General Procedure for the Reaction of Cyclic Aminals with Isocyanates.[7a,8] A solution of 0.1 mol of butyl isocyanate (or phenyl isocyanate) in 30 mL of dry toluene was added dropwise to a solution of 0.1 mol of cyclic aminal in 20 mL of dry toluene. The reaction was exothermic and the rate of addition was adjusted in order to maintain the temperature below 30 °C. At the end of the addition the solution was stirred at room temperature until no more isocyanate was detected by IR spectroscopy (1–2 h). The solvent was removed on a rotary evaporator. In the case of reactions that provided a mixture of urea aminal and urea imine, every attempt to separate the components by conventional techniques (distillation, recrystallization, solvent extraction, and chromatography) was unsuccessful. The yields are reported in Tables I and III. The physical characteristics of the products are listed in Table VI.

Acknowledgment. We thank M. Sturny for assistance in the syntheses.

Registry No. **1a**, 31952-00-8; **1b**, 70231-94-6; **1c**, 124821-12-1; **1d**, 124821-13-2; **1e**, 124821-14-3; **1f**, 51461-66-6; **1g**, 61327-69-3; **3**, 124821-48-3; **4**, 70233-87-3; **7A**, 124821-15-4; **7B**, 124821-16-5; **7E**, 124821-19-8; **7F**, 124821-21-2; **7G**, 124821-23-4; **7H**, 124821-25-6; **7K**, 124821-29-0; **7L**, 124821-30-3; **7M**, 124821-31-4; **7N**, 124821-32-5; **8C**, 124821-17-6; **8D**, 124821-18-7; **8E**, 124821-20-1; **8F**, 124821-22-3; **8G**, 124821-24-5; **8H**, 124821-26-7; **8I**, 124821-27-8; **8J**, 124821-28-9; **9a**, 124821-33-6; **9b**, 75817-16-2; **9c**, 124821-34-7; **9d**, 42163-87-1; **10c**, 124821-35-8; **10d**, 42163-96-2; **11A**, 124821-36-9; **11B**, 124821-38-1; **11C**, 124821-40-5; **11D**, 75817-27-5; **11E**, 124821-42-7; **11F**, 124821-44-9; **11G**, 124821-46-1; **11H**, 124821-47-2; **12A**, 124821-37-0; **12B**, 124821-39-2; **12C**, 124821-41-6; **12D**, 75817-28-6; **12E**, 124821-43-8; **12F**, 124821-45-0; $MeNH(CH_2)_3NH_2$, 6291-84-5; $HOCH_2CH_2NH(CH_2)_3NH_2$, 4461-39-6; $NH_2(CH_2)_3NH_2$, 109-76-2; HCHO, 50-00-0; *i*-PrCHO, 78-84-2; PhCHO, 100-52-7; *p*-$NO_2C_6H_4CHO$, 555-16-8; $Me(CH_2)_3NCO$, 111-36-4; PhNCO, 103-71-9; $HCOC(CH_3)_3$, 630-19-3; $MeNHCH_2CH_2NH_2$, 109-81-9; $PhNHCH_2CH_2NH_2$, 5700-56-1; $OCN(CH_2)_6NCO$, 822-06-0; cyclohexanone, 108-94-1.

Supplementary Material Available: IR spectral data of aminals and of the reaction products of aminals with isocyanates (2 pages). Ordering information is given on any current masthead page.

Amine-Induced Reactions of Diacyl Peroxides

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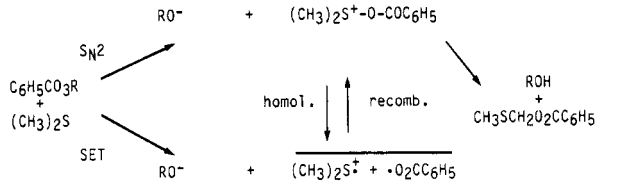
Received September 11, 1989

The decompositions of 3-chlorobenzoyl cyclobutylformyl peroxide (**3a**), and 3-chlorobenzoyl cyclopropylacetyl peroxide (**3b**) induced by 1-azabicyclo[2.2.2]octane (Q), N^1,N^1,N^4,N^4-tetramethyl-1,4-benzenediamine (W), 1,4-diazabicyclo[2.2.2]octane (DABCO), and *N,N*-dimethylaniline (DMA) were investigated. Peroxides **3** were selected for study because distinctive product patterns were expected from decompositions induced by the alternative S_N2 and SET pathways. Q and W were selected as amines likely to react by the S_N2 and SET pathways, respectively. Q reacted with **3** to give products characteristic of the intermediacy of an ion pair (general structure: $R_3NOCOC_4H_7^+ArCO_2^-$) formed by the S_N2 pathway, while W reacted with **3** to give rapid formation of the $C_4H_7CO_2$ radical, indicative of an SET pathway. Based on the results with Q and W, we interpret the results with DABCO and DMA to indicate that both induce the decomposition of **3** by the S_N2 pathway. Thus, peroxides **3** have been shown to be structurally sensitive to the modes of their induced decomposition, and are, potentially, mechanistic probes for ascertaining the mechanism of induced peroxide decomposition by closed-shell molecules.

Background and Introduction

Organic peroxides have varied applications ranging from the initiation of industrially useful free-radical polymerizations to their use in hair dye and acne medication formulations. Studies have shown that peroxides are carcinogenic and mutagenic.[1] For example, peroxide **3a** has been found to be marginally mutagenic in the *Salmonella* LT-2 and *B. subtilis* FB-13 tester strains.[1c] Little is known, however, about their mechanism of action. Pryor has pointed out that peroxides in vivo likely undergo bimolecularly assisted rupture of the O–O bond to initiate their decomposition.[2] Such induced decomposition of peroxides by odd-electron as well as closed-shell molecules is well known in peroxide chemistry. The mechanism by which closed-shell electron donors cause O–O bond rupture has received intensive study.[3-5] These reactions occur by

Scheme I



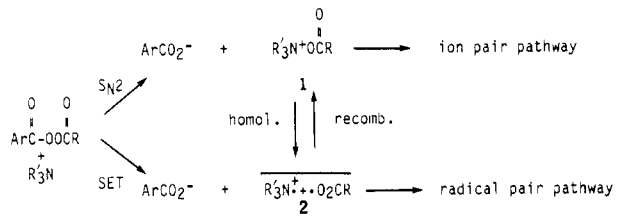
(1) (a) Fishbein, L.; Glamm, W. O.; Falk, H. L. *Chemical Mutagens*; Academic Press: New York, 1970; pp 269–73. (b) Kotin, P.; Falk, H. L. *Radiation Res. Suppl.* **1963**, *3*, 93–211. (c) Streips, U. N. Department of Microbiology and Immunology, University of Louisville, K. G. Taylor, unpublished work.

(2) Pryor, W. A. In *Free Radicals in Biology*; Pryor, W. A., Ed.; Academic Press: New York, 1976; Vol. 1, pp 1–49.

(3) Lead references: (a) Plesnicar, B. In *The Chemistry of Functional Groups, Peroxides*; Patai, S., Ed.; J. Wiley and Sons: New York, 1983; Chapter 17. (b) Oae, S.; Fujimori, K. In *The Chemistry of Functional Groups, Peroxides*; Patai, S., Ed.; J. Wiley and Sons: New York, 1983; Chapter 18. (c) Bouillon, G.; Carlo, L.; Schank, K. In *The Chemistry of the Functional Groups, Peroxides*; Patai, S., Ed.; J. Wiley and Sons: New York, 1983; Chapter 10. (d) Koenig, T. In *Free Radicals*; Kochi, J. K., Ed.; J. Wiley and Sons: New York, 1973; Chapter 3. (e) Martin, J. C. In *Free Radicals*; Kochi, J. K., Ed.; J. Wiley and Sons: New York, 1973; Vol. 2, Chapter 20.

