Reaction of α-Peroxy Lactones with C, N, P, and S Nucleophiles: Adduct Formation and Nucleophile Oxidation by Nucleophilic Attack at and Biphilic Insertion into the Peroxide Bond

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The reactions of the α-peroxy lactones **1** with a variety of carbon, nitrogen, phosphorus, and sulfur nucleophiles yield, on S_N2 attack at the more electrophilic alkoxy oxygen of the peroxide bond, diverse addition and oxygen transfer products, together with the catalytic Grob-type fragmentation. The nature of the nucleophile determines the fate of the open-chain intermediate **I**. Thus, protic nucleophiles such as primary and secondary amines and thiols lead to the second intermediate **I′** through proton shift subsequent to the S_N2 step, while nonprotic amines and sulfides, as well as diazoalkanes, lead to oxidation products or to the cycloadducts **10**−**15**. Trivalent phosphorus nucleophiles such as phosphines and phosphites and diisopropyl sulfoxylate prefer biphilic insertion, as documented by the fact that the nucleophilicity rather than the steric demand of these reagents controls their reactivity. The labile adducts undergo a variety of transformations to the final stable products. For protic nucleophiles, the amine adducts **5** and **6** are sufficiently persistent for isolation, whereas the sulfenic esters formed by thiol addition are further oxidized to the sulfinic esters **7** and **8** or react with excess thiol to the corresponding disulfides. For aprotic nucleophiles, the dipolar intermediates **I** decompose into acetone and CO_2 with regeneration of the nucleophile (Grob-type fragmentation), as seen for DABCO and pyridine *N*-oxide, or they extrude the α-lactone to afford the oxygen transfer product. The corresponding ketones, pyridine *N*-oxide, sulfoxides, and sulfones are obtained by this route from diazoalkanes, pyridine, sulfides and sulfoxides. Additionally, the diazoalkane intermediates **I** also cyclize to the cycloadducts **10**−**12**. The thermally labile phosphorus adducts **13**−**15**, which were observed by low-temperature NMR spectroscopy, decompose to the α-lactone and the phosphorus oxides. Analogously, diisopropyl sulfite is obtained from the sulfoxylate adduct. As for the fate of the α-lactones (the reduction products of the α-peroxy lactones), the dimethyl derivative either oligomerizes to the oligoester **2a** or is trapped by methanol as the α-methoxy acid **4a**, while the spiroadamantyl α-lactone decarbonylates to adamantanone.

Introduction

Reactions of the strained cyclic peroxides 1,2-dioxetanes[1,2] and dioxiranes[3] with nucleophiles have been well studied during the last decades. Numerous early examples of such transformations of dioxetanes are their deoxygenation by phosphines[1a,b] and sulfides[1c−e] and their reduction by thiols.[1f] More recently we have carried out extensive mechanistic investigations on the reaction of 3,3-disubstituted 1,2-dioxetanes with a variety of heteroatom,[2a] π[2b,c] and carbon[2d,e] nucleophiles. We established that the S_N2 mechanism operates for these reactions, in which the nucleophile attacks the peroxide bond at the sterically exposed oxygen atom to produce anionic or zwitterionic adducts; the latter transform to a variety of oxidized products. While these studies have provided valuable mechanistic information on oxygen transfer processes, the oxidations with dioxiranes have become a general and selective preparative method for the oxyfunctionalization of organic and organometallic substrates.[3]

Most recently we have directed our attention to the α-peroxy lactones **1**, four-membered cyclic peroxyesters which were made available by us in earlier times. Their chemical behavior, except its thermal decomposition with characteristic chemiluminescence,[1g] had remained largely unexplored. We have shown that olefins[4] react with the dimethyl α-peroxy lactone (**1a**) through an S_N2 attack preferentially at the alkoxy oxygen of the peroxide bond due to the inherent polarization by the acyl group. The final oxidized product may derive from epoxidation and/or adduct formation, which constitute characteristic reaction modes, respectively, of dioxiranes and 1,2-dioxetanes. The preferred reaction type proved to be sensitive to subtle steric and electronic effects of the attacking nucleophile.

Herein we focus our attention on the reaction of the α-peroxy lactones **1** with a variety of carbon and heteroatom nucleophiles. Primary and secondary amines

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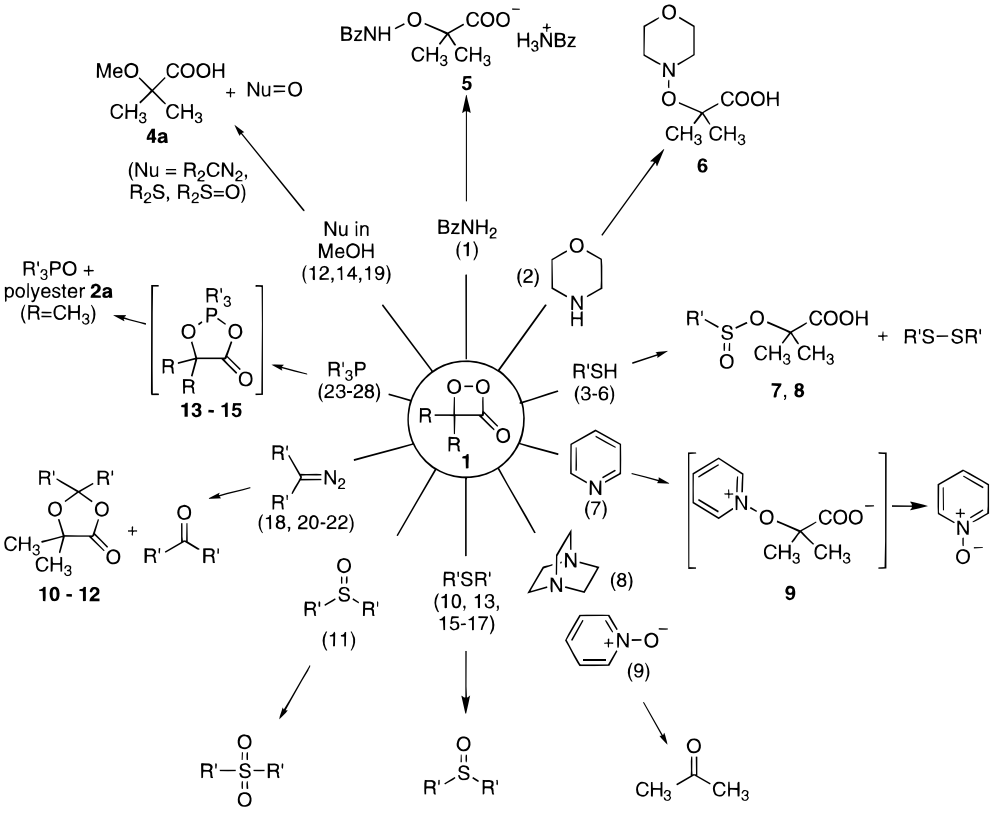
Scheme 1. Reactions of α-Peroxy Lactones 1 with C, N, P, and S Nucleophiles (numbers in brackets indicate the corresponding entries in Table 1)



