61.2 mmol of Me_3N in 180 mL of H_2O was heated at 100 °C for 20 h with an initial pressure (room temperature) of 17.7 atm of N_2, 29.3 atm of O_2, and 208.8 atm of Ar. Samples of the head gas were taken before and after the reaction and were analyzed by mass spectroscopy. The analyses of O_2 and N_2 were also confirmed by GC on a 10 ft molecular sieve column. N_2 was added as an internal standard for the analysis of O_2 by G.C. The results are shown in the table below.

	O_2	N_2	Ar	CO_2	H_2
before reaction[a]	9.6 (±0.3)	6.6 (±0.4)	82.6 (±0.8)	0	<0.02
after reaction	5.5 (±0.3)	7.3 (±0.4)	87.0 (±0.8)	0.011	0.1

[a] The balance is Me_3N.

The organic products were determined by $^{13}C\{^1H\}$ NMR spectroscopy. The IR spectra of the head gas also indicate the absence of N_2O, NO, and NO_2.

Deoxygenation of Me_3NO. A preliminary experiment indicates that no reaction occurs if an aqueous solution of Me_3NO (0.5 M) is heated first at 100 °C for 19 h and then at 150 °C for 5 h under 500 psi of argon atmosphere.

An aqueous solution of 0.92 M Me_3NO (160 mL) was heated at 200 °C and 500 psi of argon atmosphere. Samples were taken and analyzed by $^{13}C\{^1H\}$ NMR spectroscopy. Me_3NO disappeared with a half-life of 2.5 h; Me_3N accounted for about half of the product. At the end of the reaction, CO_2, but not O_2, was found in the sample of the head gas.

Acknowledgment. This study was supported by the U.S. Department of Energy, Division of Chemical Sciences, Office of Basic Energy Sciences, under Contract No. W-31-109-ENG-38.

Registry No. Me_3N, 75-50-3; Me_3NO, 1184-78-7; Me_2NH, 124-40-3; $HCONMe_2$, 68-12-2.

Steric Control of Epoxidation by Carbamate and Amide Groups. Evidence for the Carbonyl-Directed Epoxidation

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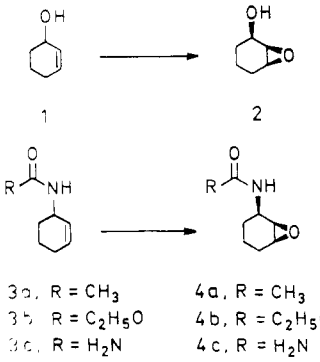
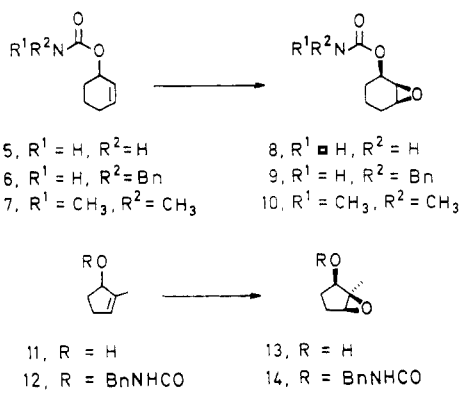
Allylic and homoallylic carbamoyloxy groups show a pronounced syn stereodirecting effect on peroxy acid epoxidation similar to that of hydroxy groups (**5** → **8**). Carbonyl oxygen of the ambident carbamoyloxy group has been found to be responsible for this steering. A similar effect operates in olefinic amides (**64** → **66**).

The hydroxyl-directed epoxidation of allylic alcohols (**1** → **2**; Scheme I) has evolved into a reliable and highly stereoselective method for the construction of vicinal chiral centers.[1-3] A similar syn directing effect has been found for amido[4] (**3a**), urethano[5] (**3b**), and ureido olefins[6] (**3c**) and for unsaturated acetals,[7] sulfones,[8] and sulfoxides[9,10] both in the aliphatic and alicyclic series. In contrast, epoxidation of esters[1,11] and carbonates[5g,12] of allylic alcohols proceeds either nonstereoselectively or produces predominantly *trans*-epoxides, while β,γ-unsaturated carboxylic acids afford mixtures of both cis and trans products.[13] In preliminary communications, we have described the syn epoxidation of various carbamates derived from allylic and homoallylic alcohols.[14,15] In this paper we report on the scope of this stereocontrolled epoxidation and discuss its mechanism.