0022-3263/90/1955-1779$02.50/0

Scheme II



mechanisms classed as either single-electron-transfer (SET) or two-electron-transfer (S_N2) processes, and distinguishing between these pathways is difficult. As Pryor and Hedrickson, Jr., have noted,[4b] neither acceleration of radical production, nor Hammett ρ values, nor rates of acceleration of peroxide decomposition, nor solvent polarity effects allow a distinction to be made. To this list Schuster[5a] would also add that the ^{18}O isotopic distribution in products from labeled peroxides can be ambiguous. Pryor and Hendrickson, Jr.,[4b] used deuterium-labeled nucleophiles and the associated β-deuterium kinetic isotope effects as a measurement for distinguishing the two pathways. They found that the reaction of dimethyl sulfide with dibenzoyl peroxide, a reaction previously characterized as S_N2,[6] gave $k_H/k_D = 0.88$, while the reaction of dimethyl sulfide with *tert*-butyl peroxybenzoate, a reaction characterized as SET,[4c] gave $k_H/k_D = 1.08$. Schuster and co-workers[5a] correlated the rate of reaction of phthaloyl peroxide with the one-electron oxidation potential of several π-electron donors.[7] In addition, using nanosecond laser spectroscopy, they observed the radical cation products of three excited state π-electron donors which reacted with phthaloyl peroxide. They concluded that all the electron donors studied reacted by the SET pathway.

Pryor and Hendrickson, Jr.,[4b,c] observed the formation of identical product classes from the S_N2-induced decomposition of dibenzoyl peroxide and the SET-induced decomposition of *tert*-butyl peroxybenzoate by dimethyl sulfide. (Methylthio)methyl benzoate was formed in high yield in both reactions, accompanied by high yields of benzoic acid (from dibenzoyl peroxide) and *tert*-butyl alcohol (from *tert*-butyl peroxybenzoate). Scheme I summarizes these results. The formation of the ester product from the decomposition of *tert*-butyl peroxybenzoate presumably results from the (exceptionally) efficient recombination reaction of benzoyloxyl radical (or benzoate ion) with the radical cation of dimethyl sulfide; the yield of free radicals by the SET pathway was only 2%.[4c] Thus, the efficient recombination of radical pairs can mask an SET-induced reaction. Also, efficient homolysis of an S_N2-produced intermediate could mask an S_N2-induced reaction, as has been the case with amine-induced reactions of diacyl peroxides.[3,8] For example, the accelerated decomposition of dibenzoyl peroxide by *N,N*-dimethylaniline has been characterized as both an SET reaction[9] and an S_N2 reaction[8,10] (Scheme II).

Table I. Recombination Reactions of Acyloxyl Radicals Thermally Generated from Symmetrical Diacyl Peroxides, $(RCO_2)_2$[a]

R	solvent	temp, °C	cage return,[b] %	ester yield,[c] %
C_6H_5	i-C_8H_{18}	80	4.6	3
CH_3	i-C_8H_{18}	80	38	15
c-C_4H_7	CCl_4	80	3.0	–
	$CHCl_3$	60	–	~0[d]
c-$C_3H_5CH_2$	CCl_4	45	0	–
	$CHCl_3$	40	–	~0[d]

[a] Taken from ref 3b unless noted otherwise. [b] Acyloxyl radical pair recombination, as measured by rate of ^{18}O scrambling in recovered labeled peroxide. [c] Ester produced by acyloxyl–alkyl radical-pair recombination. [d] Reference 12.

Table II. Recombination Reactions of Acyloxyl Radicals Thermally Generated from *tert*-Butylperoxy Esters, $RCO_2OC_4H_9$-t[a]

R	solvent	temp, °C	cage return,[b] %
C_6H_5	cumene	105.5	19
CH_3	cumene	105.5	42
i-C_3H_7	i-C_8H_{18}	103	0.3
	i-C_8H_{18}	50.6	0.5
t-C_4H_9	cumene	50.5	2.5

[a] Data taken from ref 3b. [b] Acyloxyl–*tert*-butoxyl radical-pair recombination as measured by rate of ^{18}O scrambling in recovered, labeled perester.

We believed that peroxides of appropriate structure would, in fact, produce product classes that reflected the reaction mechanism that produced them. As Tables I and II illustrate, aliphatic acyloxyl radicals larger than acetoxyl are very inefficient in cage recombination reactions, and this is because β-scission to give CO_2 and an alkyl radical is very fast. The failure to observe CIDNP effects attending ester formation from the decomposition of aliphatic diacylperoxides larger than acetoxy[13] has been taken as evidence that the decarboxylation of acyloxyl radicals proceeds at a rate faster than that required for singlet–triplet mixing ($>10^{10}$ s^{-1}).[3b,12,14] Even though ester formation from the thermal decomposition of these peroxides proceeds, in great majority, by an ion-pair pathway,[12] CIDNP effects would be expected to be observable from a radical-pair component of the reaction should that pathway be responsible for only a few percent of product. This expectation is based on the ready observation of CIDNP effects attending the formation of cyclobutyl 3-chlorobenzoate in the thermolysis of 3-chlorobenzoyl cyclobutaneformyl peroxide, a reaction which yields a typical array of radical-derived products in total yield of about

(4) (a) Pryor, W. A. In *Organic Free Radicals*; Pryor, W. A., Ed.; American Chemical Society: Washington, DC, 1978; pp 33–62. (b) Pryor, W. A.; Hendrickson, W. H., Jr. *J. Am. Chem. Soc.* **1975**, *97*, 1582–83. (c) Pryor, W. A.; Hendrickson, W. H., Jr. *J. Am. Chem. Soc.* **1975**, *97*, 1580–82.

(5) (a) Zupancic, J. J.; Horn, K. A.; Schuster, G. B. *J. Am. Chem. Soc.* **1980**, *102*, 5279–85 and references therein. (b) Schuster, G. B. *Acc. Chem. Res.* **1979**, *12*, 366–73.

(6) Pryor, W. A.; Bickley, H. T. *J. Org. Chem.* **1972**, *37*, 2885–93.

(7) For similar correlations of the reactions of nucleophiles in typical nucleophilic displacement reactions, see: (a) Banti, S.; Noyd, D. A. *J. Am. Chem. Soc.* **1973**, *95*, 8203–05. (b) Davis, R. E.; Suba, L.; Klimishin, P.; Carter, J. *J. Am. Chem. Soc.* **1966**, *91*, 104–07, and earlier work by Davis et al. (c) Edwards, J. O.; Pearson, R. G. *J. Am. Chem. Soc.* **1962**, *84*, 16–24.

(8) Hiatt, R. In *Organic Peroxides*; Swern, D., Ed.; J. Wiley and Sons: New York, 1970; Vol. 2, pp 867–75.

(9) (a) Graham, D. M.; Mesrobian, R. B. *Can. J. Chem.* **1963**, *41*, 2938–44. (b) Horner, L.; Anders, B. *Chem. Ber.* **1962**, *95*, 2470. (c) Filliatre, C.; Lalande, R.; Pometan, J.-P. *Bull. Soc. Chim. Fr.* **1975**, 1147–51.

(10) (a) Walling, C.; Indictor, N. *J. Am. Chem. Soc.* **1958**, *80*, 5814–18. (b) Fayadh, J. M.; Jessop, D. W.; Swan, G. A. *J. Chem. Soc. C* **1966**, 1605–07.

(11) Grossi, L.; Lusztyk, J.; Ingold, K. U. *J. Org. Chem.* **1985**, *50*, 5882–85. Photochemically generated benzoyloxyl radical decarboxylates 2 orders of magnitude, or more, faster.

(12) Taylor, K. G.; Govindan, C. K.; Kaelin, M. S. *J. Am. Chem. Soc.* **1979**, *101*, 2091–99.

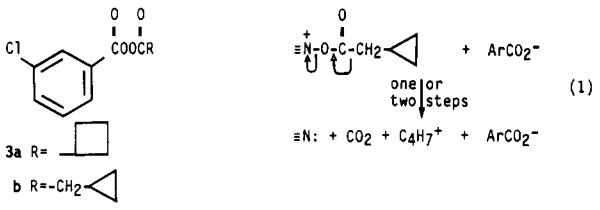
(13) Acetoxyl radical, thermally generated from diacetyl peroxide, decarboxylates with a rate constant of $\sim 6 \times 10^9$ s^{-1} (110 °C).[13] This is slow enough to permit singlet–triplet mixing of the acetoxyl–methyl radical pair which results in a CIDNP net effect (*E*, OCH_3) in the formation of methyl acetate. (a) Kaptein, R.; Brokken-Zijp, J.; de Kanter, F. J. J. *J. Am. Chem. Soc.* **1972**, *94*, 6280–87. (b) Braun, W. Rajbenbach, L.; Eirich, F. R. *J. Phys. Chem.* **1962**, *66*, 1591–95.