and thiols were chosen as protic nucleophiles, for which the S_N2 adducts were expected to be sufficiently persistent for isolation. For comparison, it was of interest to examine the reactivity of tertiary amines and sulfides as nonprotic nucleophiles. For the sulfide nucleophiles, additionally the question of competitive sulfide *versus* sulfoxide oxidation was to be assessed with the mechanistic probe thianthrene 5-oxide.[5] Moreover, the possibility of biphilic insertion was to be investigated with trivalent phosphorus nucleophiles[1a,b] and diisopropyl sulfoxylate[1d] for the hitherto unknown, sterically hindered spiroadamantyl-substituted α-peroxy lactone **1b**, for which steric effects should be negligible if a biphilic mechanism applied. Finally, diazoalkanes were chosen as carbon nucleophiles to determine whether formal cycloaddition, the predominant reaction mode for 1,2-dioxetanes,[2d] or carbon oxidation, the characteristic process for dioxiranes,[3b] would prevail. The results are displayed in the rosette of Scheme 1 and the details of the product distribution in Table 1. Clearly, we observe that the primary mechanistic event is S_N2 attack on the peroxide bond of the α-peroxy lactone by most nucleophiles, but biphilic insertion takes place for phosphines, phosphites, and sulfoxylates.

Results

Synthesis of Spiro-Adamantyl α-Peroxy Lactone (1b). The new spiro-adamantyl α-peroxy lactone (**1b**) (Scheme 2) was synthesized from the corresponding α-hydroperoxy acid, which was obtained by autoxidation of the lithium dianion of 2-adamantanecarboxylic acid in THF at −80 °C. Cyclization of the α-hydroperoxy acid with dicyclohexyl carbodiimide,[6] separation of the formed dicyclohexyl urea by low-temperature filtration over florisil, and recrystallization from pentane afforded the pure **1b** as the first isolated crystalline α-peroxy lactone. Attempts to obtain an X-ray structure at low temperature unfortunately failed.

Reactions of α-Peroxy Lactone 1a with Protic Amines. The reactions of α-peroxy lactone **1a** with benzylamine and morpholine (Table 1, entries 1 and 2) yielded the α-aminoxy acids **5** and **6**, which were isolated and fully characterized. The free acid functionality of the morpholine adduct **6** is evidenced by IR bands around 1700 cm^{-1} and ^{13}C NMR shifts around δ 180. The benzylamine adduct was isolated as its benzylammonium salt **5**, as shown by the presence of two signals for the benzylic methylene group in the ^1H and ^{13}C NMR spectra.

Reactions of α-Peroxy Lactone 1a with Thiols. α-Peroxy lactone **1a** afforded with benzyl mercaptan and thiophenol (Table 1, entries 3−6) the α-sulfinoxy acids **7** and **8**, which were isolated after treatment with diazomethane as the methyl esters **7′** and **8′**. Due to the labile nature of these products (decomposition during silica gel chromatography), the yields of isolated material were low. The sulfinic ester group was assigned by its IR bands around 1190 cm^{-1} and the ^1H NMR shifts of the adducts **7′** and **8′**. Thus, the benzylic protons of **7′** are diastereotopic due to the chirality of the sulfinic ester functionality and appear as an AB system (J_{gem} = 12.8 Hz), while the aromatic protons of **8′** in the *meta* position show a low-field shift to δ 7.90 by the sulfinic ester substituent. Further evidence for the structures of **7′** and **8′** is given by their independent syntheses from the corresponding sulfinic acid chlorides and methyl α-hydroxy isobutyrate (eq 1), which also allowed their complete characterization. Together with the adducts **7** and

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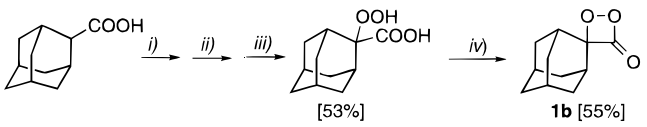
Table 1. Product Studies for the Reaction of α-Peroxy Lactones 1 with C, N, P and S Nucleophiles

