(*S*)-acetate **4a** and the (*S*)-alcohol **1a** (hexane/ethyl acetate = 9/1 and 8/2) with a ratio depending on the incubation time.

a. At 60% conversion, (*S*)-(−)-**1a** (0.51 g, 34%) was obtained; $[\alpha]_D$ −39° (>98% ee). The 60-MHz NMR spectrum was identical with the one previously reported for (*R,S*)-**1a**, and a correct elemental analysis was found.

b. At 40% conversion, the (*S*)-(+)-acetate **4a** (0.6 g, 32%) was isolated; $[\alpha]_D$ +25° (>98% ee). The chemicophysical data were in agreement with the structure.

Enzymatic Transacetylation of (*R,S*)-Epoxy Alcohol 1b. The experimental procedure was as for **1a**. Starting from (*R,S*)-**1b** (1.83 g, 9.15 mmol), the reaction reached 60% conversion to the acetate **4b** in 2 h and, after purification, (*S*)-(−)-**1b** (0.658 g, 36%) was obtained; $[\alpha]_D$ −12.6° (96% ee). When the reaction was carried out on the same amount of (*R,S*)-**1b** and at 40% conversion (1 h), the (*S*)-(+)-acetate **4b** (0.84 g, 38%) was isolated; $[\alpha]_D$ +5.9° (96% ee). The chemicophysical properties of compound **1b** were in agreement with the literature data (ref 17), and for the acetate **4b** the properties were in accord to the structure.

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Registry No. (±)-**1a**, 135107-04-9; (5)-**1a**, 135214-52-7; (±)-**1b**, 135214-51-6; (*s*)-**1b**, 103680-90-6; **2a**, 30457-89-7; **2b**, 103680-89-3; **3a**, 20593-63-9; **3b**, 84515-42-4; (*s*)-**4a**, 135107-05-0; (*s*)-**4b**, 135107-06-1; PFL, 9001-62-1; vanadium acetylacetonate, 13476-99-8; vinyl acetate, 108-05-4.

Divergent Response of a Hindered Cyclopropene to Strong Oxidizing Agents

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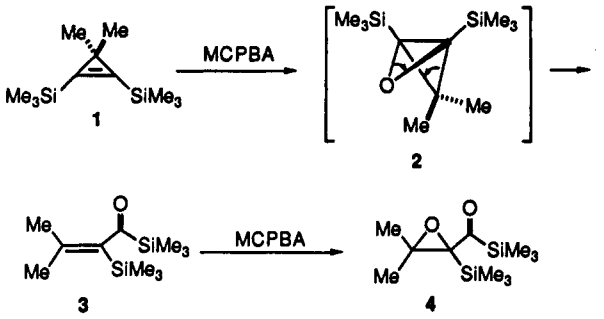
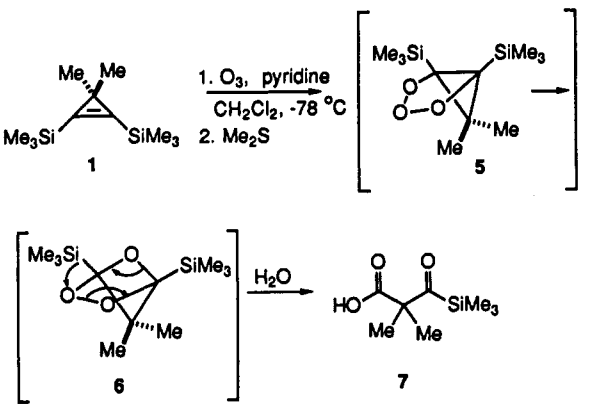
The inability to produce oxabicyclobutanes by direct epoxidation of a cyclopropene has been recognized for some time.[2] No member of this structurally interesting class of compounds has yet been characterized, presumably due to the substantial structural strain present in this highly condensed heterocyclic framework and the existence of a facile isomerization pathway under the conditions customarily employed. With the recent advent of dimethyldioxirane[3] and its trifluoromethyl analogue[4] on the chemical scene,[5] the combination of high reactivity, neutral pH, and ease of workup offered by these reagents suggested that they be examined for the possible elaboration of this extremely sensitive class of compounds.