(14) Cooper, R. A.; Lawler, R. G.; Ward, H. R. *J. Am. Chem. Soc.* **1972**, *94*, 545–51.

5%.[12] Thus, the failure to observe net CIDNP signals attributable to acyloxyl–alkyl radical-pair recombination is reasonable circumstantial evidence for the short lifetime of such pairs. Falvey and Schuster[15] have estimated the rate of decarboxylation of photogenerated 9-methylfluoren-9-ylformyloxyl radical to be 1.8×10^{10} s^{-1}, a result compatible with the CIDNP-based conclusions concerning decarboxylation rates. We conclude that a radical pair **2** where R = primary, secondary alkyl (Scheme II) formed by the SET path would not be expected to cross over efficiently to the "ion-pair pathway" by a recombination reaction, and, consequently, should give products which follow from its mechanistic origin.

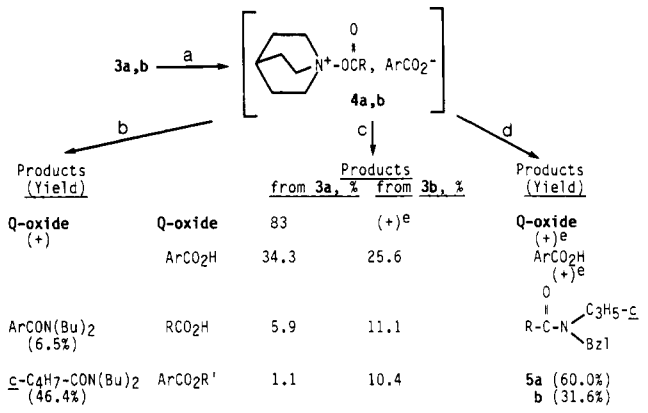
Crossover from the S_N2 pathway by homolysis of cation **1** (Scheme II) is possible. Certain cations **1** prepared by reaction of a tertiary amine oxide with a carboxylic acid anhydride do induce the polymerization of styrene and/or acrylic esters.[16,17] But, the reactions of ion pairs incorporating **1** vary significantly with the nature of R, R′, anion, and solvent,[17] and formation of radicals from **1**, is, typically, a low-yield process.[17] Thus, the selection of an appropriate diacyl peroxide for reaction with tertiary amines, i.e., a peroxide which would give an unstable acyloxyl radical via SET, should permit dilineation of the reaction pathway (SET or S_N2) by characterization of the products.

Accordingly, we have examined the decomposition of peroxides **3a,b**[12] induced by the following tertiary amines: quinuclidine (Q), *N*¹,*N*¹,*N*⁴,*N*⁴-tetramethyl-1,4-benzenediamine (W), 1,4-diazabicyclo[2.2.2.]octane (DABCO), and *N*,*N*-dimethylaniline (DMA). We selected peroxides **3** because the aliphatic acyloxyl radicals derived therefrom should, judging from their inefficiency in cage return and ester forming reactions (Table I), decarboxylate at a rate which would compete very favorably with the recombination reaction (scheme II).[18] Also, we anticipated that, with an electron donating R group in **1** (R = C_4H_7), a heterolytic decomposition process producing amine, CO_2, and the $C_4H_7^+$ isomeric carbocations[12] (captured as $ArCO_2C_4H_7$) might contribute to a product array distinctive for the presence of such an intermediate (reaction 1).



We selected amines Q and W as examples which should react with **3** by the S_N2 and SET pathways, respectively. The high ionization potential (8.02 eV)[20] and oxidation potential (0.96–1.1 V)[21] of Q would seem to preclude an SET reaction pathway for it, and W ($E_{1/2}$ = 0.12 V) produces a stable radical cation—a Wurster salt—upon (facile) electrochemical oxidation.[22] DABCO also produces a radical cation upon oxidation (IP = 7.52 eV;[21] $E_{1/2}$ = 0.6 V[22]), the oxidized N being stabilized by through-bond conjugation with the other bridgehead N.[23] Thus, DABCO, in contrast to Q, might be a candidate for SET-induced decomposition of **3**. Complete understanding of the mechanism of the DMA-induced reaction of benzoyl peroxide is lacking,[8-10,24] and we hoped its reactions with **3** would shed additional light on the problem.

Scheme III[a]



[a] (a) 1.0 g of **3**, 20 mL of $CHCl_3$; −40 °C; add 1.0 equiv of Q; (b) warm to room temperature; 24 h; add excess *N*,*N*-di-*n*-butylamine; (c) warm to room temperature; 24 h; 5% $NaHCO_3$ quench; separate acids, bases, neutrals; (d) −30 °C; add benzylcyclopropylamine; (e) product identified, but yield not determined.

Results and Discussion

Scheme III summarizes the product analyses of the reaction of peroxides **3** with Q. Upon admixture of Q at −40 °C with a $CHCl_3$ (or $CDCl_3$) solution of **3a**, the peroxide rapidly disappeared (see the NMR study below). The reaction was allowed to warm and was then treated with excess *N*,*N*-di-*n*-butylamine; quinuclidine *N*-oxide (Q-oxide), *N*,*N*-di-*n*-butyl-3-chlorobenzamide, and *N*,*N*-di-*n*-butylcyclobutanecarboxamide were obtained in the indicated yields (reaction b). This was indicative of the initial formation of ion pair **4a** followed by acylation of 3-chlorobenzoate anion to produce the *N*-oxide and the corresponding mixed carboxylic anhydride. Analogous results had been obtained by Huisgen and Kolbeck from the reaction of benzoquinuclidine with dibenzoyl peroxide.[25] Aqueous bicarbonate workup (reaction c) facilitated analysis of acid and ester formation. Indeed, **4a** and **4b** produced the trio of C_4H_7 3-chlorobenzoates[26] ($ArCO_2R'$ in Scheme III and later schemes) in an isomer ratio typical for the intermediacy of C_4H_7 carbocations: cyclobutyl–cyclopropylmethyl–3-butenyl = 1.0:2.1:0.4. Given the relative rates of ionization of cyclobutyl and cyclopropyl substrates,[12] it would be expected that **4b**

(15) Falvey, D. E.; Schuster, G. B. *J. Am. Chem. Soc.* **1986**, *108*, 7419–20.

(16) (a) Horner, L.; Brüggeman, H.; Knap, K. H. *Justus Liebigs Ann. Chem.* **1959**, *626*, 1–19. (b) Boekelheide, V.; Harrington, D. L. *Chem. Ind. (London)* **1955**, 1423.

(17) (a) Oae, S.; Asai, N.; Fujimori, K. *Bull. Chem. Soc. Jpn.* **1979**, *52*, 2409–12. (b) Huisgen, R.; Bayerlein, F.; Heydcamp, W. *Chem. Ber.* **1959**, *92*, 3223–43.

(18) Skell and co-workers[19] have reported that the relative rates of decarboxylation of $RCO_2^•$ are *t*-Bu < *i*-Pr < *n*-Pr, and attribute this reactivity order to a steric retardation of the necessary widening of the OCO angle along the reaction coordinate. Data on the efficiency of the cage return reaction shown in Table II seem to support these results. However, in the $RCO_2^•$ formed from **3**, steric crowding should be low or absent, and decarboxylation should be rapid, as seems to be the case.

(19) (a) May, D. D.; Skell, P. S. *J. Am. Chem. Soc.* **1982**, *104*, 4500–02. (b) Peyerimhoff, S. D.; Skell, P. S.; May, D. D.; Buenker, R. J. *J. Am. Chem. Soc.* **1982**, *104*, 4515–20. (c) Skell, P. S.; May, D. D. *J. Am. Chem. Soc.* **1983**, *105*, 3999–4008.

(20) Bischoff, P.; Hashmall, J. A.; Heilbronner, E.; Hornung, V. *Tetrahedron Lett.* **1969**, 4025–28.

