38–39 °C.

The thermal stability of **3c,4c** was examined by heating a **3c/4c** mixture in toluene at 100 °C for 20 h. ^1H NMR and HPLC analysis showed that neither decomposition nor rearrangements took place. Analogously, no changes in the ^1H NMR spectrum and in the HPLC were observable when a solution of **5c** in toluene was heated for 23 h at 80 °C.

4. Diphenylnitrone 1 and 2-Phenylbutadiene (2d). Nitrone 1 (986 mg, 5.00 mmol), diene **2d** (900 mg, 6.91 mmol), and toluene (1 mL) were heated in a nitrogen atmosphere at 80 °C for 7 h. Toluene was removed under reduced pressure to give a product mixture that was separated by MPLC (RP 18, methanol) to give three fractions: unreacted 1 (120 mg, 12%), a crude mixture of cycloadducts (1.34 g, 82%), and a mixture of hydrocarbons (100 mg, probably dimers of **2d**), which showed the same ^1H NMR spectrum as a sample obtained by heating a solution of **2d** in toluene. Chromatography (MPLC) of the cycloadduct fraction on a diol phase with pentane as eluent gave a fraction containing **3d**, **4d** and **5d** (443 mg, 27%) and a second fraction containing **3d'** and **4d'** (458 mg, 28%). Pure **3d** was obtained from the first fraction by crystallization with methanol. Compounds **4d** and **5d** were isolated from the mother liquors by a combination of MPLC (RP 18, methanol/water = 98/2 and 80/20) and fractional crystallization. In a similar way, compound **4d'** was obtained from the **3d'/4d'** mixture by treatment with methanol, and separation of the mother liquor by MPLC (RP 18, methanol/water = 80/20 afforded **3d'**. Total yields (isolated) were **3d** (mp 100–101 °C/methanol) 14.1%, **4d** (mp 59–61 °C/methanol) 3.8%, **5d** (mp 106–107 °C/methanol) 3.1%, **3d'** (mp 83–85 °C/methanol) 4.2%, **4d'** (mp 86–87 °C/methanol) 19.5%.

The thermal stability of the cycloadducts was examined for the major products **3d** and **4d'**. Both compounds remained unchanged when heated in toluene at 100 °C for 18 h. While **3d** decomposed to a complex mixture of products (not containing **5d**) when heated in toluene at 130 °C for 12 h, compound **4d'** remained almost unchanged when treated under these conditions for 36 h. Approximately 50% decomposition of **4d'** took place, when heated at 140 °C for 34 h. The complex mixture of products was not identified.

5. Diphenylnitrone 1 and 1-Phenyl-3-methylbutadiene (2e). Nitrone 1 (207 mg, 1.05 mmol), diene **2e** (150 mg, 1.04 mmol), and toluene (0.5 mL) were heated in a nitrogen atmosphere at 80 °C for 23 h. After evaporation of toluene in vacuo, the mixture was purified by MPLC (RP 18, methanol) to give 330 mg of a 2:1 mixture (^1H NMR) of **3e** and **4e**, which was separated by MPLC (RP 18, methanol/water = 95/5) to yield **3e** (221 mg, 62%) and **4e** (93 mg, 26%). Recrystallization from methanol gave analytically pure samples of **3e** (mp 78–80 °C) and **4e** (mp 80–81 °C).

6. Diphenylnitrone 1 and 1-Methyl-3-methylenecyclohexene (2f). In a silicon-rubber-sealed flask, nitrone 1 (642 mg, 3.26 mmol), diene **2f** (555 mg, 5.13 mmol), and toluene (1 mL) were heated in a nitrogen atmosphere at 80 °C for 8 h. Excess **2f** and toluene were removed in vacuo, and the residue was separated by MPLC (RP 18, methanol) to give compounds **4f** (332 mg, 33%) and **3f** (375 mg, 38%), which were recrystallized from methanol; mp 117–119 °C (**4f**) and 69–70 °C (**3f**).