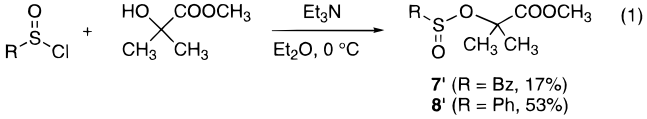
	α-peroxy	reaction conditions[b]				product distribution[c]			
entry[a]	lactone	nucleophile[d]	temp [°C]	time[e] [h]	mb[f] [%]	addition	oxidation	reduction	fragn
1	**1a**	$BzNH_2$ (3.0)	−20	0.05	97	95 (**5**)	−	−	2
2	**1a**	morpholine (1.0)	−20	0.05	96	91 (**6**)	−	−	5
3	**1a**	BzSH (0.75)	−20	0.05	92[g]	42 (**7**)	2 (RSSR)	**2a**, **3a**[h,i]	6
4	**1a**	BzSH (2.39)	−20	0.05	96[g]	39 (**7**)	6 (RSSR)	**2a**, **3a**[h,i]	12
5	**1a**	PhSH (0.63)	−20	0.05	88[g]	31 (**8**)	6 (RSSR)	**2a**, **3a**[h,i]	20
6	**1a**	PhSH (1.80)	−20	0.05	97[g]	36 (**8**)	10 (RSSR)	**2a**, **3a**[h,i]	15
7a	**1a**	pyridine (1.0)	−20	0.5	70[j]	65 (**9**)	−	−	5
7b	**1a**	pyridine (1.0)	20	168	>95	−	76 (*N*-oxide)[k]	27 (**2a**)	−
8	**1a**	DABCO (1.0)	−50	0.05	86[j]	−	−	−	86
9	**1a**	pyridine *N*-oxide (1.0)	−20	0.35	91[j]	−	−	−	91
10	**1a**	MeSMe (1.16)	−20	0.05	69	−	57 (RSOR)[l]	−	11
11	**1a**	MeSOMe (1.10)	−20	0.05	98	−	95 (RSO_2R)	54 (**2a**)	3
12	**1a**	MeSOMe (1.10)[m]	−20	0.05	>95	−	>95 (RSO_2R)	>95 (**4a**)	−
13	**1a**	PhSPh (1.07)	−20	0.05	81	−	53 (RSOR)[n]	25 (**2a**)	22
14	**1a**	PhSPh (1.10)[m]	−20	0.05	>95	−	86 (RSOR)	>95 (**4a**)	−
15	**1a**	SSO (1.33)[o]	−20	0.05	94	−	78[p]	78 (**2a**)	16
16	**1a**	$^iPrOSO^iPr$ (1.10)[q]	−20	0.05	>95	−	95 [ROS(O)OR]	>95 (**2a**)	−
17	**1b**	$^iPrOSO^iPr$ (2.89)[q]	−50	0.05	94	−	90 [ROS(O)OR]	−	94
18	**1a**	CH_2N_2 (ca. 5)[r]	−20	0.05	73	24 (**10**)	−	49 (**2a**)	−
19	**1a**	CH_2N_2 (ca. 4)[s]	−20	0.05	10	−	−	10 (**4a**)	−
20	**1a**	Ph_2CN_2 (1.0)	−20	3	>95	13 (**11**)	43 (R_2CO)	−	40
21	**1a**	fluorene-CN_2 (1.0)	−20	2	93	16 (**12**)	67 (R_2CO)	77 (**2a**)	−
22	**1a**	$(CH_3OOC)_2CN_2$ (4.0)	20	24	>95	−	−	−	>95
23a	**1a**	Ph_3P (1.1)	−60	0.05	>95	75 (**13a**)	*h*	17 (**2a**)	8
23b	**1a**	Ph_3P (1.1)	20	24	>95	−	>95 (R_3PO)	>95 (**2a**)	−
24a	**1a**	$C_5H_9O_3P$ (1.0)[t]	−60	0.05	91	23 (**14a**)	68 (R_3PO)	53 (**2a**)	−
24b	**1a**	$C_5H_9O_3P$ (1.0)[t]	20	24	>95	−	95 (R_3PO)	96 (**2a**)	−
25	**1a**	$(EtO)_3P$ (5.0)	−60	0.05	>95	−	>95 (R_3PO)	92 (**2a**)	2
26a	**1b**	Ph_3P (1.2)	−60	0.05	>95	50 (**13b**)	*h*	−	50
26b	**1b**	Ph_3P (1.2)	20	24	>95	−	>95 (R_3PO)	−	70
27a	**1b**	$C_5H_9O_3P$ (1.0)[t]	−60	6[u]	>95	48 (**14b**)	52 (R_3PO)	−	*h*
27b	**1b**	$C_5H_9O_3P$ (1.0)[t]	20	24	>95	−	>95 (R_3PO)	−	50
28a	**1b**	$(EtO)_3P$ (3.0)	−60	0.15[v]	>95	47 (**15b**)	55 (R_3PO)	−	46
28b	**1b**	$(EtO)_3P$ (3.0)	20	24	>95	−	>95 (R_3PO)	−	60

[a] For the "b" runs, the reaction mixtures of the "a" runs were allowed to warm up to room temperature for thermal decomposition. [b] In $CDCl_3$ unless indicated. [c] In $CDCl_3$ determined by ^1H NMR spectroscopy with hexamethyldisiloxane as internal standard, in CH_3CCl_3 determined gravimetrically; product structure is indicated in brackets. [d] Number of equivalents in brackets. [e] Conversion >95% unless indicated. [f] Mass balance relative to α-peroxy lactone **1**; includes the yields of addition, oxidation (or reduction), and fragmentation products. [g] Yield of adducts **7** and **8** accounts for 2 equiv of α-peroxy lactone **1a**. [h] Not quantified due to overlap with other product NMR signals. [i] α-Hydroxy acid **3a** detected in form of the corresponding methyl ester after treatment with diazomethane. [j] No other products were observed. [k] Also 21% unidentified products. [l] Also 1% dimethyl sulfone was observed. [m] Run in 1:1 $CDCl_3/CD_3OD$ as solvent. [n] Also 6% diphenyl sulfone was observed. [o] Thianthrene 5-oxide. [p] 67% SOSO and 11% SSO_2, $x_{SO} = 0.16$. [q] Under oxygen-free reaction conditions (freeze-pump-thaw method), no change in the product distribution was observed. [r] Run in CH_3CCl_3, yield of volatile oxidation and fragmentation products not determined. [s] Run in 1:1 CH_3CCl_3/CH_3OH, yield of volatile oxidation and fragmentation products not determined. [t] 4-Methyl-2,6,7-trioxa-1-phosphabicyclo[2.2.2]octane. [u] Conversion 70%. [v] Conversion 67%.