(21) Chow, Y. L.; Danen, W. C.; Nelsen, S. F.; Rosenblatt, D. H. *Chem. Rev.* **1978**, *78*, 243–84. This article contains an extensive collection of oxidation potentials of aliphatic amines.

(22) Dvorak, V.; Nemec, I.; Zyken, J. *Microchem. J.* **1967**, *12*, 350–70.

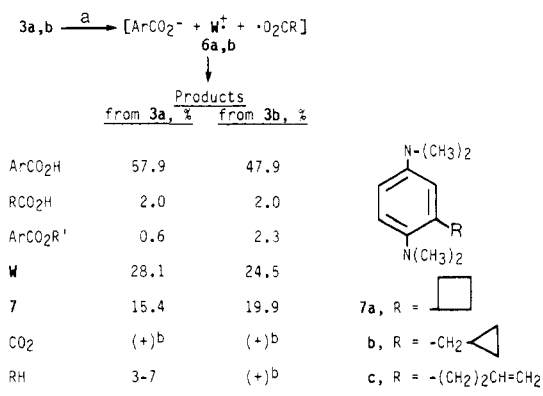
(23) Heilbronner, E.; Muszkat, K. A. *J. Am. Chem. Soc.* **1970**, *92*, 3818–21.

(24) (a) Huisgen, R.; Heydkamp, W.; Bayerlein, F. *Chem. Ber.* **1960**, *93*, 363–74. (b) Roy, R. B.; Swan, G. A. *Chem. Commun.* **1966**, 427–28.

(25) Huisgen, R.; Kolbeck, W. *Tetrahedron Lett.* **1965**, 783–87.

(26) The extensive chemistry of the heteroaromatic *N*-oxide relatives of **4** has been reviewed: Oae, S.; Ogino, K. *Heterocycles* **1977**, *6*, 583–675.

Scheme IV[a]



[a] (a) 1.0 g of 3, 20 mL of $CHCl_3$; −55 °C; add 1.0 equiv of W; (b) compound identified, but yield not determined.

should yield more ester than **4a**, and this was observed. We found that ion pairs **4** could be intercepted directly by the introduction of benzylcyclopropylamine into the reaction while it was maintained at low temperature (reaction d). This gave amides **5** in the yields indicated in Scheme III. 3-Chlorobenzoic acid was also isolated, but the corresponding 3-chlorobenzamide derivative was *not* formed under these conditions.

^1H NMR spectroscopy at low temperatures was used to monitor reaction progress. In these cases a 2–4-fold excess of amine was used to bring the decomposition of **3** to completion rapidly. Under the conditions of 4-fold excess of Q, **3a** was converted to **4a** within 30 min at −40 °C. This was evidenced by the disappearance of the α C–H (m, δ 3.36) and aromatic signals of **3a** (key signal: H4 at δ 7.60), the appearance of the α C–H signal of **4a** (m, δ 3.10), and the distinctive resonances of 3-chlorobenzoate anion (H2, δ 7.8; H4,5, 7.1; H6, 7.7). Accompanying the α C–H signal of **42** were the NCH_2 and $NCCH_2$ signals of **4a** at δ 3.2 and 1.9, respectively. These last signals were downfield from the corresponding signals of Q (δ 2.9 and 1.6) and different from those of Q-oxide (δ 3.4 and 1.8). The integration of the signals attributable to **4a** was consistent with the assignments made. Attending the addition of benzylcyclopropylamine to such reactions was the disappearance of signals assigned to **4a**, and the appearance of signals distinctive for Q-oxide and amide **5a** (NCH_2, δ 4.45; α CH, 3.38; CH_2CH_2, 0.7).

The chemistry observed for the reaction of peroxide **3b** with Q was analogous to that described above. While we did not make a detailed comparison, ion pair **4b** seemed less stable than **4a**. Thus, the ^1H NMR spectrum of **3b** reacting with 1 equiv of Q at −20 °C revealed product signals attributable to Q-oxide and mixed anhydride ($COCH_2$, d, δ 2.41, $J \sim 6.6$ Hz, tentative). A transient, partially overlapped doublet ($J \sim 6$ Hz) was observed at δ 2.2 at low temperature. By analogy with **4a**, this would be an appropriate chemical shift for the CH_2 of **4b**, but a definitive assignment could not be made.

The above evidence supports an S_N2 reaction pathway involving the initial formation of ion pair **4** followed by product formation resulting from unimolecular and bimolecular reactions of the ion pair.

Scheme IV summarizes the results of the decomposition of **3** by W, a reaction dramatically different from that between **3** and Q. Immediately upon the addition of W to **3a** at −55 °C to −40 °C, the characteristic blue color of the Wurster salt, $W^{\bullet+}$, appeared,[27] and vigorous evolution of CO_2 commenced (confirmed by $BaCO_3$ precipitation).

Monitoring the reaction at −40 to −20 °C by ^1H NMR spectroscopy showed the disappearance of **3a** (loss of H4 signal at δ 7.60) by the time the first spectrum was recorded (5–10 min). Also, the aromatic signal of W (δ 6.84) disappeared immediately, and the $N-CH_3$ signal (δ 2.84) was broadened even when excess W was employed. This phenomenon is attributable to a redox exchange between W and $W^{\bullet+}$,[28] and this exchange has been observed previously by NMR spectroscopy.[29] The signal for cyclobutane at δ 1.95 appeared immediately, along with that of 3-chlorobenzoic acid. In well-resolved spectra the cyclobutane signal was seen as a "doublet" with a peak separation of approximately 0.01 ppm. We attributed this to the presence of C_4H_7D arising from abstraction of D from the solvent $CDCl_3$. A ^2H NMR spectrum of the crude reaction mixture confirmed the presence of a deuterated compound having the anticipated chemical shift. Upon warming to room temperature the aromatic signal of W reappeared, and the NCH_3 signal sharpened. This was accompanied by the appearance of the characteristic aromatic (δ 7.0) and NCH_3 (δ 2.9 and 2.6) signals of **7a**. Given the absence of C_4H_7-containing isomers of **7a**, this product is formed by a reaction of cyclobutyl radical with $W^{\bullet+}$ or W (see below). The late appearance of the signals for **7a** may indicate that **7a** is also involved in a redox exchange reaction which generates $\mathbf{7a}^{\bullet+}$.[30]

Peroxide **3b** reacted with W in an analogous fashion. Both peroxides gave very low yields of ester, *and* of other products (e.g., acid) containing the RCO group. In reactions employing equivalent amounts of amine and peroxide it is difficult to rule out ester formation by way of the slow thermolysis of residual peroxide. However, the quantitative results are corrected for the presence of esters in the starting peroxide. Thus, we believe that the esters do arise from N–O bond formation and subsequent heterolysis during the reaction of W with **3**. The interesting feature of the reaction of **3b** is the isolation of the isomeric products **7b,c**. This result establishes the process leading to products **7** as a recombination reaction between $W^{\bullet+}$ and C_4H_7 radical, and not an alkylation of W (or WH^+) by C_4H_7 radical. We have studied the radical alkylation of faster reacting aromatics, such as quinoxaline and 4-cyanopyridine,[31] with C_4H_7 radical generated from bis(cyclopropylacetyl) peroxide and have found that the alkylated products contained 3-butenyl groups exclusively.[32] Thus, the radical alkylation of closed-shell aromatic compounds is not fast enough to trap cyclopropylmethyl radical before ring opening is completed. The reaction producing **7b,c** must, therefore, be faster, and a cage recombination reaction has the requisite velocity. Using the ratio of **7b** to **7c** (16.3%:3.6%) and the rate of ring opening of cyclo-

(27) The presence of $W^{\bullet+}$ was confirmed by epr spectroscopy.

(28) Kowert, B. A.; Marcoux, L.; Bard, A. J. *J. Am. Chem. Soc.* **1972**, *94*, 5538–50.

(29) Johnson, C. S., Jr. *J. Chem. Phys.* **1963**, *39*, 2111–14.