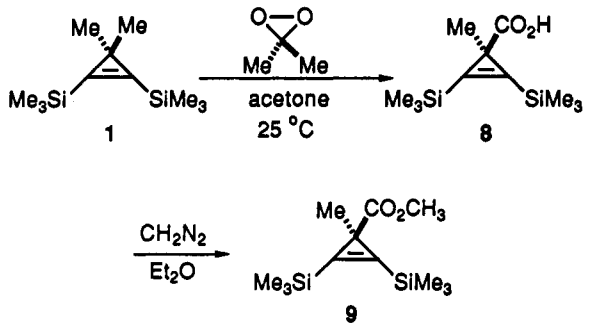
Scheme I



Scheme II



Scheme III



The stability of **1** and the beneficial steric shielding offered by its substitution prompted its selection for initial study.[6] This paper records the entirely different response exhibited by **1** toward *m*-chloroperbenzoic acid (MCPBA), ozone, and dimethyldioxirane (DMD).

The oxidation of **1** with MCPBA was carried out under several sets of conditions. Invariably, the major products were the α,β-unsaturated acylsilane **3** and its epoxide **4** (Scheme I). The oxidation was observed to proceed sluggishly, a reasonable rate materializing only when the reaction was conducted near room temperature. In accord with previous reports,[2] the appearance of **3** and **4** is considered to stem from transient formation of oxabicyclobutane **2** with ensuing electronic reorganization as shown.

Hindered alkenes often react with ozone to produce the epoxide rather than the expected products of ozonolysis.[7]

(1) The Ohio State University Fellow, 1986–1987; National Need Fellow (Department of Education), 1988–1989; American Chemical Society Organic Division Fellow (Eli Lilly Co.), 1989–1990.

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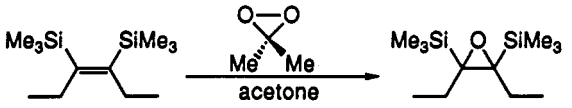
Cyclopropene 1 does not conform to this reactivity pattern. Exposure of 1 in cold (−78 °C) dichloromethane solution to ozone resulted in rapid reaction to produce acylsilane 7 as the sole product (Scheme II). Presumably, 1,3-dipolar cycloaddition to the three-membered ring double bond to generate molozonide 5 is not seriously impeded. Once subsequent conversion to ozonide 6 is complete, isomerization to the trimethylsilyl ester 7 is made possible. Hydrolysis during handling provides the free carboxylic acid.

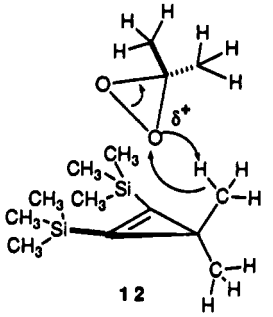
The preceding two oxidative transformations and the suggested mechanistic models provide a useful frame of reference for assessing the reactivity of 1 toward DMD. When 1 was admixed with DMD in acetone solution at room temperature, a slow reaction occurred. Several equivalents of DMD were required to effect complete consumption of starting material. In the end, carboxylic acid 8 was identified as the major product (Scheme III) without evidence for concurrent attack on the double bond! Recourse to the more reactive trifluoromethyl-substituted dioxirane led to the formation of several unidentified products.

In order to rule out the possibility that this unusual reactivity pattern may arise because of a general lack of reactivity of bis(trimethylsilyl)alkenes toward DMD, 10[8] was treated comparably with DMD in acetone at room temperature. Quantitative conversion to epoxide 11 occurred in 5 h.