7. Synthesis and Thermolysis of the Amine Oxide 11a. 1-(Chloromethyl)-2-(2-methoxy-2-phenylethyl)-3,3,4,4,5,5-hexamethylcyclopentene (12).[34] A solution of $ZnCl_2$ (163 mg, 1.20 mmol) in ether (0.19 mL) and CH_2Cl_2 (2.2 mL)[10] was added to a solution of α-methoxybenzyl chloride (1.57 g, 10.0 mmol) in CH_2Cl_2 (10 mL) at −65 °C. A solution of **2a** (1.78 g, 10.0 mmol) in CH_2Cl_2 (5 mL) was added dropwise within 10 min. After 2 h,

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Table VI. Determination of the Rates of Cycloadditions of 1 with 2a,b,f, in Toluene

			retention times/min						
	[1]/M^{-1}	[2]/M^{-1}	1	3	4	5	Ph–$C_{12}H_{25}$	temp/°C	k_2/M^{-1} s^{-1}
2a	0.453	0.456	2.38	6.29	7.03	7.67	11.16	80	1.1×10^{-5}
								100	6.0×10^{-5}
2b	0.200	0.201	2.40	3.97	3.70	4.74	14.19	80	3.3×10^{-4}
2f	0.251	0.250	2.35	3.77	4.04		11.94	80	4.4×10^{-5}

the cold mixture was poured on concentrated aqueous ammonia (50 mL), and the organic layer was washed with water (20 mL) and dried over $MgSO_4$. Evaporation of the solvent and successive Kugelrohr distillation (240 °C/1.5 mbar) afforded 2.72 g (81%) of **12**: IR (neat) 2974, 2939, 2870, 2815, 1462, 1452, 1375, 1367, 1150, 1097, 755, 718, 700, 663 cm^{-1}; ^{1}H NMR: δ 0.75 (s, 3 H), 0.80 (s, 6 H), 0.97 (s, 3 H), 1.00 (s, 3 H), 1.02 (s, 3 H), ABX system with ν_A = 2.31, ν_B = 2.65, ν_X = 4.30 and J_{AB} = 14.1 Hz, J_{AX} = 6.1 Hz, J_{BX} = 7.6 Hz (3 H), 3.19 (s, 3 H), AB system with ν_A = 3.80, ν_B = 4.10 and J_{AB} = 11.4 Hz (2 H), 7.34 (m, 5 H); ^{13}C NMR δ 21.06 (q), 21.62 (q), 24.29 (q), 24.70 (q), 24.85 (q), 25.03 (q), 35.18 (t), 38.62 (t), 46.36 (s), 49.46 (s), 50.65 (s), 56.89 (q), 83.36 (d), 126.65 (d), 127.64 (d), 128.36 (d), 139.43 (s), 142.47 (s), 145.21 (s); MS (70 eV), m/z = 334 (M$^+$, 0.1), 298 (0.2), 163 (2), 122 (9), 121 (100), 91 (4), 77 (4). Anal. Calcd for $C_{21}H_{31}ClO$ (334.9): C, 75.31; H, 9.33. Found: C, 75.62; H, 9.23.