(30) The appearance of the NMR signal for cyclobutane was accompanied by the appearance of two *singlets* at δ 2.16 and 3.78. Since the reaction of W with both **3a** and **3b** produced the same set, the signals must arise from a reaction product of W. These signals remained in the spectrum at temperatures up to −20 °C, but then disappeared simultaneously on further warming as the signals for **7a** (or **7b,c**) appeared, and sharpened. The chemical shifts suggest the presence of $(CH_3)_2N$-alkyl, and $(CH_3)_2{}^+N=$ groups, respectively. We believe the pair of signals are those of an unstable reaction *product*, perhaps one that decays to **7a** (or **7b,c**), or perhaps an *ipso* substitution product resulting from the recombination of $W^{\bullet+}$ and cyclobutyl or some other radical.

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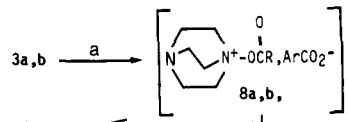
(32) Taylor, K. G.; Tso, S. Joint Central and Great Lakes Regional American Chemical Society Meeting, Dayton, OH, May 1981; *Abstract* ORGN 245, and unpublished results.

Scheme V[a]



Products (Yield)		Products from 3a, %	Products from 3b, %	Products (Yield)
DABCO-oxide (+)[e]	DABCO-oxide	(+)[e]	(+)[e]	DABCO-oxide (+)[e]
	$ArCO_2H$	36.8	33.9	
$ArCON(Bu)_2$ (8.9%)	RCO_2H	24.6	10.9	**5a** (56%) **5b** (39%)
	$ArCO_2R'$	2.2	4.9	
$c\text{-}C_4H_7\text{-}CON(Bu)_2$ (1.3%)	CH_2O[f]	23.2	19.9	
	piperazine[g]	(+)	(+)	

[a] (a) 1.0 g of **3**, 20 mL of $CHCl_3$; −40 °C; add 1.0 equiv of DABCO; (b) warm to room temperature; 24 h; add excess *N,N*-di-*n*-butylamine; (c) warm to room temperature; 24 h; 5% $NaHCO_3$ quench; separate acids, bases, neutrals, water soluble compounds; (d) −20 °C; add benzylcyclopropylamine; (e) product identified, but yield not determined; (f) isolated as the 2,4-dinitrophenylhydrazone derivative; (g) identified as the N^1,N^4-dibenzoyl derivative.

propylmethyl radical at −20 °C (1.2×10^7 s^{-1}),[33] and assuming equal rates of reaction of $W^{\bullet+}$ with the isomeric C_4H_7 radicals, we estimate a recombination rate constant at −20 °C of 1.1×10^8 L mol^{-1} s^{-1}.[31a] Also, a volatile product, which displayed ^1H NMR signals at δ 0.94 (d, J = 6.4 Hz) and 0.54 (m), was tentatively assigned the structure of methylcyclopropane (CH_3 and methine H signals).[34]

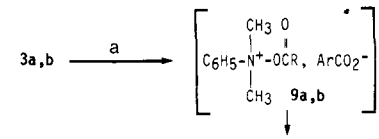
The results indicate that the reaction of W with **3** rapidly produces acyloxyl radicals even at temperatures down to −55 °C. W induces the decomposition of **3** considerably faster than does Q. But W is methylated by dimethyl sulfate in $CDCl_3$ by a second-order reaction with a $t_{1/2}$ of 271 s (29.1 °C), conditions under which the rate of methylation of Q is too fast to measure. Therefore, it is unlikely that the acyloxyl radicals are produced by homolysis of the N–O bond of an S_N2-produced intermediate. Thus, we believe that W reacts with **3** by an SET mechanism which rapidly, if not directly, produces a species such as **6**.

Scheme V summarizes the product analyses of the reactions of peroxides **3** with DABCO. The results are similar to those obtained from the reactions of **3** with Q, with an important exception. The yields of amides produced after warming and dibutylamine treatment (reaction sequence a + b, Scheme V) are lower in this case. We attribute this to a Grob-type fragmentation of intermediate **8a**, which competes with nucleophilic attack of *m*-chlorobenzoate on **8a**. Evidence for this was obtained from reaction sequence a + c (Scheme V): formaldehyde and piperazine were isolated, a result also obtained by Huisgen and Kolbeck[25] from the reaction of dibenzoyl peroxide and DABCO. Ion pairs **8** were intercepted at low temperatures by the addition of benzylcyclopropylamine (reaction sequence a + c, Scheme V).

The reaction of **3a** with DABCO was also monitored at low temperatures using ^1H NMR spectroscopy. A spectrum taken 5 min after mixing equivalent amounts of **3a** and DABCO at −20 °C revealed the formation of 3-chlorobenzoate ion. Also, there appeared a pair of "triplets" ($J \sim 6$ Hz), of equal integral, centered at δ 3.27 and 3.18, downfield from the signal of unreacted DABCO (δ 2.80). These signals are assigned to the protons at positions 2 and 3, respectively, of **8a**. In the presence of a 4-fold excess of DABCO, peroxide **3a** was completely converted to **8a** within 30 min at −40 °C. The addition of benzylcyclopropylamine to this reaction resulted in the appearance of the signals of **5a** and of DABCO-oxide (δ 3.31 and 3.11).[35] Low-temperature ^1H NMR studies of **3b** and DABCO gave results similar to those obtained with **3b** and Q.

All the results indicate that **3** reacts with DABCO by the S_N2 pathway.

Scheme VI[a]



Products from 3a, %	Products from 3b, %
$ArCO_2H$ 24.6	50.0
RCO_2H' 36.8	
$ArCO_2R'$ 10.4	9.2-22.4
$C_6H_5N(CH_3)_2$ 8.5[b]	17.5[b]
$C_6H_5NHCH_3$ 19.6	12.4
$C_6H_5N(CH_3)COR$(**10**) 13.0-15.0	6.0
$C_6H_5N(CH_3)CO_2R$(**11**) 1.5-2.4	1.5
CH_2O (+)[c]	(+)[c]
RH[d] 23±3	nd

[a] (a) 1.0 g of **3**, 20 mL of $CHCl_3$; −40 °C; add 1.0 equiv of DMA; warm to room temperature; or −10 °C; add DMA; −10 to 0 °C, 24 h; (b) recovered; GC determination; (c) product identified, but yield not determined; (d) cyclobutane; measured as percentage of the total integral of cyclobutyl protons in NMR spectra of crude reaction mixtures maintained at 0 °C or below.

As expected,[8-10,24] the reactions of **3** with DMA (IP = 7.14 eV;[36] $E_{1/2}$ = 0.68 V[22]) gave a complex array of products. Most of these are summarized in Scheme VI. When **3a** and DMA were mixed at −30 °C, a bright yellow solution formed, slow evolution of CO_2 commenced, and NMR monitoring showed slow disappearance of **3**. At −10 °C, cyclobutane (δ 1.96, isotopic doublet) formation was evidenced after 10-min reaction. The half-life of **3a** at −10 °C was approximately 40 min, by which time signals attributable to 3-chlorobenzoic acid (H4, doublet at δ 7.31, $J \sim 7$ Hz, slightly upfield from the analogous H of **3a**), *N*-methylaniline (NCH_3 at δ 2.95, slightly upfield from $N(CH_3)_2$), $C_6H_5N(CH_3)COC_4H_9$ (**10a**) (NCH_3 at δ 3.17; CH_2 at 1.67), and [4,4′-bis(dimethylamino)diphenyl]methane (**12**) (CH_2 at δ 3.41) could be seen in the spectrum. *N*-Methylaniline, **10a**, and **12** are distinctive products of the Polonovski demethylation reaction,[17] a reaction considered to proceed through an intermediate such as **9**. Additional products which arise by this route are the carboxylic acids and formaldehyde (Scheme VI). We take as further evi-

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(34) Crawford, R. J.; Erickson, G. L. *J. Am. Chem. Soc.* **1967**, *89*, 3907–08.

(35) The downfield signals of DABCO-oxide showed some dependence of chemical shift on temperature and concentration of 3-chlorobenzoic acid. At room temperature the DABCO-oxide signals were seen at δ 3.38 and 3.10. The differences in shifts of the signals of **8a** and DABCO-oxide are small but reproducible.