Scheme 2[a]



[a] (i) 2 LDA, −20 °C, THF; (ii) $^3O_2$, −70 to −90 °C, THF; (iii) HCl (10%), −80 °C, THF; (iv) DCC, CH_2Cl_2, −40 °C.



(1)

8, the disulfides of the thiols were obtained in low yields. Variation in the ratio between oxidized thiol and α-peroxy lactone **1a** had little influence on the product distribution. Together with the sulfur products, the oligomeric ester **2a** and methyl α-hydroxy isobutyrate were also observed. The latter derives from the corresponding α-hydroxy acid **3a** after reaction of the crude product mixture with diazomethane.

Reactions of α-Peroxy Lactone 1a with Nonprotic Amines. Pyridine was oxidized by α-peroxy lactone **1a** to its *N*-oxide through the intermediate **9** (entries 7a and 7b). The α-pyridinoxy acid **9** was identified *in situ* by its NMR spectral data, but complete characterization was not possible due to its decomposition to pyridine *N*-oxide. Although adduct **9** was the only product observed right after completion of the reaction, besides pyridine *N*-oxide also ca. 21% unidentified products were observed in the ^1H NMR spectrum of the crude reaction mixture (cf. footnote k). With 1,4-diazabicyclo[2.2.2]cyclooctane (DABCO) and pyridine *N*-oxide (entries 8 and 9), only catalytic decomposition of α-peroxy lactone **1a** into acetone was observed without consumption of the nucleophile.

Reactions of α-Peroxy Lactones 1a and 1b with Nonprotic Sulfur Nucleophiles. The oxidation of sulfides and sulfoxides by α-peroxy lactones **1a** and **1b** (Table 1, entries 10−15) yielded as main products the corresponding sulfoxides and sulfones, *i.e.* the respective oxidation products by transfer of a single oxygen atom. Small amounts of the sulfones were also observed in the oxidation of sulfides (cf. footnotes l, n). In the oxidation of sulfides and sulfoxides run in $CDCl_3$ as solvent (entries 10, 11, and 13), oligoester **2a** was observed as reduction product in moderate yields together with unidentified material. In methanol as cosolvent (entries 12 and 14), α-methoxy acid **4a**, the known methanol trapping product of the α-lactone, was obtained quantitatively. Furthermore, the reaction of α-peroxy lactone **1a** with thian-

threne 5-oxide (entry 15) afforded the 5,10-dioxide (SOSO) and the 5,5-dioxide (SSO_2) in 67% and 11% yields (cf. footnote p).

As for the reaction of the diisopropyl disulfoxylate with the α-peroxy lactones **1** (entries 16 and 17), the corresponding sulfites were obtained by extrusion of one oxygen atom. In the case of the α-peroxy lactone **1a** (entry 16), deoxygenation led quantitatively to the oligoester **2a**, while for the spiroadamantyl derivative **1b** (entry 17) only adamantanone was detected as reduction product. When the latter reaction was directly monitored by ^{1}H NMR spectroscopy at −50 °C, no reaction intermediate was observed as precursor to the final products adamantanone and diisopropyl sulfoxylate. Moreover, no changes in the product composition were found when the reaction was conducted under rigorously deoxygenated conditions by applying the freeze-pump-thaw method (Table 1, footnote q).

Reactions of α-Peroxy Lactone 1a with Diazomethane Derivatives. The reaction of α-peroxy lactone **1a** with diazomethanes (Table 1, entries 18−22) yielded the cycloadducts **10**−**12** together with substantial amounts of catalytic decarboxylation of the α-peroxy lactone **1a** and oxidation of the diazo compound to the corresponding ketone. Only with the less nucleophilic mesoxalic ester derivative occurred no reaction at −20 °C, but at room temperature thermal decomposition of the α-peroxy lactone **1a** took place (entry 22).

For the diphenyl and fluorenyl derivatives, the adducts **11** and **12** were isolated and fully characterized. The 1,3-dioxolan-4-ones **10**−**12** showed a typical carbonyl IR band at 1765 cm^{-1} and ^{13}C NMR shifts at δ 176. The diazomethane adduct **10** was identified and quantified by GC analysis and coinjection with an independently synthesized sample.[7] Since the reactions with diazomethane (entries 18 and 19) were run in nondeuterated solvents, the volatile oxidation product of diazomethane, namely formaldehyde, was not detected, and the extent of oxidation was quantified in terms of the oligoester **2a**, the known reduction product of α-peroxy lactone **1a**.[8] Fragmentation of α-peroxy lactone **1a** into acetone was also not quantified in these cases, which accounts for the low mass balance. When the reaction of α-peroxy lactone **1a** with diazomethane was carried out in methanol as cosolvent, the α-methoxy acid **4a** was obtained from α-lactone as trapping product.[9]

Loss due to evaporation of the volatile products **10** and **4a** during the workup accounts for the low yield of isolated products on the preparative scale.