1-(*N*-Anilinomethyl)-2-(2-methoxy-2-phenylethyl)-3,3,4,4,5,5-hexamethylcyclopentene. Compound **12** (2.45 g, 7.32 mmol) and aniline (4.50 g, 48.3 mmol) were heated in an N_2 atmosphere at 85 °C for 18 h. After this cooled, 50 mL of $CHCl_3$ was added to the partially solidified mixture. After agitation, the suspension was filtered and the residue was washed with 20 mL of $CHCl_3$. The combined filtrates were washed with saturated aqueous $NaHCO_3$ solution and dried over $MgSO_4$. Solvents and excess aniline were evaporated in vacuo and the residue was purified by Kugelrohr distillation (240 °C/0.6 mbar) to afford 2.67 g (93%) of a colorless oil which solidified spontaneously: mp 76–77 °C (methanol); IR (KBr) 3345, 3011, 2971, 2933, 2812, 1600, 1513, 1495, 1470, 1454, 1436, 1425, 1374, 1365, 1310, 1255, 1221, 1176, 1153, 1098, 1057, 1013, 745, 695 cm^{-1}; ^{1}H NMR δ 0.83 (s, 3 H), 0.85 (s, 3 H), 0.95 (s, 3 H), 0.99 (s, 3 H), 1.01 (s, 3 H), 1.07 (s, 3 H), ABX system with ν_A = 2.23, ν_B = 2.59, ν_X = 4.33 and J_{AB} = 14.3 Hz, J_{AX} = 4.4 Hz, J_{BX} = 10.0 Hz (3 H), 3.25 (s, 3 H), AB system with ν_A = 3.42, ν_B = 3.49, and J_{AB} = 11.8 Hz (2 H), 4.63 (br, s, 1 H), 6.58–6.72 (m, 3 H), 7.16–7.31 (m, 7 H); ^{13}C NMR δ 20.79 (q), 22.13 (q), 24.52 (q), 24.93 (q), 25.06 (q), 25.17 (q), 35.97 (t), 38.89 (t), 46.26 (s), 49.78 (s), 50.64 (s), 56.57 (q), 82.82 (d), 112.64 (d), 116.33 (d), 126.50 (d), 127.63 (d), 128.46 (d), 129.11 (d), 140.81 (s), 141.84 (s), 142.57 (s), 149.32 (s); MS (70 eV), m/z = 391 (M$^+$, 28), 359 (9), 283 (11), 181 (17), 121 (100), 106 (19), 93 (30), 77 (12). Anal. Calcd for $C_{27}H_{37}NO$ (391.6): C, 82.81; H, 9.52; N, 3.58. Found: C, 82.95; H, 9.55; N, 4.00.

7,7,8,8,9,9-Hexamethyl-3,4-diphenyl-3-azabicyclo[4.3.0]-non-1(6)-ene (13). The secondary amine $C_{27}H_{37}NO$ (2.67 g, 6.82 mmol), anhydrous NaI (2.36 g, 15.7 mmol), and trimethylsilyl chloride (11.1 g, 102 mmol) were heated at 85 °C in dry acetontrile with stirring for 15 h (N_2 atmosphere). After cooling, 50 mL of CH_2Cl_2, 15 mL of saturated aqueous $NaHSO_3$, and 15 mL of water were added. Solid $NaHCO_3$ was then added in small portions until the CO_2 evolution had ceased. The aqueous layer was extracted with two 50-mL portions of CH_2Cl_2, and the combined organic layers were dried over $MgSO_4$. After evaporation of the solvent, Kugelrohr distillation (220 °C/0.5 mbar) afforded 1.79 g (73%) of **13**, an air-sensitive oil, which can be converted into the more stable hydrochloride by bubbling dry HCl through a solution of **13** in CCl_4, from which the hydrochloride precipitates. Purification of the hydrochloride is achieved by dissolving it in a small volume of CH_2Cl_2, adding dry ether, and cooling the mixture for crystallization. The free base **13** is obtained from its hydrochloride by treating it with a concentrated aqueous solution of Na_2CO_3.