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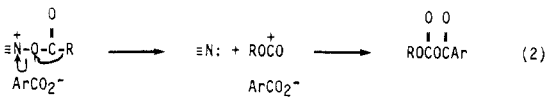
Table III. Hypothetical ΔG Values for Reactions of Peroxides with Nucleophiles Calculated from E_{red} and E_{ox} Data

peroxide	(E_{red}, V)	nucleophile	(E_{ox}, V)[a]	ΔG, kcal mol^{-1}	mechanism
dibenzoyl	(−0.16)[b]	$(CH_3)_2S$	(1.26)[c]	25.4	S_N2[d]
3	(−0.15)[e]	Q	(1.0)[f]	18.5	S_N2
3	(−0.15)	DMA	(0.7)[f]	11.5	S_N2
3	(−0.15)	DABCO	(0.60)[g]	9.2	S_N2
TBP[h]	(−0.9)[i]	$(CH_3)_2S$	(1.26)	8.3	SET[d]
3	(−0.15)	W[g]	(0.1–0.05)	−1.4 to −2.5	SET

[a] All determined vs Ag/Ag$^+$ using Pt electrodes. [b] $E_{1/2}$ vs SCE in C_2H_5OH/C_6H_6; ref 42. [c] Reference 36. [d] Reference 4c. [e] Estimated from data of ref 42. [f] Ref 21. [g] Ref 22. [h] *tert*-Butyl peroxybenzoate. [i] $E_{1/2}$ vs SCE; ref 43.

dence of formation of intermediate **9** the production, in significant yield, of 3-chlorobenzoate esters, formed via reaction 1 (see above).

A unique reaction product is seen in urethanes **11**. Presumably, these substances are formed by reaction of *N*-methylaniline with carbonic anhydrides, the latter produced by a version of the Leffler "carboxy inversion reaction"[12] (see reaction 2). The reaction of **3** with DMA



produced little or no 2-hydroxy-*N*,*N*-dimethylaniline derivatives. Such products are produced from intermediates such as **9** by an intramolecular rearrangement.[17a] But this reaction path competes poorly with the Polonovski and other reactions in solvents of low polarity,[17] so the absence of such products in the present case cannot be taken as evidence against the intermediacy of **9**.

The results indicate that **9** is formed in a yield much too high to be attributable to a pathway involving SET followed by recombination as outlined in Scheme II; thus, the S_N2 pathway is indicated. Cyclobutane formation, therefore, must result from decarboxylation of the cyclobutylformyloxyl radical produced by homolysis of the N–O bond of **9a**. Competing homolysis and heterolysis reactions of the N–O bond of **9** finds abundant analogy in the heterolysis and homolysis of the O–O bond of peroxides.[12]

We conclude from the above that peroxides **3** give products which reflect their mechanism of origin. Further, the results indicate that Q, DABCO, and DMA react with **3** by an S_N2 mechanism, while W induces the decomposition of **3** by an SET process.

Both the S_N2 and SET reactions are single-electron-transfer processes.[38] The differentiating mechanistic feature is that in S_N2 reactions, the single-electron shift occurs concomitantly with bond interchange between nucleophile and electrophile (donor (D) and acceptor (A)), while in SET reactions, the electron shift precedes bond interchange. The former process produces D^+–D^- molecules; the latter produces $D^{\bullet+}$ and $A^{\bullet-}$ species. Factors favoring the SET process in the competition between these two pathways are (1) a strong D–A interaction; (2) steric hindrance between D and A; (3) a weak D–A bond; and (4) radical delocalization in $D^{\bullet+}$ and/or $A^{\bullet-}$.[38b,c] In the present case, steric differences among the amines (D) are expected to be a minor factor in reactivity differences. Further, given the high lability of the N^+–O bond in $\equiv N^+$–O–acyl species in general, we believe differences in N–O bond strengths will be a minor factor in the present case, perhaps manifesting themselves more apparently in the decomposition of the species once formed. The strength of donor–acceptor interactions can be gauged from the difference of the vertical ionization potential (donor) and electron affinity (acceptor) of the D, A pair, and this is a prime factor governing S_N2–SET competition.[38c] If these differences are gauged using oxidation and reduction potentials, i.e., using potentials obtained under conditions much closer to adiabatic (polarography, cyclic voltammetry), then the fourth factor noted above, namely radical delocalization, should be reflected in the value of the potential, more faithfully than from gas-phase ionization potentials.[39] Indeed, the ΔG for electron transfer can be estimated from solution phase oxidation and reduction potentials of D and A, respectively.[40] A high exergonicity of this energy change has been related to a low $\Delta G^{\ddagger}$ of electron transfer between D and A[40,41] (see eq 3). Such

$$\Delta G \approx E(D^+/D) - E(A/A^-) \quad (3)$$

ΔG values for the reactions of three peroxides with amine and sulfur nucleophiles are collected in Table III. Special care must be exercised in interpreting the ΔG–$\Delta G^{\ddagger}$ relationship in the case of irreversible SET reactions such as would be encountered in the present cases,[41] but the data collected in Table III are suggestive of a predictive value for calculated ΔG values. From the data therein it appears that a nucleophile-dependent ΔG might be found below which the SET mechanism operates, and above which the S_N2 mechanism operates.

Experimental Section

NMR spectra were recorded on Varian XL-300 and EM-390 spectrometers. Chemical shifts are reported as δ TMS for ^1H and ^{13}C NMR spectra. Mass spectra were obtained at the Midwest Mass Spectrometry Center, University of Nebraska—Lincoln, and at the Department of Pharmacology and Toxicology of the University of Louisville. Elemental analyses were done by Midwest Microlabs, Inc., Indianapolis, IN. VPC analyses were performed on a Varian 3700 research chromatograph with flame ionization detector as described in ref 12. The three 6 ft × 0.125 in. stainless steel tubing columns used for VPC analyses were 15% DEGS on chrom W (AW and DMCS), 5% carbowax on chrom W (AW and DMCS), and 5% SE-30 on anachrom ABS.

Peroxides **3**, and the C_4H_7 aroyl esters, and *N*,*N*-di-*n*-butyl aroyl and alkanoyl amides which were used as identifying standards were prepared, characterized, and quantitated as described in ref 12. Amines Q, W, DABCO, DMA, and *N*-methylaniline were obtained from Aldrich Chemical Co. They were purified by recommended methods prior to use.

1-Azabicyclo[2.2.2]octane *N*-Oxide (Q-oxide) and 1,4-Diazabicyclo[2.2.2]octane *N*-Oxide (DABCO-oxide). These

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two *N*-oxides were prepared by stirring the corresponding amines in methanol with excess 30% hydrogen peroxide for 48 h, according to the method of Huisgen et al.[17b] The excess hydrogen peroxide was carefully destroyed with platinum black, the solution was filtered to remove the platinum black, and the solvent was distilled in vacuo to obtain white, hygroscopic crystals; Q-oxide (hygroscopic) (lit.[44a] mp about 110 °C, hygroscopic); DABCO-oxide mp 119–21 °C (lit.[45] mp 121–123 °C); ^{1}H NMR ($CDCl_3$) of Q δ 2.90 (m, 6 H, NCH_2), 1.82 (m, 1 H, CH), 1.62 (m, 6 H, CH_2); of Q-oxide δ 3.6 (m, 1 H, CH?), 3.4 (t, 6 H, CH_2), 1.8 (t, 6 H, CH_2) (lit.[44] reports δ CH_2 at 3.4 and 2.0, respectively); ^{13}C NMR ($CDCl_3$) δ 62.37 (CH_2), 26.05 (CH_2), 19.58 (CH); ^{1}H NMR of DABCO-oxide ($CDCl_3$) δ 3.35 (t, CH_2), 3.18 (t, CH_2), integrals equal.

***N*-Benzyl-*N*-cyclopropylcyclobutanecarboxamide (5a).** Amide **5a** was prepared by the treatment of 1.0 g of cyclobutanecarbonyl chloride in benzene with 1.2 mol equiv of benzylcyclopropanamine. The resulting solution was heated in a water bath for 10 min. The crude product, obtained in the benzene layer, was washed with 1 N HCl, 5% $NaHCO_3$, and distilled water. After drying (Na_2SO_4), purification of the amide, an oil, was carried out by silica gel column chromatography followed by vacuum distillation: ^{1}H NMR ($CDCl_3$) δ 7.8 (5 H, m, C_6H_5), 4.45 (2 H, s, NCH_2), 3.38 (1 H, quint, CHCO), 1.7–0.9 (7 H, m, $(CH_2)_3$ plus NCH), 0.46 (4 H, m, cyclopropyl CH_2); mass calcd for $C_{15}H_{19}NO$ ($M^{\bullet+}$) 229.147, found ($M^{\bullet+}$) 229.147.