Reactions of α-Peroxy Lactones 1a and 1b with Phosphorus Nucleophiles. The reactions of α-peroxy lactones **1a** and **1b** with phosphorus nucleophiles (Table 1, entries 23−28) were run in deuterochloroform at −60 °C and directly monitored by ^{1}H NMR spectroscopy at that temperature to detect possible reaction intermediates. The corresponding insertion products, namely the dioxaphospholanones **13**−**15**, were observed in all cases except in the reaction between α-peroxy lactone **1a** and triethyl phosphite (entry 25). In the latter case, the quantitative oxidation of the phosphite to the phosphate was observed with concomittant formation of the oligoester **2a**. Also in the other cases simultaneous direct formation of the phosphorus oxidation product was observed at low temperature. As for the dioxaphospholanones **13**−**15,** the phosphorus coupling constants with the ring carbon atoms show typical values of 3−13 Hz for a two-bond interaction, and the ^{31}P NMR shifts are characteristic for such cycloadducts. Thus, the adducts **14a**, **14b**, and **15b** of the insertion of the corresponding phosphites into the peroxide bond of α-peroxy lactones **1a** and **1b** showed resonances between δ 50 and 60, which are in good agreement with reported values for analogous pentacovalent phosphorus compounds.[1a,b,9a,b] The assignment of the five-membered ring structure is also unequivocal in the case of the adamantyl derivative **13b**, which has a ^{31}P NMR shift of δ 24.9, again in good accordance with reported values.[1a,b] In contrast, the phosphorus shift of the dimethyl adduct **13a** occurs at higher field (δ 9.4). Since negative phosphorus shifts are reported for the open, betainic form of analogous dioxaphospolanes,[9b] the measured value of δ 9.4 is an indication that adduct **13a** equilibrates fast between the closed five-membered ring and the open zwitterionic form.

Table 2. Rate Studies of the Reaction of Spiroadamantyl α-Peroxy Lactone 1b with Phosphorus Nucleophiles[a]

entry	nucleophile	solvent	k^b
1	Ph_3P	CH_2Cl_2	22 ± 10
2	Ph_3P	CH_3CN	26 ± 2
3	$C_5H_9O_3P$[c]	CH_2Cl_2	0.074 ± 0.005
4	$C_5H_9O_3P$[c]	CH_3CN	0.124 ± 0.001
5	none	CH_2Cl_2	(9.7 ± 0.3) × 10^{-5}
6	none	CH_3CN	(9.2 ± 0.2) × 10^{-5}

[a] At 10 ± 0.5 °C. [b] Entries 1−4 are second-order [s^{-1} M^{-1}] and entries 5 and 6 first-order [s^{-1}] rate constants. [c] 4-Methyl-2,6,7-trioxa-1-phosphabicyclo[2.2.2]octane.

For mechanistic purposes, the rates for the reaction of the adamantyl α-peroxy lactone **1b** with triphenylphosphine and the bicyclic phosphite methyltrioxaphosphabicyclooctane were measured in dichloromethane and acetonitrile[9c] at 10 °C by using the chemiluminescence decay method (Table 2). As expected, the results show a greater reactivity (approximately two orders of magnitude higher) for the triphenylphosphine compared to the bicyclic phosphite; however, the solvent effect is small since the rates in acetonitrile are only slightly (twofold) higher for the bicyclic phosphite (entries 3 and 4) and within the experimental error for triphenylphosphine (entries 1 and 2).

While all adducts **13**−**15** decomposed on standing at room temperature, they showed different thermal persistence at low temperatures. Thus, the triphenylphosphine adducts **13a**,**b** persisted for a few hours at −20 °C, while the phosphite adducts **14a**,**b** and **15b** decomposed slowly at that temperature. In all cases, the total decomposition of the adducts led quantitatively to the corresponding phosphine oxides and phosphates. However, a difference in chemical behavior was found between the dimethyl adducts **13a** and **14a**, which also quantitatively led to the oligoester **2a**, and the adamantyl derivatives **13b**, **14b** and **15b**. Thermal decomposition of the latter gave substantial amounts of adamantanone (50−70%) and the corresponding phosphine oxide or phosphate quantitatively.

Discussion

Our results of the reaction between α-peroxy lactones **1a** and **1b** and a set of C, N, P, and S nucleophiles (Table

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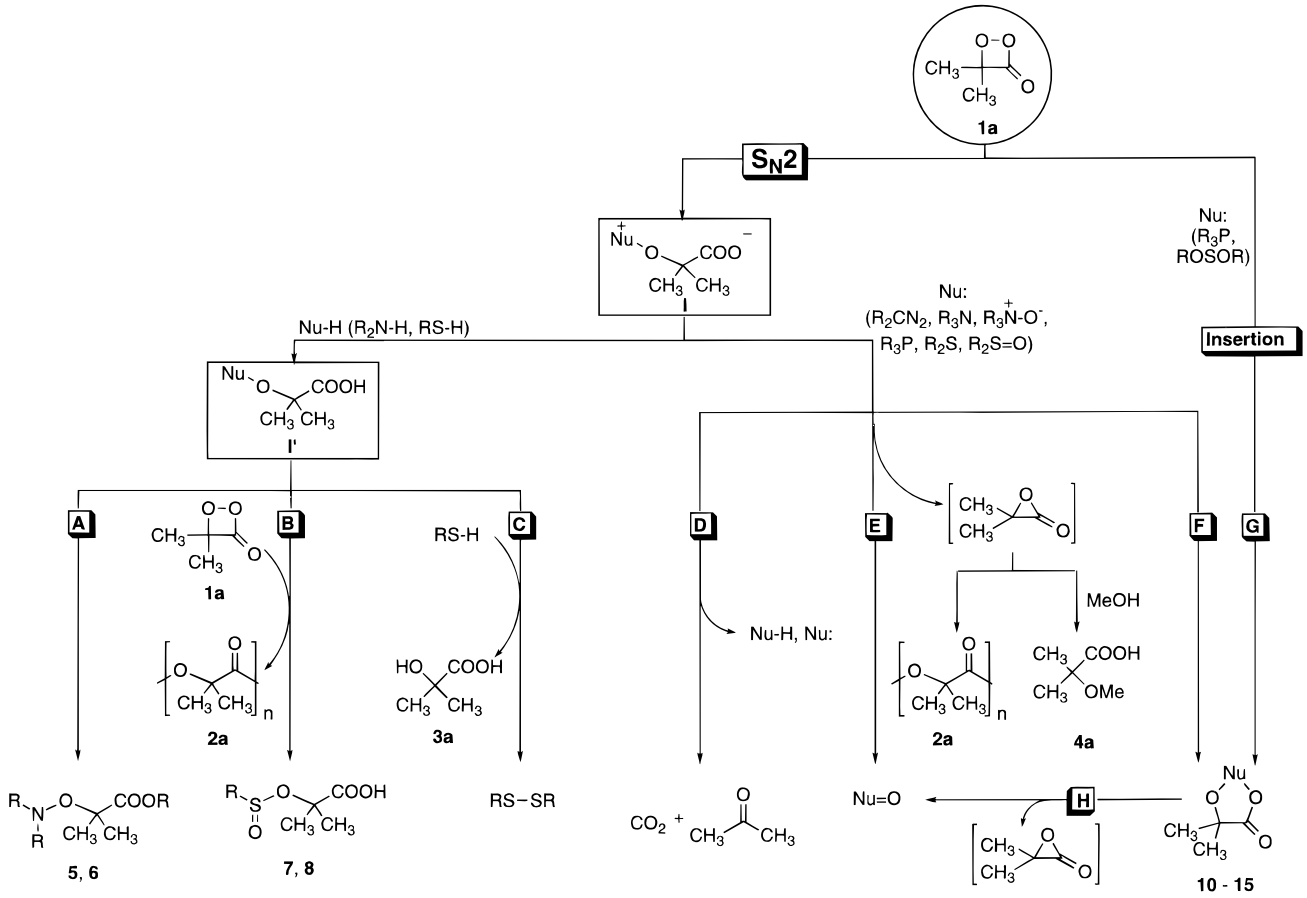
Scheme 3. Mechanism for the Reaction of α-Peroxy Lactone 1a with C, N, P, and S Nucleophiles