Scheme I



Scheme II



Results and Discussion

As a part of a broader program aimed at developing novel stereo- and regioselective methods by employing neighboring groups to control addition reactions,[16] we have now investigated the stereochemistry of epoxidation of allylic (**5–7**, **12**, **16**, **17**, **22**, **28**, and **34**) and homoallylic (**48–50**) carbamates.[17] We have found that carbamate **5**, *N*-benzylcarbamate **6**, and *N,N*-dimethylcarbamate **7**, derived from cyclohexenol (Scheme II), are predominantly oxidized with *m*-chloroperoxybenzoic acid (MCPBA) in noncoordinating solvents (such as CH_2Cl_2 or $CHCl_3$) at 0 °C in a syn fashion to afford *cis*-epoxides **8–10**, respectively, as the major products (Table I). Cyclopentenol **11** and its *N*-benzylcarbamate **12** follow the same pattern. The configuration of the epoxides thus obtained was es-

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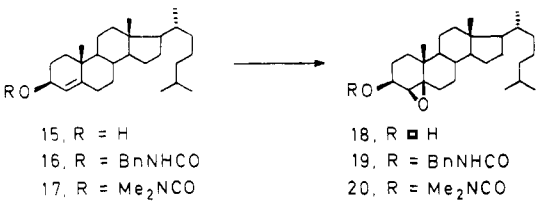
Table I. Epoxidation of Substituted Olefins with *m*-Chloroperoxybenzoic Acid

compd	substituent	product(s)	cis/trans ratio[a]	stereochemistry	ref
1	OH	2	10:1	syn	11a
5	H_2NCO_2	8	3:1	syn	-
6	$BnNHCO_2$	9	5:1	syn	-
7	Me_2NCO_2	10	10:1	syn	-
11	OH	13	>20:1	syn	-
12	$BnNHCO_2$	14	>20:1	syn	-
15	OH	18	major	syn	1
16	$BnNHCO_2$	19	>20:1	syn	-
17	Me_2NCO_2	20	>20:1	syn	-
21	OH	23 + 24	3:1	syn	21
22	$BnNHCO_2$	25 + 26	<1:10[b]	anti	-
27	OH	29	<1:10	anti	3h
28	Me_2NCO_2	30	<1:10	anti	-
33	OH	35	<1:10[c]	anti[c]	3h
34	Me_2NCO_2	36	<1:10	anti	-
39	C_2H_5OCONH	42	>20:1	syn	-
40	CH_3CONH	43	single product	syn	4g
44	CH_3CONH	45	8:1[d]	syn	-
46	OH	51 + 56	5:1	syn	27a
47	$C_6H_5CO_2$	52 + 57	1:10	anti	27b
48	H_2NCO_2	53 + 58	6:1	syn	-
49	$BnNHCO_2$	54 + 59	>10:1	syn	-
50	Me_2NCO	55 + 60	1:1	nonselective	-
64	$BnNHCOCH_2$	66 + 68	12:1	syn	-
65	$i\text{-}C_3H_7NHCOCH_2$	67 + 69	>20:1	syn	34
70	$CH_3O_2CCH_2$	71 + 72	4:1	syn	-

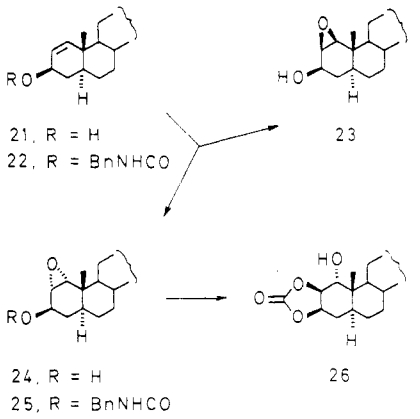
[a] Determined by high-field ^1H NMR spectra of the crude reaction product. [b] Ratio estimated; isolated yields: 69% of **25** and 27% of **26**. [c] Formation of epoxide **35** is assumed. Pure product could not be isolated as it immediately undergoes fission to polar products.[3h] [d] The minor product was not identified. The ^1H NMR spectrum of the crude mixture suggests the structure of isomeric epoxide.

Scheme III



tablished either by chemical correlation or by ^1H NMR spectra. *cis*-Epoxy carbamates **8** and **9** were prepared directly from the parent epoxy alcohol **2** by treatment with trichloroacetyl isocyanate[14b] or *N*-benzylisocyanate, respectively. Similarly, **14** was synthesized from *cis*-epoxy alcohol **13**. Although the (*N*,*N*-dimethylcarbamoyl)oxy epoxide **10** could not be obtained by analogous derivatization,[14a] its configuration was inferred from its ^1H NMR spectra. The oxirane protons appear in the range characteristic for *cis*-epoxy derivatives (br s around 3.30 ppm), while the same protons in trans isomers invariantly resonate around 3.15 ppm.