Amides 5b, *N*-Benzyl-*N*-cyclopropyl-3-chlorobenzamide, *N*-methyl-*N*-phenylcyclobutanecarboxamide (10a), and *N*-methyl-*N*-phenylcyclopropylacetamide (10b) were prepared and characterized in a similar manner: ^{1}H NMR of **5b** ($CDCl_3$) key resonances δ 4.45 (NCH_2), 1.95 (CH_2CO); of **10a** ($CDCl_3$) δ 7.29, 7.19 and 7.05 (2 H, 1 H, and 2 H, *m*-, *p*-, and *o*-H's of NC_6H_5), 3.17 (3 H, s, NCH_3), 2.98 (1 H, m, CHCO), 2.29 (2 H, m, CH_2), 1.67 (4 H, m, CH_2's); of **10b** ($CDCl_3$) δ 7.18, 7.12 and 6.97 (2 H, 1 H, and 2 H, *m*-, *p*-, and *o*-H's of NC_6H_5), 3.17 (3 H, s, NCH_3), 1.96 (2 H, d, J = 6.3 Hz, CH_2CO), 1.02 (1 H, m, CH), 0.44 (2 H, m, CH_2), ~0 (m under TMS, CH_2(?)); mass calcd for $C_{12}H_{15}NO$ (**10**) ($M^{\bullet+}$) 189.116, found ($M^{\bullet+}$) 189.079.

***N*-Methyl-*N*-phenylcyclobutyl- and -cyclopropylurethanes (11).** Urethanes 11 were prepared by reacting the corresponding alkyl chloroformate[12] with an excess (1:3) of *N*-methylaniline. Characterization included GC–MS and NMR spectroscopy: ^{1}H NMR ($CDCl_3$) of **11a** δ 7.5–7.2 (5 H, m, NC_6H_5), 5.10 (1 H, quint, CHO), 3.34 (3 H, s, NCH_3), 2.38 (2 H, m, CH_2), 2.10 (2 H, m, CH_2), 1.78 and 1.67 (1 H and 1 H, m and m, CH_2); of **11b** ($CDCl_3$) δ 7.35–7.15 (5 H, m, NC_6H_5), 3.93 (2 H, d, J = 7.5 Hz, CH_2O), 3.31 (3 H, s, NCH_3), 1.15 (1 H, m, CH), 0.51 and 0.25 (2 H and 2 H, m and m, CH_2CH_2); mass calcd for $C_{12}H_{15}NO_2$ ($M^{\bullet+}$) 205.110, found 205.114.

2-Cyclobutyl-N^1,N^1,N^4,N^4-tetramethyl-1,4-phenylenediamine (7a). Diamine W was added to a stirred solution of peroxide **3a** in chloroform, maintained at −40 °C (see below for general method). After 2 h of stirring, the reaction mixture was allowed to warm to room temperature. It was washed with 1 N HCl to separate the basic fraction containing the desired compound. The acidic solution was neutralized with $NaHCO_3$ and extracted several times with ether. The combined ether extracts were dried and concentrated in vacuo. The product thus obtained was purified by silica gel chromatography, eluting with hexane–ethyl acetate (1:1). Compound **7a** was eluted in the first fraction and was characterized by NMR spectroscopy: ^{1}H NMR ($CDCl_3$) δ 7.01 (1 H, d, J = 7.8 Hz, $H6_{arom}$), 6.84 (1 H, d, J ~ 3 Hz, $H3_{arom}$), 6.59 (1 H, q, J = 7.8, 3 Hz, $H5_{arom}$), 4.01 (1 H, quint, CH), 2.90 (6 H, s, 4-NCH_3), 2.59 (6 H, s, 1-NCH_3), 2.35, 2.16, 2.02 and 1.86 (2 H, 2 H, 1 H, and 1 H, m's, $(CH_2)_3$). Further purification was carried out by recrystallization from CH_3OH/ether of the dihydrochloride salt, prepared by treatment of **7a** in dry ether with dried HCl gas. Anal. Calcd for $C_{14}H_{24}N_2Cl_2$: C, 57.73; H, 8.31, N, 9.62; Cl, 24.34. Found: C, 57.73; H, 8.53; N, 9.49; Cl, 24.41.

The isomeric diamines **7b,c** were isolated in similar fashion as a mixture of free bases from the reaction of **3b** with W. The ratio of **7b** to **7c** was determined by VPC using the carbowax column and 1-propyl 3-chlorobenzoate as internal standard. (The response factors for **7a** and **7b** plus **7c** were identical within experimental error.) The oven was programmed from 160 °C to 180 °C at 10 °C per minute; injection port was maintained at 220 °C: ^{1}H NMR ($CDCl_3$) δ 7.09 (d, J = 8 Hz, $H6_{arom}$), 6.90 (d, J = 3 Hz, $H3_{arom}$), 6.64 (q, J = 8, 3 Hz, $H5_{arom}$), 5.94 (m, vinyl CH, **7c**), 5.04 (m, vinyl CH_2, **7c**), 2.88, 2.86 (s, s, NCH_3's), 2.8–2.7 (m, CH_2's of **7c**), 2.58 (s, NCH_3's), 2.36 (m, CH_2 of **7b**), 0.98 (m, cyclopropyl CH, **7b**), 0.48 and 0.17 (m and m, cyclopropyl CH_2CH_2, **7b**); mass calcd for $C_{14}H_{22}N_2$ ($M^{\bullet+}$) 218.178, found ($M^{\bullet+}$) 218.178.

Decomposition of the Peroxides, General Method. A solution of 1.0 g of peroxide in 20 mL of $CHCl_3$ was cooled to −40 °C using an acetone–dry ice bath, while being maintained in a nitrogen atmosphere. While stirring, 1.1 mol equiv of the amine was added dropwise to this solution. The resulting solution was allowed to warm to room temperature and was stirred for 24 h. The carboxylic acids in the solution were extracted with 5% sodium bicarbonate. The basic compounds in the organic layer were extracted using 1 N HCl. The remaining layer was dried over anhydrous Na_2SO_4 to obtain the neutral compounds.

The combined bicarbonate extracts were acidified with aqueous HCl. The carboxylic acid(s) thus obtained were extracted several times with ether. The combined ether extracts were washed with distilled water, dried, and concentrated in vacuo. The yield of acids was obtained by weighing, and their ratio was ascertained by ^{1}H NMR spectroscopy.

The HCl extracts were neutralized with sodium bicarbonate solution to obtain the free bases. These bases were extracted with ether several times, washed with water, dried, and concentrated in vacuo. Quantitation of the amines, amides, and urethanes formed was done by VPC, using 1-propyl 3-chlorobenzoate as an internal standard, and the 5% carbowax column. The esters formed were quantitated by VPC using the same internal standard and the 15% DEGS column.[12]

Decomposition of Peroxides, Specific Methods. Identification of Q-oxide. The product mixture of **3a** and Q was extracted with bicarbonate solution, and the aqueous layer was treated with an anion exchange resin (OH^-) in methanol until the pH was 8, to remove 3-chlorobenzoate and cyclobutane carboxylate ions by anion exchange. The resulting solution was filtered to remove the resin and concentrated in vacuo to isolate Q-oxide (83%), which was characterized by comparing its ^{1}H NMR spectrum with that of an authentic sample prepared as described above.

Deuterium NMR Spectrum of Deuterated Cyclobutane. A sample of 32 mg of **3a** in 0.5 mL of $CDCl_3$ was placed in a 5-mm NMR tube and cooled to 0 °C. To this 15 mg of W or DMA in 0.5 mL of $CDCl_3$ was added. The deuterium NMR spectrum of the mixture was measured at 0 °C. A broad signal, ascribable to deuterated cyclobutane, was observed centered at δ 2.