13: bp 220 °C (bath)/0.5 mbar; IR (neat) 2971, 2941, 2907, 2864, 1597, 1502, 1466, 1449, 1394, 1372, 1367, 1315, 786, 746, 696 cm^{-1}; ^{1}H NMR δ 0.70 (s, 3 H), 0.75 (s, 3 H), 0.82 (s, 3 H), 0.90 (s, 3 H), 0.91 (s, 3 H), 1.00 (s, 3 H), ABLMX system with ν_A = 2.38, ν_B = 2.70, ν_L = 3.56, ν_M = 3.88, ν_X = 5.22, and J_{AB} = 16.5 Hz, J_{AX} = 1.7 Hz, J_{BX} = 5.8 Hz, J_{LM} = 16.0 Hz, J_{AL} = 1.9 Hz, J_{AM} = 1.0 Hz, J_{BL} = 3.0 Hz, J_{BM} = 3.0 Hz (5 H), 6.70–6.91 (m, 3 H), 7.07–7.26 (m, 7 H); ^{13}C NMR δ 20.87 (q), 22.12 (q), 23.43 (q), 23.57 (q), 23.87 (q), 24.15 (q), 28.06 (t), 42.89 (t), 47.30 (s), 48.96 (s), 49.00 (s), 56.08 (d), 114.43 (d), 117.47 (d), 126.45 (d), 126.76 (d), 127.83 (d), 129.07 (d), 135.43 (s), 135.86 (s), 142.42 (s), 149.80 (s); MS (70 eV), m/z = 359 (M$^+$, 24), 344 (10), 275 (10), 182 (18), 181 (100), 180 (18), 91 (10), 77 (17). HCl salt: mp 257–258 °C/subl. (CH_2Cl_2/Et_2O). Anal. Calcd for $C_{26}H_{34}NCl$ (396.0): C, 78.86; H, 8.65; N, 3.54. Found: C, 78.52; H, 8.67; N, 3.76.

Amine Oxide 11a. A solution of *m*-chloroperbenzoic acid (347 mg of 75% material = 1.5 mmol) in 10 mL of CH_2Cl_2 was added dropwise (20 min) to a solution of **13** (0.43 g, 1.2 mmol) in CH_2Cl_2 (10 mL) at 0 °C. After stirring for 1 h, 15 mL of saturated aqueous Na_2CO_3 solution was added to the cold solution, and the organic layer was separated. The aqueous layer was extracted with 10 mL of CH_2Cl_2, and the combined organic layers were dried over $MgSO_4$. After evaporation of the solvent 0.44 g (98%) of a colorless solid (**11a**) with mp (dec) 61–65 °C was obtained: IR (KBr) 3056, 2970, 2942, 2908, 2864, 1595, 1484, 1454, 1375, 1369, 1155, 1112, 1099, 1027, 770, 756, 723, 696 cm^{-1}; ^{1}H NMR δ 0.94 (s, 3 H), 0.97 (s, 3 H), 1.03 (s, 3 H), 1.05 (s, 3 H), 1.07 (s, 3 H), 1.10 (s, 3 H), ABX system with ν_A = 2.44, ν_B = 2.71, ν_X = 4.81, and J_{AB} = 18.3 Hz, J_{AX} = 9.0 Hz, J_{BX} = 4.5 Hz (3 H), 4.64 (br s, 2 H), 7.00–7.58 (m, 10 H); ^{13}C NMR δ 21.48 (q), 21.56 (q), 23.63 (q), 23.71 (q), 23.84 (q), 23.87 (q), 26.62 (t), 47.75 (s), 49.44 (s), 49.70 (s), 69.15 (t), 80.58 (d), 122.68 (d), 127.52 (d), 127.80 (d), 128.91 (d) 129.26 (d), 131.15 (d), 134.11 (s), 134.73 (s), 137.71 (s), 150.15 (s); MS (70 eV), m/z = 375 (M$^+$, 22), 267 (62), 181 (69), 163 (100), 149 (63), 97 (78).

A part of this material was converted into the perchlorate: Compound **11a** (101 mg, 0.27 mmol) was dissolved in methanol (2 mL). After addition of 0.5 mL of $HClO_4$ (70%), methanol was removed in vacuo, and 10 mL of water was added. An oily precipitate formed which was dissolved in 2 mL of CH_2Cl_2. When 6 mL of ether was added, the perchlorate **11a**·$HClO_4$ (52 mg, 41%) was obtained by filtration and washing of the crystals with dry ether; mp (dec) 184–186 °C. Anal. Calcd for $C_{26}H_{34}NClO_5$ (476.0): C, 65.60; H, 7.20; N, 2.94. Found: C, 65.62; H, 7.02; N, 3.15.

