an oil bath at 100 °C. After 18 h the vial was removed from the bath and allowed to reach room temperature. The usual workup afforded, after chromatography (silica gel, 2:1 C_6H_6–hexane), 0.53 g (53.5%) of pheryl benzoate, crystals from hexane, mp 68–69 °C (lit.[29] mp 71 °C).

Phenyl acetate was prepared in a similar fashion from 1-phenylethanol.

Registry No.—**1**, 13080-90-5; **2**, 55044-07-0; **3**, 13492-22-3; **4**, 570-90-1; **5**, 566-66-5; 5β-**6**, 61990-52-1; 5α-**6**, 61990-53-2; **8**, 6249-79-2; **9**, 3347-62-4; **10**, 61990-54-3; **11**, 7231-31-4; 2,3-epoxycyclohexanone, 6705-49-3; 2,3-epoxy-3-phenylpropiophenone, 5411-12-1; 2,3-epoxy-2,6-dimethyl-8-nonanone, 61990-55-4; α-4,5-epoxy-3,20-dione, 17503-05-8; β-4,5-epoxy-3,20-dione, 17597-24-9; 3,4-epoxy-4-methyl-2-pentanone, 4478-63-1; cholesterol, 57-88-5; benzyl acetate, 140-11-4; phenyl-2-propanol, 698-87-3; diphenylcarbinol, 91-01-0; phenyl benzoate, 93-99-2; 2-cyclohexenol, 822-67-3; 4-phenyl-3-buten-2-ol, 17488-65-2; 1,3-diphenylpropenol, 4663-33-6; 1-hexen-3-ol, 4798-44-1; 2,6-dimethyl-2-nonen-8-ol, 40596-76-7; 4-methyl-3-penten-2-ol, 4325-82-0.

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(22) Oxidation of primary alcohols by the nitroxide catalyzed process generally yields carboxylic acids by a Baeyer–Villiger reaction on the initially produced aldehyde (ref 2). This process suffers as a preparative method, however, in most cases owing to the difficulty of separating the products from *m*-chlorobenzoic acid.
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(25) *m*-Chloroperbenzoic acid is also decomposed by the nitroxide catalyst (ref 1); however, the rate of this decomposition is slower than the alcohol oxidation, thus does not interfere with it.
(26) Cyclopropyl methyl ketone is particularly unreactive in the Baeyer–Villiger reaction, but can be oxidized by trifluoroperacetic acid (ref 23).
(27) Melting points were determined on a Thomas-Hoover melting point apparatus. Infrared spectra were recorded on a Beckman IR-5A spectrophotometer using sodium chloride disks or potassium chloride pellets. Mass spectra were determined on an LKB 9000 gas chromatograph–mass spectrometer system operated with an accelerating voltage of 3.5 kV, an ionizing current of 60 μA, an electron energy of 70 eV, and an ion source temperature of 250 °C or on a Hewlett-Packard 5982 A gas chromatograph–mass spectrometer system with an ion source temperature of 180 °C, ionizing current 0.15 μA, and an electron energy of 70 eV. Aliquots of crude reaction and isolated products were monitored using gas chromatographic columns described below. Gas chromatography was performed on a Varian 2700 gas chromatograph equipped with a FID detector using 6 ft × 0.25 in. glass columns: column A, 3% OV-1 on 80/100 mesh Supelcoport; column B, 5% Carbowax 1540 on 40/60 mesh Chromosorb T. The phrase "worked up in the usual fashion" means that the organic phase was washed successively with 1.0 M NaOH, water, and brine, then dried by passage through a cone of anhydrous sodium sulfate.
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Reevaluation of the Use of Peroxycamphoric Acid as an Asymmetric Oxidizing Agent

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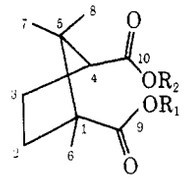
The usual method for preparation of monopercamphoric acid for asymmetric synthesis is shown to afford significant quantities of two isomers giving opposite stereochemical senses of asymmetric induction. One of the isomers can be obtained crystalline and use of this single isomer for asymmetric induction leads to optical yields of chiral sulfoxides, epoxides, and oxaziridines 50–100% greater than previously reported to result from use of the mixed isomers. In one of the more favorable cases, 2-*tert*-butyl-3-(*p*-bromophenyl)oxaziridine (**4**) was obtained in 60% enantiomeric excess using the crystalline peracid.