10 25 °C 11

On this basis, the steric hindrance present in 1 would seem to be important in forcing the oxidation of a methyl group to be the kinetically faster process. Highly selective oxidations of nonactivated C–H bonds in hydrocarbons by DMD have been reported.[9] Recently, 4,4-dimethylcholesterol and its acetate were noted to undergo such C–H oxidation more rapidly than olefin epoxidation.[10] The sluggish reactivity of 1 suggests that the relative size of the DMD molecule may cause it to be denied access to the cyclopropene double bond (see 12).[11] As a consequence, DMD may be useful in situations where selective epoxidation is sought on the basis of disparate steric requirements.



12

The facile conversion of a 3-methyl group in 1 to a carboxylic acid group is remarkable. Literature reports indicate that the initial oxidation of hydrocarbons to alcohols is quite slow. Subsequent oxidations from the alcohol through the aldehyde to the acid proceed rapidly.[4,9] Finally, the steric situation in 8 is clearly sufficient to protect its double bond from oxidation during the several hours required to consume the balance of unreacted 1 oxidatively.

Experimental Section

Oxidation of 1 with MCPBA. To a solution of MCPBA (122 mg of 80%, 0.565 mmol) in CH_2Cl_2 (5 mL) at −78 °C under argon was added 1[6] (100 mg, 0.471 mmol) with magnetic stirring. The reaction mixture was allowed to warm to room temperature over 6 h, poured into water (10 mL), diluted with CH_2Cl_2 (10 mL), separated, washed with saturated sodium bicarbonate solution (3 × 10 mL), dried over sodium sulfate, filtered, and evaporated to provide 139 mg of oil. Preparative TLC (silica gel, elution with 4% ethyl acetate in petroleum ether) gave 20.0 mg of 3 and 54.0 mg of a 2:1 mixture of 4 and 3 (65% combined yield). Pure samples were obtained by preparative GC (2.5 in 5% SE-30 on Chromosorb W, 12 mL/min, 150 °C).

For 3: colorless liquid; IR (neat, cm^{-1}) 1605; ^1H NMR (300 MHz, C_6D_6) δ 1.57 (s, 3 H), 1.45 (s, 3 H), 0.14 (s, 18 H); ^{13}C NMR (75 MHz, C_6D_6) δ 249.75, 147.61, 142.22, 23.18, 22.83, −0.43, −3.28; GC/MS m/z (M^+) calcd 228, obsd 228.

For 4: colorless oil; IR (neat, cm^{-1}) 1627; ^1H NMR (300 MHz, C_6D_6) δ 1.10 (s, 3 H), 1.05 (s, 3 H), 0.22 (s, 9 H), 0.11 (s, 9 H); ^{13}C NMR (75 MHz, C_6D_6) δ 254.78, 74.28, 62.63, 23.16, 22.72, −2.07, −3.06; GC/MS m/z (M^+) calcd 244, obsd 244.

Ozonolysis of 1. A solution of 1 (310 mg, 1.46 mmol) in CH_2Cl_2 (40 mL) containing 2 drops of pyridine was cooled to −78 °C and treated with ozone until the color was blue (5 min), stirred at this temperature while being purged with oxygen for 30 min, and treated with 2 mL of freshly distilled dimethyl sulfide. After being warmed to 0 °C, the solution was dried, filtered, and evaporated to leave 2.5 g of light yellow liquid. Removal of the DMSO at room temperature and 0.1 Torr left 220 mg (80%) of 7 as a yellow viscous oil that decomposed on attempted purification. For 7: IR (neat, cm^{-1}) 3260, 2960, 2900, 1720; ^1H NMR (300 MHz, C_6D_6) δ 10.00 (s, 1 H), 1.24 (s, 6 H), 0.18 (s, 9 H); GC/MS m/z ($M^+ - CO_2$) calcd 133, obsd 133.