1) show three formal reaction types: *addition* of the nucleophile to the peroxide bond of α-peroxy lactone **1**, which leads either to the open-chain adducts **5**−**9** or to the cycloadducts **10**−**15**, *oxidation* of the nucleophile by oxygen transfer with concomitant *reduction* of the α-peroxy lactone, and decarboxylation of the latter to the corresponding ketone by *fragmentation*. Our reaction modes are rationalized in Scheme 3 by the open-chain adducts **I** and **I′**, which arise from the attack of the nucleophile at the more electrophilic alkoxy oxygen of α-peroxy lactone **1**, in analogy to our recent findings for the reaction of α-peroxy lactone **1a** with olefins.[4] Additionally, direct insertion of the nucleophile into the peroxide bond to afford cycloadducts is postulated.

In our previous studies on the reaction of the related 3,3-disubstituted 1,2-dioxetanes with a series of nucleophiles, which yielded a comparable set of products,[2] we postulated the intermediacy of an adduct from the S_N2 attack of the nucleophile on the less hindered oxygen of the peroxide bond. Furthermore, for the reactions of sterically hindered tetrasubstituted 1,2-dioxetanes with trivalent phosphorus,[1ab,10] arsenic and antimony[11] nucleophiles, as well as di- and trisubstituted 1,2-dioxetanes with sulfoxylates,[1d] which lead to the corresponding heteroatom-substituted dioxolanes, a biphilic insertion mechanism has been postulated on the basis of kinetic measurements (Hammett correlations[10a] and isotopic effects[10b]). Biphilic insertion has also been postulated for monovalent metal complexes.[12]

In the present study, the S_N2 adducts **I** are formed for all protic nucleophiles, namely amines (Table 1, entries 1 and 2) and thiols (entries 3−6), as well as for pyridine (entry 7). Adduct **I′** results after nucleophilic attack on the α-peroxy lactone **1** and subsequent intramolecular and/or intermolecular protonation. The adduct **I′** was isolated for morpholine in form of acid **6** (entry 2), while the benzylamine adduct reacted further with excess base to the salt **5** (entry 1), which was isolated (Scheme 3, path A). The different behavior of the amine adducts derives from the higher basicity of benzylamine, which is protonated by the acid functionality.

The benzylmercaptan and thiophenol adducts **I′** (Table 1, entries 3−6) exhibited two subsequent transformations, namely oxidation of the sulfenic to the isolated sulfinic esters **7** and **8** by a second α-peroxy lactone **1a** (Scheme 3, path B) and reaction with a thiol molecule to the corresponding disulfide (Scheme 3, path C).[13] In parallel, the oligoester **2a**, the reduction product of the α-peroxy lactone **1a**, and the α-hydroxy acid **3a**, produced by the S_N2 attack on the sulfenate, were observed. No sulfenic ester was detected even when the reaction was carried out with an excess of thiol (entries 4 and 6), which displays the higher reactivity of the sulfenate toward oxidation in comparison with the thiol. Indeed, oxidation of sulfenic esters by singlet oxygen[14] or mCPBA[15] is known, and it is instructive to compare the present results with our previous results for the reaction of 3,3-disubstituted 1,2-dioxetanes with thiophenol.[2a] In the