In recent years, a monoperoxycamphoric acid (MPCA) ascribed structure **1** has found use as a chiral oxidant for the asymmetric syntheses of chiral sulfoxides,[1–3] epoxides,[3–6] and oxaziridines.[3,7–9] In most instances, the degree of asymmetric induction afforded by MPCA is rather low. In this paper, we report an experimental modification that substantially increases the optical yields of products afforded by oxidation with MPCA.

Ordinarily, MPCA is prepared by reaction of camphoric anhydride with hydroperoxide ion, as originally described by Milas and McAlevy.[10] So far as can be ascertained from most published procedures ,the MPCA used for asymmetric synthesis is isolated via an extractive workup and does not appear to be purified further (apart from drying and iodometric standardization) before use *even though Milas and McAlevy originally reported it to be a crystalline solid.* Use of the unpurified extract is tantamount to a general de facto assumption that MPCA **1** is the only significant peracid in the

Table I. ^{13}C Chemical Shifts[a] of Camphoric Acid and Percamphoric Acid Isomers



Carbon atom	Camphoric acid,[b] R_1 = R_2 = H	1,[c] R_1 = H; R_2 = OH	2,[c] R_1 = OH; R_2 = H	3,[c] R_1' = R_2' = OH
1	56.66	56.07	55.39	56.20
2	33.19	32.29	31.87	32.16
3	23.12	22.58	22.58	22.58
4	53.04	50.16	52.34	52.79
5	46.63	47.30	47.63	46.88
6	21.99	21.67	21.38	21.60
7	21.51	21.18	21.08	21.08
8	23.12	22.58	22.58	22.58
9	175.66	175.17	179.71	180.26
10	177.55	181.79	176.66	182.25

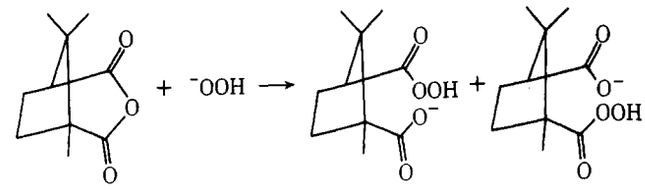
[a] All chemical shifts ± 0.06 ppm. Single-frequency off-resonance decoupling was used to assist in spectral assignments. [b] In acetone-d_6, ~ 250 mg/2 mL. [c] In chloroform-d, ~ 500 mg/2 mL.

Table II. Oxidation of *p*-Bromobenzylidene-*N*-*tert*-butylamine with MPCA at −78 °C[a]

Entry	Solvent	Ratio of oxidants[b] 1	2	3	Enantiomeric excess, % (±1%)[c]
1	CH_2Cl_2[d]	15	1	~0	40
2	CH_2Cl_2[d]	2	1	1	<1
3	CH_2Cl_2[d]	4	2	1	24
4	$CHCl_3$/CH_2Cl_2 (4:1)	15	1	~0	60

[a] The reaction mixture was kept at this temperature for 12 h, then allowed to warm to room temperature over a 5–6 h period. [b] Estimated from the intensities of ^{13}C NMR peroxycarbonyl resonances. [c] An excess of the (−) isomer[12] was obtained in each instance, in an overall yield of >80%. [d] 95% of the theoretical amount of camphoric acid had precipitated at the conclusion of the reaction.

extract. It is logical to expect that MPCA isomer **2** might also be present (eq 1); the question is, to what extent?