Oxidation of 1 with DMD. Dimethyldioxirane was prepared as per the literature procedure[3] except that 0.5 g of Na_2EDTA was added to the generation flask. To a magnetically stirred solution of dimethyldioxirane (60 mL of 0.05 M, 3 mmol) in acetone at rt was added 1 (85.0 mg, 0.400 mmol). After 35 h at rt, the acetone was evaporated, the moist residue was diluted with CH_2Cl_2 (10 mL), and the organic phase was dried, filtered, and evaporated to provide 71 mg of impure 8 as pale yellow oily crystals. This material was taken up in ether (10 mL) and treated with an ethereal solution of diazomethane until a yellow color persisted. Evaporation gave 65.1 mg of yellow oil, preparative gas chromatography (1.5 m 5% SE-30 on Chromosorb W) of which proceeded with considerable loss due to volatility to provide 18.6 mg (18%) of pure 9 as a colorless oil.

For 8: IR (KBr, cm^{-1}) 1667; ^1H NMR (300 MHz, C_6D_6) δ 11.40 (br s, 1 H), 1.30 (s, 3 H), 0.20 (s, 18 H); ^{13}C NMR (75 MHz, C_6D_6) δ 185.62, 131.56, 24.03, 22.18, −1.30; MS m/z (M^+) calcd 242.1158, obsd 242.1122.

For 9: IR (neat, cm^{-1}) 1705; ^1H NMR (300 MHz, $CDCl_3$) δ 3.55 (s, 3 H), 1.32 (s, 3 H), 0.19 (s, 18 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 199.00, 131.35, 51.22, 23.61, 22.14, −1.34; MS m/z (M^+) calcd 256.1315, obsd 256.1321.

Oxidation of 10 with DMD. An excess of dimethyldioxirane in acetone (22 mL of 0.08 M, 1.76 mmol) was added to a solution of 10[8] (40.0 mg, 0.175 mmol) in acetone (5 mL). The reaction mixture was stirred at rt and monitored by GC/MS. Starting material was completely consumed after 5 h. The reaction mixture was concentrated under reduced pressure, diluted with CH_2Cl_2 (5 mL), dried, filtered, and concentrated to provide 11 as a pure colorless liquid (42.8 mg, 100%): ^1H NMR (300 MHz, $CDCl_3$) δ 1.79 and 1.46 (2 6-line dq, $J \approx 14$, 7 Hz, 4 H), 0.91 (t, $J = 7.4$ Hz, 6 H), 0.16 (s, 18 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 62.30, 24.63, 10.46, 0.13; MS m/z (M^+) calcd 244.1679, obsd 244.1690.

Acknowledgment. This investigation was supported by the National Science Foundation.

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Registry No. 1, 107736-03-8; 3, 135192-92-6; 4, 135192-93-7; 7, 135192-94-8; 8, 135192-95-9; 9, 135192-96-0; 10, 135192-97-1; 11, 135192-98-2; MCPBA, 937-14-4; DMD, 74087-85-7; ozone, 10028-15-6.

Supplementary Material Available: ^{1}H NMR spectra of 3, 4, 7–9, and 11 (6 pages). Ordering information is given on any current masthead page.

Di-*tert*-butyl *N*-Acylimidodicarbonates as Isolable Acylating Agents: Mild Conversion of Primary Carboxamides to Substituted Amides

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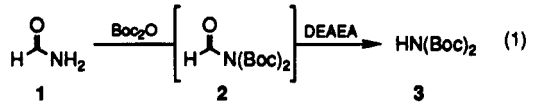
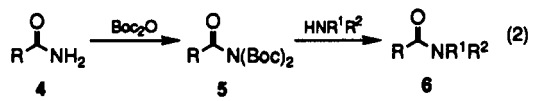
During the course of our work on the synthesis of platelet-activating factor antagonists, we required a mild, general means of converting primary amides to secondary and tertiary amides. This can be accomplished by hydrolysis of amides to acids followed by coupling with the requisite amine; however, this hydrolysis may be incompatible with acid- or base-sensitive functional groups.[1]

A possible solution was suggested by the pioneering work of Grehn and Ragnarsson, which described the exhaustive *tert*-butoxycarbonylation of amide nitrogens[2] and the cleavage of *N*-Boc-acylamides with hydrazine and 2-(diethylamino)ethylamine (DEAEA).[3,4] These workers also describe the synthesis of di-*tert*-butyl imidodicarbonate (3) by exhaustive *tert*-butoxycarbonylation of formamide followed by aminolysis of the unstable di-*tert*-butyl *N*-formylimidodicarbonate (2; eq 1).[5,6] We viewed com-