Rate of Methylation of Q and W. Dimethyl sulfate, 0.095 mmol, was added to 0.053 mmol of W in 0.2 mL of $CDCl_3$. The reaction was monitored at 29.1 °C by ^{1}H NMR spectroscopy. The decrease in dimethyl sulfate concentration was measured by integrating the methyl signal of dimethyl sulfate at δ 4.0. The rate of formation of methylated W was measured by integrating the methyl signal of methylated W at δ 3.7. The reaction was found to be of second-order with $t_{1/2}$ = 271 s.

The methylation of 0.05 mmol of Q with 0.10 mmol of dimethyl sulfate in 0.2 mL of $CDCl_3$ was complete before the reaction could be monitored by ^{1}H NMR spectroscopy.

Identification of 5 in Reactions of 3 with Q and DABCO. Peroxide **3** (60–85 mg) in 0.5 mL of chloroform ($CDCl_3$) placed in a 5-mm NMR tube was cooled to −40 °C using an acetone dry–ice bath. To this, 4 equiv of Q (or DABCO) were added, and the reaction was allowed to continue at −40 °C for 30 min. This was sufficient time for **3** to react completely. Then, 1 equiv of benzylcyclopropanamine was added to the reaction mixture, and ^{1}H NMR spectra of the reaction were taken at 10–15-min intervals, while warming the reaction mixture to room temperature. The spectra revealed the disappearance of the signals due to benzylcyclopropanamine (NCH_2 at 3.6 ppm) with the simultaneous appearance and increase in the signal intensity due to amide **5a** (NCH_2, 4.45 ppm). After workup, **5a** was identified by comparison of its VPC trace (carbowax column) with that of authentic **5**, and

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quantitated using 1-propyl 3-chlorobenzoate as internal standard.

Identification of Formaldehyde, Piperazine, and DABCO-oxide as Products of the Reaction of 3 with DABCO. Peroxide **3a** was decomposed as described above with DABCO. To this mixture 2,4-dinitrophenylhydrazine was added, followed by the addition of deionized water. A yellow precipitate formed, which was isolated by filtration. After washing with 5% $NaHCO_3$ and water, further purification was carried out by passing a chloroform solution of the precipitate through a silica gel column. Pure formaldehyde 2,4-dinitrophenylhydrazone was eluted with chloroform and methanol (1:1): yellow crystals; 23%; mp 164-165 °C (lit. mp 166 °C); mixture mp undepressed; the hydrazone was further characterized by comparison of its ^1H NMR spectrum with that of an authentic sample.

To a 3-mL aliquot of a reaction of **3a** with DABCO were added 10 mL of H_2O and 2 mL of benzoyl chloride, followed by the addition of portions of solid NaOH. The mixture was shaken, and the addition of NaOH was continued until the solution was basic. The product was extracted with $CHCl_3$, and the $CHCl_3$ layer was washed with dilute HCl and H_2O and then dried over $CaCl_2$. Evaporation of the $CHCl_3$ yielded white crystals: mp 191 °C (lit.[46] mp 191 °C); mixture mp undepressed; and ^1H NMR spectrum identical with that of an authentic sample.

DABCO-oxide was identified by matching the NMR signals (triplets at δ 3.38 and 3.10) seen in a reaction aliquot with those of authentic DABCO-oxide admixed with 1 equiv of 3-chlorobenzoic acid in $CDCl_3$.

Identification of Formaldehyde, 10, 11, and 12, and the Absence of 2-(*N*,*N*-Dimethylamino)phenol in the Reactions of 3 with DMA. Formaldehyde was isolated as its 2,4-dinitrophenylhydrazone as described for the reaction of **3** with DABCO: mp 165-66 °C; ^1H NMR spectrum identical with that of an authentic sample.

Amides **10** and urethanes **11** were identified and quantitated by comparison with authentic samples using VPC analysis (carbowax column, 1-propyl 3-chlorobenzoate internal standard) of the neutral fractions of reaction products of **3** with DMA.

The basic fraction from the decomposition reaction of **3b** and DMA was separated as described above. The base mixture was passed through a column of silica gel and eluted with hexane-chloroform (1:1), followed by elution with hexane-acetone (1:1).

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The hexane-chloroform fraction contained three components as indicated by TLC. These compounds were separated by rechromatography on silica gel, eluting with toluene-chloroform (1:2). Compound **12** eluted in the first fraction: yellow crystals; mp 90-91 °C (lit.[10b] mp 89-90 °C); ^1H NMR ($CDCl_3$) δ 6.50 and 6.90 (d and d, J = 8.4 Hz, 4 H and 4 H, arom H's), 3.65 (s, 2 H, CH_2), 2.70 (s, 12 H, NCH_3's).

Further elution with chloroform gave a low-melting solid tentatively identified as 4-(4-(*N*,*N*-dimethylamino)benzyl)-*N*-methylaniline, the desmethyl homologue of **12**: ^1H NMR ($CDCl_3$) δ 6.95-7.15 and 6.10-6.70 (m and m, 4 H and 4 H, arom H's), 3.70 (s, 2 H, CH_2), 3.45 (s, 1 H, NH), 2.87 (s, 6 H, $N(CH_3)_2$), 2.75 (s, 3 H, NCH_3).

NMR Experiments. All low-temperature spectra were recorded on the Varian XL-300 spectrometer. A solution of ~0.05 g (0.0002 mol) peroxide in 0.5 mL of $CDCl_3$ (5-mm tube) was cooled to -40 °C, 2-4 mol equiv of cooled amine (1 mole equiv in the case of amine W) was added, and the reaction was monitored on the spectrometer. Typically, spectra at -40, -30, -20, -10, 0, 10 °C, and room temperature were recorded after maintaining the reaction for 10 min or so at each temperature. (In the case of W-induced decomposition, the spectra were recorded starting from -60 °C.) The experimental conditions used for the acquisition of the spectra was 10 μs pulse-width, 4-8 scans, and 4000-Hz spectral width. $CDCl_3$ was used for the lock signal.

Acknowledgment. We thank the following sources for partial support of this work: the National Institutes of Health, Grant CA22365, and the Commission on Academic Excellence of the University of Louisville (grant to S.S.). Also, we wish to thank Dr. Harrell Hurst of the Department of Pharmacology and Toxicology, University of Louisville, for mass spectral determinations; we also acknowledge the help of the Midwest Center for Mass Spectrometry, University of Nebraska—Lincoln, which is supported by the National Science Foundation.

Registry No. **3a**, 70458-21-8; **3b**, 70458-22-9; **5a**, 125302-96-7; **5b**, 125302-97-8; **7a**, 125302-98-9; **7b**, 125302-99-0; **7c**, 12530-00-6; **10a**, 71473-94-4; **10b**, 125303-02-8; **11a**, 125303-01-7; **11b**, 125303-03-9; Q, 100-76-5; Q oxide, 25289-67-2; W, 100-22-1; DABCO, 280-57-9; DABCO oxide, 18503-52-1; DMA, 121-69-7; *m*-$ClC_6H_4CONBu_2$, 35306-68-4; c-C_4H_7-$CONBu_2$, 125302-95-6; *N*,*N*-di-*n*-butylamine, 111-92-2; benzylcyclopropylamine, 13324-66-8; cyclobutanecarbonyl chloride, 5006-22-4.

A Route to Linear, Bridged, or Spiro Polycyclic Compounds: Sequential Use of the Intermolecular Diels-Alder Reaction and Radical Cyclization

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Received August 21, 1989

The intermolecular Diels-Alder reaction in which either the diene or the dienophile carries a suitably located homolyzable substituent, such as a phenylseleno group, represents a convenient method for assembly of compounds that can undergo radical cyclization. The technique can be used to generate polycyclic structures that are fused in a linear, bridged, or spiro manner. The hetero Diels-Alder version is equally versatile in this connection.

The utility of radical cyclization[1] in synthetic chemistry depends very much on the ease with which structurally complex radical precursors can be assembled, and we have evaluated a number of classical processes, such as the Ireland ester enolate rearrangement[2] and the Michael addition,[3] in this regard. The Diels-Alder reaction is especially suitable for integration with radical chemistry, although it has not yet seen extensive use for this purpose. Our experiments, which are described below,[4] and the two other publications[5] in this area, show that the Diels-Alder

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