Scheme IV



In his pioneering paper, Henbest showed that the syn directing effect of hydroxy groups is strong enough to override the steric bias of the steroid skeleton,[1] whose α-side is usually less hindered,[11b,18] and to drive the epoxidation to occur predominantly from the β-side (**15** → **18**; Scheme III).[1,3h,19] Accordingly, both the *N*-benzyl-

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(2) (a) Sharpless, K. B.; Michaelson, R. C. *J. Am. Chem. Soc.* **1973**, *95*, 6136. (b) Katsuki, T.; Sharpless, K. B. *J. Am. Chem. Soc.* **1980**, *102*, 5974. (c) Gao, Y.; Hanson, R. M.; Klunder, J. M.; Ko, S. Y.; Masamune, H.; Sharpless, K. B. *J. Am. Chem. Soc.* **1987**, *109*, 5765. For reviews, see: (d) Berti, G. *Top. Stereochem.* **1973**, *7*, 93. (e) Rao, A. S.; Paknikar, S. K.; Kirtang, J. G. *Tetrahedron* **1983**, *39*, 2323. (f) Pfenninger, A. *Synthesis* **1985**, 89. (g) Dryuk, V. G. *Usp. Khim.* **1985**, *54*, 1674. (h) Finn, M. G.; Sharpless, K. B. In *Asymmetric Synthesis*; Morrison, J. D., Ed; Academic: New York, 1985; Vol. 5, p 247. (i) Kočovský, P.; Tureček, F.; Hájíček, J. *Synthesis of Natural Products: Problems of Stereoselectivity*; CRC Press: Boca Raton, FL, 1986; Vols. I and II.

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(8) Hardinger, S. A.; Fuchs, P. L. *J. Org. Chem.* **1987**, *52*, 2739.

(9) Joyce, R. P.; Galnor, J. A.; Weinreb, S. M. *J. Org. Chem.* **1987**, *52*, 1177.

(10) For other directive groups, see ref 2d and the following text.

(11) (a) Chamberlain, P.; Roberts, M. C.; Whitham, G. H. *J. Chem. Soc. B* **1970**, 1374. (b) Kirk, D. N.; Hartshorn, M. P. *Steroid Reaction Mechanisms*; Elsevier: Amsterdam, 1968.

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(14) (a) Kočovský, P. *Tetrahedron Lett.* **1988**, *29*, 2475. (b) Kočovský, P. *Tetrahedron Lett.* **1986**, *27*, 5521.

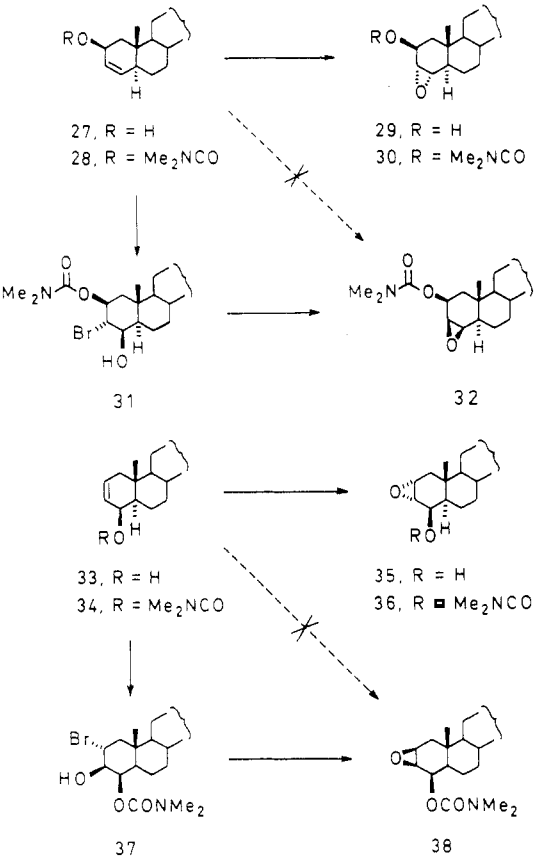
(15) For the first report on the syn epoxidation of carbamates derived from homoallylic cyclopentenols, see: Ponsold, K.; Schubert, G.; Wunderwald, M.; Tresselt, D. *J. Prakt. Chem.* **1981**, *323*, 819.

(16) (a) Kočovský, P.; Stieborová, I. *J. Chem. Soc., Perkin Trans. 1* **1987**, 1969. (b) Kočovský, P.; Starý, I.; Zajíček, J.; Tureček, F.; Vašičková, S. *J. Chem. Soc., Perkin Trans. 1* **1988**, 2297. (c) Kočovský, P. *J. Org. Chem.* **1988**, *53*, 5816. (d) Kočovský, P.; Stieborová, I. *Tetrahedron Lett.* **1989**, *30*, 4295. (e) Starý, I.; Kočovský, P. *J. Am. Chem. Soc.* **1989**, *111*, 4981.

(17) Preparation of all the model carbamates will be published separately.

(18) Fieser, L. F. *Experientia* **1950**, *6*, 312.