Thermal Rearrangement of 11a. A solution of **11a** (120 mg) in toluene (2 mL) was heated in a N_2 atmosphere for 4 h at 80 °C. Toluene was removed under reduced pressure to give a residue, which contained neither **11a** nor **5a** according to ^{1}H NMR. Purification by MPLC (RP 18, methanol) afforded 71 mg (59%) of **14**: viscous oil; IR (KBr) 3052, 3017, 2966, 2938, 2861, 1598, 1488, 1450, 1392, 1378, 1373, 1367, 1217, 1152, 1085, 1061, 1026, 1007, 800, 745, 706, 695 cm^{-1}; ^{1}H NMR δ 0.56 (s, 3 H), 0.80 (s, 3 H), 0.84 (s, 3 H), 0.90 (s, 3 H), 1.00 (s, 3 H), 1.05 (s, 3 H), ABX system with ν_A = 2.55, ν_B = 2.88, ν_X = 5.28, and J_{AB} = 15.5 Hz, J_{AX} = 6.2 Hz, J_{BX} = 5.5 Hz, further split by long-range couplings (3 H), AB system with ν_A = 4.04, ν_B = 4.10, and J_{AB} = 15.9 Hz, further split by long-range couplings (2 H), 6.90–7.42 (m, 10 H); ^{13}C NMR δ 21.08 (q), 22.07 (q), 23.31 (q), 24.25 (q), 24.76 (q), 24.80 (q), 32.00 (t), 46.20 (s), 49.54 (s), 50.26 (s), 57.71 (t), 85.15 (d), 115.98 (d), 121.73 (d), 126.51 (d), 127.51 (d), 128.11 (d), 128.69 (d), 136.14 (s), 137.37 (s), 142.17 (s), 152.22 (s); MS (70 eV), m/z = 375 (M$^+$, 43), 267 (95), 197 (42), 163 (83), 149 (64), 97 (100); high-resolution MS, m/z calcd for $C_{26}H_{33}NO$ 375.25622, found 375.25658.

8. Kinetics of the Cycloadditions of 1 with Some Dienes. Equimolar amounts of the cycloaddends **1** and **2** and *n*-dodecylbenzene (internal standard) were dissolved in toluene to give a total of 5 mL. This solution was placed in a flask, flushed with nitrogen, sealed with a rubber septum, and placed into a thermostat (oil bath, 80.0 °C). After certain intervals, samples (25 μL) were taken with a syringe, dissolved in 1 mL of a CH_3OH/CH_2Cl_2 solution (1:1), and stored in the freezer (−25 °C) until they were analyzed by HPLC (RP 18, CH_3OH:H_2O = 95:5 (v/v), UV detection at 254 nm). Linear plots of $[1]^{-1}$ vs time were evaluated

to yield the second-order rate constants k_2 (Table VI).

9. Thermolysis of the Cycloadducts 3a,b, 4a,b, and 5a,b. One of the cycloadducts **3a,b–5a,b** and dodecylbenzene (standard) were dissolved in toluene, distributed to several vials (flushed with N_2), and placed into a thermostated oil bath. The mixtures, which were removed from the thermostat after various times, were analyzed by HPLC as described above. For results see Table V.