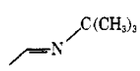
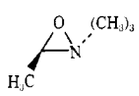
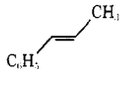
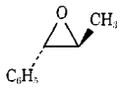
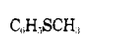
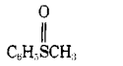
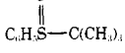
1 **2**

Using the usual procedure and workup, we obtained a solution that, by iodometry, contained essentially only MPCA. However, six signals (three pairs) are evident in the carbonyl region of the ^{13}C NMR spectrum of this material (Table I). None of these signals arise from the anhydride or diacid. By means of ^{13}C NMR, it was ascertained that monoperacids **1** and **2** were both present as was a small amount of bisperacid **3**, presumably formed by exchange. In our hands, the proportion of monoperacid **1** varies (50–80% of total) depending upon the care taken in regulating reaction temperature and the rate of anhydride addition. Although hardly astonishing, this observation has considerable impact in terms of asymmetric induction. By concentrating the crude ethereal extract under vacuum, diluting with CH_2Cl_2, and storing at −30 °C for several days, colorless prisms (ca. 50%, mp 65–68 °C) were obtained. The ^{13}C NMR spectrum of this material is consistent with its being a 15:1 mixture of monoperacids **1** and **2**. One additional recrystallization raises the melting point to 70–71 °C.[11] Crystalline **1** shows no demonstrable decomposition after storage at −30 °C for 1 month. However, when crystalline **1** is dissolved in CH_2Cl_2 and stored for several days at 25 °C, or 2 weeks at −30 °C, noticeable conversion of **1** to **2**, **3**, and camphoric acid occurs. Monoperacid **2** has not been isolated although the mother liquors from the crystallization of **1** are substantially enriched in **2**.

From the results of asymmetric synthesis of 2-*tert*-butyl-3-(*p*-bromophenyl)oxaziridine (**4**) using MPCA of different isomeric compositions, it may be inferred that peracids **1** and **2** have opposite stereochemical preferences. Oxidation with a fresh solution of crystalline **1** affords **4** in 40% ee (Table II, entry 1), use of the crude extract affords **4** in 24% ee (entry 3), and use of the mother liquors affords essentially racemic oxaziridine (entry 2).

These results raise the possibility that, in prior reports of the use of MPCA, optical yields might have been significantly

Table III. Asymmetric Oxidations of Various Substrates with MPCA

Starting material[a]	Product[b]	Solvent	Temp, °C	Enantiomeric excess, % Lit. or crude extract	Crystalline
		CH_2Cl_2	−78	10 (−)	14 (−)[13]
		$CHCl_3$	0	4.6 (*S*)[5]	7.8 (*S*)
		$CHCl_3$	0	5.1 (1*S*,2*S*)[5]	9.2 (1*S*,2*S*)
		$CHCl_3$	0 4 −50	3.8 (*R*)[1] 6.4 (*R*)[2]	 6.4 (*R*) 9.0 (*R*)
		$CHCl_3$	0 4 −30	1.3 (*S*)[1] 1.6 (*S*)[2]	 4.4 (*S*)

[a] Registry no. are, respectively, 62058-77-9, 100-42-5, 873-66-5, 100-68-5, 3019-19-0. [b] Registry no. are, respectively, 62107-41-9, 20780-54-5, 4518-66-5, 4850-71-9, 62076-10-2.

higher (and possibly sometimes of the opposite sense) had crystalline MPCA been used instead of crude extract. To check upon the generality of this hypothesis, several previously reported MPCA asymmetric oxidations were repeated using crystalline **1**. The results of these comparisons and of the asymmetric synthesis of several other oxaziridines, again using different compositions of the MPCA isomers, appear in Table III. In general, the use of crystalline **1**, rather than the crude extract, increases optical yield by 50–100%. In some instances, optical yields are still fairly low. However, the 60% optical yield obtained in the case of oxaziridine **4** (Table II) demonstrates that crystalline **1** sometimes functions as quite an efficient chiral oxidant.

Acknowledgment. This work has been partially supported by grants from the National Institutes of Health and the National Science Foundation.

Registry No.—**1**, 16211-85-1; **2**, 62058-73-5; **3**, 39923-07-4; (−)-**4**, 62058-74-6; (±)-**4**, 62058-75-7; camphoric acid, 5394-83-2; *p*-bromobenzylidene-*N*-*tert*-butylamine, 62058-76-8.