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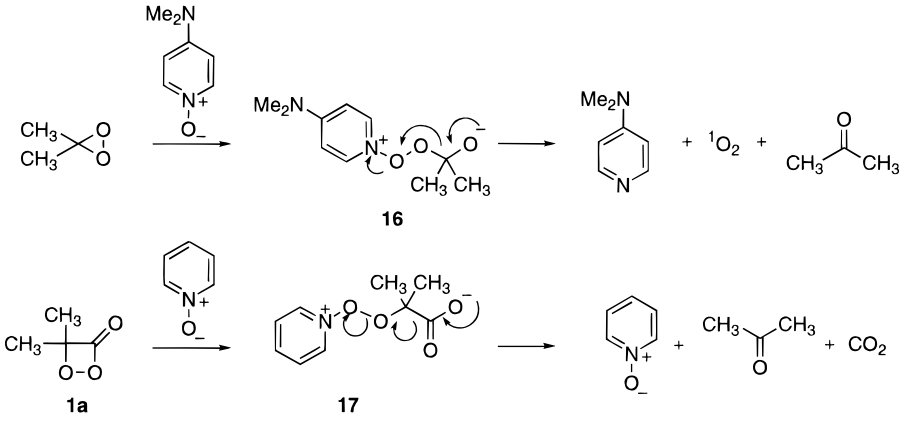
Scheme 4. Grob-Type Fragmentations of the Dipolar Intermediates 16 and 17 Produced in the S_N2 Reaction of Pyridine *N*-Oxides with Dimethyldioxirane and α-Peroxy Lactone 1a



latter case the postulated intermediary sulfenic esters were not further oxidized but reacted with excess thiophenol to give phenyl disulfide. As expected, the more electrophilic α-peroxy lactone **1a** is a stronger oxidant than 1,2-dioxetanes since it is capable to oxidize the sulfenic esters in the presence of excess thiol. This is analogous to the oxidation of thiols to sulfinic acids by the strong oxidant mCPBA.[16]

As for pyridine (entry 7), the type **I** adduct **9** could be observed at low temperature and was converted to pyridine *N*-oxide as major product (Scheme 3, path E), in contrast to its known behavior in basic aqueous media, in which Grob-type fragmentation and ring-opening by nucleophilic attack of hydroxide ion are observed.[17] For DABCO (entry 8) and pyridine *N*-oxide (entry 9), no intermediates or addition products could be detected. Instead, catalytic decarboxylation of the α-peroxy lactone **1a** to acetone was observed. Participation of the intermediate **I** is plausible in these cases in analogy to what is known for other peroxides. Thus, for DABCO a zwitterionic adduct was detected in the reaction with 1,2-dioxetanes,[2a] and the reaction with *tert*-butyl peroxy esters was also postulated to go through an S_N2 mechanism.[18] As for *N*-oxides, an adduct was also postulated as intermediate in the deoxygenation of *p*-(dimethylamino)pyridine *N*-oxide with dimethyldioxirane to afford singlet oxygen through the dipolar intermediate **16** (Scheme 4).[3c] Such a Grob-type fragmentation[19] of the dipolar intermediate **17** produced between the α-peroxy lactone and pyridine *N*-oxide (Scheme 4) would lead to acetone and CO_2 with release of the pyridine *N*-oxide nucleophile (Scheme 3, path D) and constitute catalytic decomposition of the α-peroxy lactone.

As for the aprotic sulfur nucleophiles (Table 1, entries 10−15), namely sulfides and sulfoxides, the oxygen transfer products, *i.e.* the corresponding sulfoxides and sulfones were obtained as major products. In the case of diphenyl sulfide, the primary oxidation product, diphenyl sulfoxide, was further oxidized in small amounts to diphenyl sulfone. Analogous to dimethyldioxirane,[20] the electrophilic character of the α-peroxy lactone **1a** as oxidant is confirmed by the low x_{SO} value of 0.16 in its reaction with thianthrene 5-oxide (entry 15). We propose the oxidation pathway through the intermediate **I** (Scheme 3, path E) in analogy to our findings for 3,3-disubstituted 1,2-dioxetanes and diphenyl sulfide,[2a] in which a similar dipolar adduct was detected. Additionally, a nucleophilic mechanism has been claimed for the reaction of dimethyl sulfide with benzoyl peroxide.[21]

For diisopropyl sulfoxylate (Table 1, entries 16 and 17), which is quantitatively oxidized to diisopropyl sulfite, the biphilic insertion mechanism (Scheme 3, path G) seems plausible since this nucleophile reacts readily even with the sterically severely hindered spiroadamantyl α-peroxy lactone **1b** (entry 17). Thermal decomposition of the labile sulfurane-type cycloadduct leads to diisopropyl sulfite and α-lactone (Scheme 3, path H). Indeed, sulfurane cycloadducts have been observed in the reaction of sulfoxylates with di- and trisubstituted 1,2-dioxetanes,[1d] and a concerted biphilic insertion mechanism has been postulated for this oxidation. In contrast, biphilic insertion is unlikely for the sulfides since *ab initio* calculations (RHF/6-31G**) performed on dimethyl sulfide and dimethyl sulfoxylate as model compounds show that the LUMO of dimethyl sulfide lies at higher energy than the one of dimethyl sulfoxylate, the difference is ca. 1.9 eV. Thus, the back-donation from the peroxide oxygen to the empty sulfur d orbital is quite probable for the sulfoxylate but unlikely for the sulfide, whose LUMO lies too high.

For the diazomethane and phosphorus nucleophiles, the cycloadducts **10**−**12** (Table 1, entries 18−21) and **13**−**15** (entries 23−28) were formed, but an open-chain intermediate **I** could not be observed for any of these nucleophiles even by low-temperature NMR-spectral monitoring. For the diazomethane derivatives (entries 18−22), two possible mechanisms may be considered, nucleophilic attack of the carbon atom on the peroxide bond or carbene formation from the diazoalkane with subsequent biphilic insertion. Since under the present reaction conditions (−20 °C), the diazomethane derivatives persist, no carbenes are formed, and the latter possibility is excluded. Thus, we propose a nucleophilic end-on attack along the peroxide bond axis in which steric effects determine the lower reactivity of the aromatic derivatives. After formation of the intermediate **I**, cyclization (Scheme 3, path F) or intramolecular S_N2 attack (path E) lead to the corresponding dioxolanones **10**−**12** or ketones and α-lactone. In contrast to our previous work on the reaction of diazoalkanes with 1,2-dioxetanes,[2d] for which cycloaddition occurred in high yields, in the present study oxidation of the diazoalkanes to the ketones is the major pathway. Thus, the oxygen