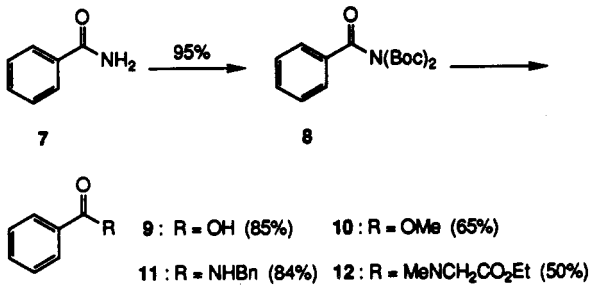




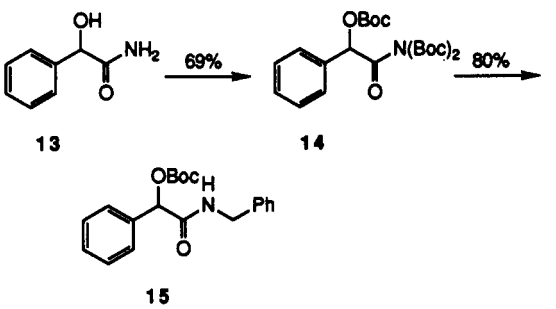
pounds such as 2 as acylating agents rather than a source of 3 and would now like to report that primary amides react with di-*tert*-butyl dicarbonate to give stable, isolable *N*-acylimidodicarbonates 5 (eq 2). These compounds are indeed active acylating agents and cleave selectively at the amide linkage upon reaction with alkoxides to give esters plus di-*tert*-butyl imidodicarbonate (3). This could have been anticipated since Grieco has shown that related *N*-Boc lactams and *N*-Boc secondary amides undergo selective cleavage upon exposure to hydroxide or alkoxides.[7] Imidodicarbonate 5 also bears some similarity to triamides, which Wasserman has shown react as activated carboxylates.[8] We now demonstrate that reaction of 5 with primary and some secondary amines gives the desired amide 6 in moderate to high yields. A series of examples are discussed below.

Treatment of benzamide with di-*tert*-butyl dicarbonate in the presence of DMAP gave a 95% yield of *N*-benzoylimidodicarbonate 8 after silica gel chromatography (Scheme I). This material could be stored indefinitely at room temperature without significant decomposition, as is the case for the other *N*-acylimidodicarbonates described herein (vide infra). Reaction of 8 with sodium hydroxide gave an 85% yield of benzoic acid (9) while methyl benzoate (10) was produced in 65% yield upon exposure to sodium methoxide. Treatment of 8 with benzylamine in methylene chloride at room temperature over 10 h gave an 84% yield of *N*-benzylbenzamide (11), which is on the same order of reactivity as other isolable acylating agents.[9]

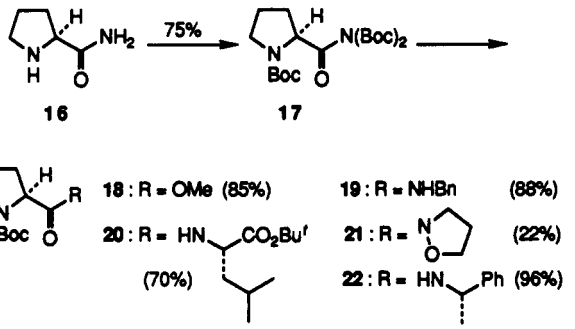
Scheme I



Scheme II



Scheme III



(1) For an overview of methods for amide hydrolysis, see: Larock, R. C. *Comprehensive Organic Transformations: A Guide to Functional Group Preparation*; VCH: New York, 1989; p 988. Also see: Greenlee, W. J.; Thorsett, E. D. *J. Org. Chem.* **1981**, *46*, 5351.

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