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Registry No. 1, 1137-96-8; **2a**, 96806-52-9; **2b**, 20968-70-1; **2c**, 513-81-5; **2d**, 2288-18-8; **2e**, 68036-69-1; **2f**, 23611-15-6; **3a**, 123186-95-8; **3b**, 123186-99-2; **3c**, 123187-03-1; **3d**, 123187-05-3; **3d'**, 123187-08-6; **3e**, 123187-10-0; **3f**, 123187-12-2; **4a**, 123186-96-9; **4b**, 123187-00-8; **4c**, 123187-04-2; **4d**, 123187-06-4; **4d'**, 123187-09-7; **4e**, 123187-11-1; **4f**, 123187-13-3; **5a**, 123186-97-0; **5b**, 123187-01-9; **5c**, 123206-03-1; **5d**, 123187-07-5; **6a**, 123186-98-1; **6b**, 123187-02-0; **6c**, 19029-47-1; **7a**, 110373-09-6; **8a**, 110373-08-5; **9**, 123187-14-4; **11a**, 110373-11-0; **11a**·$HClO_4$, 123187-20-2; **12**, 123187-16-6; **13**, 123187-18-8; **13**·HCl, 123187-19-9; **14**, 123187-21-3; $PhNH_2$, 62-53-3; PhNO, 586-96-9; (±)-PhCHClOMe, 66873-72-1; 1-(*N*-anilinomethyl)-2-(2-methoxy-2-phenylethyl)-3,3,4,4,5,5-hexamethylcyclopentene, 123187-17-7.

Supplementary Material Available: IR, ^1H NMR (200 MHz), ^{13}C NMR (50 MHz), mass spectra (EI), and microanalytical data of all compounds listed in Table I and of compound **9** (8 pages). Ordering information is given on any current masthead page.

Oxidation of Primary Amines by Dimethyldioxirane[1]

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Dimethyldioxirane oxidizes primary amines rapidly, and generally in high yield, to the corresponding nitro compounds. The method can also be used to synthesize polynitro compounds.

Introduction

Many nitro compounds are difficult to synthesize by direct nitration methods. However, some success has been achieved by direct oxidation of the corresponding amines using either peracids or hydrogen peroxide.[2-6] We earlier reported[7] that dimethyldioxirane (**1**) oxidizes some primary amines to nitro compounds. We have now followed up our earlier work by oxidizing a variety of primary amines to the corresponding nitro compounds through the use of dimethyldioxirane.[8] This reagent is more convenient to use than other oxidants and generally leads to higher yields of the desired nitro compounds. Included in the current results are several examples of the use of **1** to prepare polynitro compounds.

This work is part of a comprehensive program on the chemistry of dioxiranes. We first reported the successful isolation in solution of **I** and related dioxiranes in 1985.[8] Since that time Adam and co-workers[9] and Curci et al.[10,11] have described similar experiments. Dioxiranes are powerful and unique oxidants that oxidize substrates ranging from more reactive species such as the amines used in the present work to the generally unreactive saturated hydrocarbons.[11,12] Our work on the oxidation of amines includes the primary amines described here and in our earlier report[7] as well as secondary and tertiary amines. We recently reported[13] that oxidation of appropriate secondary amines by **1** leads to a convenient, high yield route

Table I. Oxidation of Primary Amines by Dimethyldioxirane

amine	yield,[a] % isolated	yield,[a] % GC	method
o-nitroaniline		65	*c*
m-nitroaniline		97	*b*
3,5-dinitroaniline	94		*c*
p-aminobenzonitrile		90	*b*
p-aminobenzoic acid	95		*b*
p-chloroaniline		97	*b*
p-toluidine		98	*b*
p-aminoacetophenone		95	*b*
2,6-difluoroaniline		96	*b*
2,4,6-trichloraniline		97	*b*
p-nitroaniline		98	*b*
1-naphthylamine		42[e]	*c*
p-aminobenzotrifluoride		93	*c*
1,4-diaminocubane	80		*b*
1,3,5,7-tetraamino-adamantane	91		*d*
1,6-hexanediamine	20		*b*
1,6-hexanediamine	60		*b, d*
p-phenylenediamine	82		*b, d*
o-phenylenediamine		85	*c*
endo-2-aminonorbornane	58		*b, d*
exo-2-aminonorbornane	80.8		*b*

[a] In all cases the product is the nitro compound corresponding to the amine. [b] Amine added to dioxirane solution. [c] Dioxirane added to amine. [d] Amine hydrochloride used. [e] Accompanied by 2-hydroxy-1-nitronaphthalene (20%).

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