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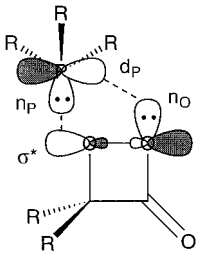

Figure 1. Favorable $n_P-\sigma^*$ and n_O-d_P HOMO/LUMO Interactions in the Transition State for the Biphilic Insertion of Trivalent Phosphorus Nucleophiles into the Peroxide Bond of α-Peroxy Lactones **1**

transfer propensity of the α-peroxy lactone **1a** toward diazoalkanes resembles the established reaction mode of dimethyldioxirane.[3b]

The dioxaphospholanones **13**−**15** are thermally labile and decomposed to the corresponding phosphorus oxides (*vide infra*) with release of the α-lactone (path H). Together with the cycloadducts, large amounts of phosphorus oxidation products (up to 70%) are formed already at −60 °C (Table 1, entries 23a−28a), conditions at which the adducts persist. The observed reactivity pattern of the trivalent phosphorus nucleophiles speaks for a stepwise S_N2 pathway to afford the phosphorus oxides through the zwitterionic intermediate (Scheme 3, path E) and through the additional insertion path G. However, the formation of the products through an end-on S_N2 attack is in disagreement with the observed reactivity with the adamantyl derivative **1b**, for which a linear S_N2 attack on the alkoxy-substituted oxygen along the peroxide bond axis is sterically impeded. As displayed by the measured rate constants (Table 2), the reactivity is determined by the nucleophilicity of the phosphorus partner rather than by its steric demand. In fact, the more nucleophilic but bulkier triphenylphosphine (entries 1 and 2) is about two orders of magnitude more reactive than the less nucleophilic but sterically less encumbered bicyclic phosphite (entries 3 and 4), which speaks for a nonlinear approach of the nucleophile on the peroxide bond. Similar trends, which have been observed for the cycloaddition of sterically encumbered tetrasubstituted 1,2-dioxetanes with phosphorus nucleophiles, have been explained in terms of a concerted insertion on the basis of isotopic and electronic substituent effects.[10a,b] Consequently, for our case, we suggest a concerted, biphilic insertion to afford the cycloadducts **13**−**15** (path G).

As for the geometry of the attack, while the absence of steric effects rules out the linear attack, the direct insertion of the phosphorus lone electron pair directly into the peroxide bond by a symmetrical, perpendicular attack must be discarded because of electrostatic repulsion between the phosphorus lone pair and the peroxide σ bond and oxygen lone pairs. As a compromise, we propose the transition state depicted in Figure 1, which minimizes the aforementioned effects and allows a secondary interaction between the empty d orbital of the phosphorus (d_P) and the oxygen lone pair (n_O) which ultimately leads to the cycloaddition. A comparison between the reaction rates in dichloromethane and acetonitrile (Table 2) shows only a nominal solvent polarity effect, which in principle supports the proposed concerted insertion process.[9c] However, the solvent effect is a composite one on the total reaction rate of two concurrent processes, namely, biphilic insertion and nucleophilic substitution, and definitive mechanistic conclusions are questionable.

A point of mechanistic interest is the fate of the α-lactone, the expected reduction product of the α-peroxy lactone **1** after oxygen transfer to the heteroatom nucleophile[4] (Scheme 3, path E). In the case of α-peroxy lactone **1a**, the intermediary α-lactone was efficiently trapped by methanol (entries 12, 14, and 19). In aprotic solvents we found low yields of the oligoester **2a**, the known oligomerization product of the α-lactone.[8] The low yield compared to the oxidized products we attribute to side reactions of the intermediary α-lactone or its dipolar valence isomer with the nucleophiles. Such side reactions are inhibited in methanol due to efficient trapping of the α-lactone (entries 12 and 14). In contrast, for the spiroadamantyl α-peroxy lactone **1b**, the main reduction product was adamantanone (entries 17 and 26−28). The α-lactone produced from the thermal decomposition of the labile cycloadducts (Scheme 3, path H) prefers to decarbonylate instead of oligomerizing due to steric effects. This behavior is in agreement with the known tendency of higher substituted α-lactones to yield the corresponding ketones through decarbonylation.[22]

In conclusion, the products obtained during the reaction of α-peroxy lactones **1** with a variety of heteroatom and carbon nucleophiles reveal the susceptibility of these electrophilic, strained cyclic peroxy esters toward S_N2 attack, a reactivity which the latter also displayed toward π nucleophiles.[4] Moreover, the α-peroxy lactones **1** show similar reaction modes than that of the related strained cyclic dioxiranes and 1,2-dioxetanes, although in their oxidizing strength they fall between dioxiranes (more reactive) and 1,2-dioxetanes (less reactive), as witnessed most effectively in the thiol reaction. The formation of the amine and thiol adducts **5**−**9** demonstrates that the nucleophilic attack occurs at the more electrophilic alkoxy oxygen atom, in spite of steric effects. Subsequently, the open-chain S_N2 adducts **I** and **I′** react through a variety of channels, namely addition (Scheme 3, paths A, B, and G), oxidation of the nucleophiles (path E), and catalytic Grob-type decarboxylation (path D). Furthermore, trivalent phosphorus nucleophiles and sulfoxylates also react through biphilic insertion (path G), in which the nucleophilicity rather than steric factors govern this cycloaddition.

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Supporting Information Available: The Experimental Section includes the synthesis and complete characterization of the products (7 pages). This material is contained in libraries on microfiche, immediately follows this article in the microfilm version of the journal, and can be ordered from the ACS; see any current masthead page for ordering information.

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