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(11) The originally reported melting point of 49–50 °C may indicate that Milas and McAlevy had in hand a mixture of **1** and **2**.
(12) A sample of this material with 39.6% ee had $[\alpha]^{23}_{D}$ −29.7° (tentatively assigned the 2*S*,3*R* configuration).[13]
(13) An NMR method for the determination of absolute configuration and enantiomeric composition of oxaziridines is being reported elsewhere.

Reduction of Amides and Lactams to Amines by Reactions with Phosphorus Oxychloride and Sodium Borohydride[1]

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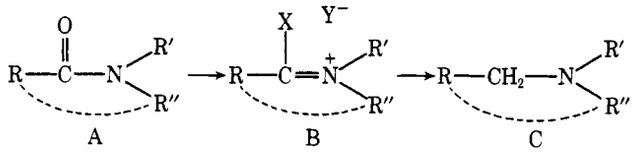
Practical and convenient procedures were developed for the reduction of carboxamides and lactams to corresponding secondary and tertiary amines by reactions with $POCl_3$ and $NaBH_4$. Optimum conditions for formation of *O*-phosphoryl (or chloroimonium) intermediates and their reductions are structure dependent. Selective reductions of amide esters and amide nitriles to amino esters and amino nitriles were obtained.

The reduction of amides and lactams to amines with lithium aluminum hydride[2] sometimes proceeds with difficulty, particularly where secondary amines are to be generated, due to NH proton acidity and formation of insoluble complexes. The use of forcing reaction conditions such as reduction in refluxing *N*-ethylmorpholine[3] does not always overcome this barrier. Alternatively, diborane may be used for such reductions but other susceptible groups, such as double bonds, can then also react. Selective reduction of amido esters to amino esters[4] with diborane usually requires a deactivated pentachlorophenyl or an aromatic acid ester. The recently developed reduction of amides to amines by a sodium borohydride–carboxylic acid complex[6] could also not be used for selective reduction of the lactam ester **18**, with both carbonyl groups lost in the reduction product. However, selective reduction of lactams in the presence of ester functions can be achieved by conversion to thiolactams and desulfurization with Raney nickel[7,8] or by formation of alkoxyimonium intermediates with triethyloxonium fluoroborate and subsequent reduction with sodium borohydride.[9,10]

Since the latter procedures suffer from being either cumbersome, experimentally difficult, or costly, a more practical preparative method for reduction of N-mono- and disubstituted amides and lactams was required, preferably with selectivity for these functional groups. This was found in the reactions of lactams and amides with $POCl_3$ followed by $NaBH_4$.[11] While a previous report of the reaction of *N*-benzylpiperidone with $POCl_3$ and subsequent borohydride reduction had indicated only dimeric amine products,[12] we found that good yields of the monomeric amine could be obtained from this lactam as well as from other examples listed in Table I.

The reaction sequence proceeds from an amide or lactam A to an imino derivative B where X and/or Y can be $OPOCl_2$



and/or Cl. While an *O*-phosphoryl derivative may be favored over the corresponding imino chloride, in analogy to observations in related studies,[13–16] either or both types of derivatives may be produced in the reaction medium. Formation of the imonium derivatives was followed by NMR spectra which showed a downfield shift of 0.8–1.0 ppm for protons α to nitrogen in tertiary amides and 0.4–0.6 ppm in secondary amides. It was also noted that alkyl groups in *N*,*N*-dialkylamides, usually nonequivalent in $CDCl_3$ solutions, became equivalent in $POCl_3$ solutions (owing to amide protonation by HCl, which could be suppressed by addition of pyridine). This equivalence was lost as the amide A was converted to the imino derivative B in *N*,*N*-dimethyl- and -diethylbenzamide and in *N*,*N*-dimethylcyclohexanecarboxamide, but not in the other examples shown in Table I. Observation of these conversions provided minimal reaction times for the first step of the reaction sequence.

Table I lists the times necessary for complete reaction of amides with $POCl_3$, plus 20–30%. A dependence of the reaction rate on steric and electronic structural parameters may be