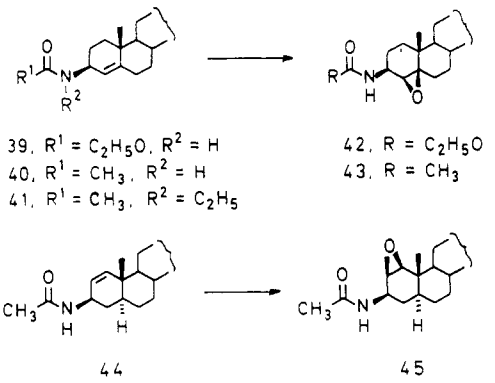
Scheme V



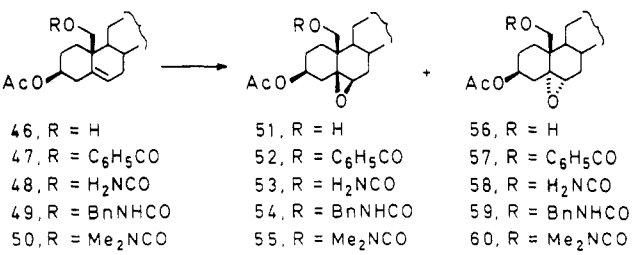
carbamate **16** and *N,N*-dimethylcarbamate **17** were found to furnish β-epoxides **19** and **20**, respectively, as the major products (Table I).[20]

Epoxidation of the isomeric allylic alcohol **21** with peroxy acids is slightly less stereoselective,[3h,21] giving a 3:1 mixture of the *cis*- and *trans*-epoxy alcohols **23** and **24** (Scheme IV), while the transition-metal-catalyzed oxidation with t-BuOOH leads solely to the corresponding α,β-unsaturated ketone.[3h] It was, therefore, of interest to probe the reactivity of a carbamate derived from **21** and to compare the relative strength of hydroxy vs carbamoyloxy group. From the previous experiments with *N*-benzylcarbamates, *N,N*-dimethylcarbamates, and N-unsubstituted carbamates (e.g. **5–7**, **16**, and **17**), it was concluded that there was not much difference in the stereocontrol of epoxidation among these allylic substrates. Hence, the most easily available *N*-benzylcarbamate **22** was selected as the probe. On treatment of the latter with MCPBA under the standard conditions, two compounds of different polarity were obtained: the lipophilic product was identified as the *trans*-epoxy carbamate **25**.[22] The polar component lacked the benzylamino group and its IR spectrum showed typical carbonyl vibration at 1808 cm^{-1} together with an OH band at 3625 cm^{-1}. Moreover, the same compound could be prepared in a quantitative yield

Scheme VI



Scheme VII



on acid treatment of the epoxide **25**, so that its structure was formulated as the carbonate **26**. Hence, it was obvious that the syn stereocontrol completely failed in the carbamate **22**, while in the parent alcohol **21** it still operated fairly well.

Further experiments were carried out with carbamates **28** and **34**, in order to gain additional information on the scope of the syn stereodirecting effect of the carbamoyloxy group. The parent alcohols **27** and **33** are known[3h] to produce stereoselectively α-epoxides **29** and **35**, respectively. This steric course appears to be a consequence of severe steric congestion of the β-side by the angular methyl which prevents the coordination of peroxy acid to the hydroxy group. In accord with the behavior of carbamate **22**, the carbamates **28** and **34** also gave α-epoxides **30** and **36**, respectively, as the major products (Scheme V). The structure of **30** was elucidated by combination of ^1H NMR spectra and chemical correlation. The coupling constants of 2-H, 3-H, and 4-H in the ^1H NMR spectrum of **30** are identical with those of **29**.[3h] Moreover, the diastereoisomeric β-epoxide **32** was prepared for comparison in two steps from olefin **28** through addition of hypobromous acid followed by alkali treatment ($KHCO_3$). The coupling pattern of 2-H, 3-H, and 4-H in the spectrum of the epoxide prepared in this way was entirely different from that of **29** and **30**. Similar arguments can be applied for **36** and **38** (details are given in the Experimental Section).

Since the above experiments indicated that the stereodirecting efficacy of the carbamoyloxy groups was lower than that of the hydroxy group, we set out to explore the stereochemistry of epoxidation of acylated allylic amines as their congeners. To this end, we prepared carbamate **39** and amides **40**,[4g] **41**, and **44** (Scheme VI). Both **39** and **40** gave on MCPBA treatment the corresponding β-epoxides **42** and **43**,[4g] respectively, as the sole products. To our surprise, the *N*-ethylacetamide **41** turned out to be inert to MCPBA or trifluoroperoxyacetic acid at room temperature for a week. Refluxing with MCPBA in 1,2-dichloromethane led to a gradual decomposition and formation of polar products. This behavior is in agreement with the recent observation by Rottela,[5f] who has also

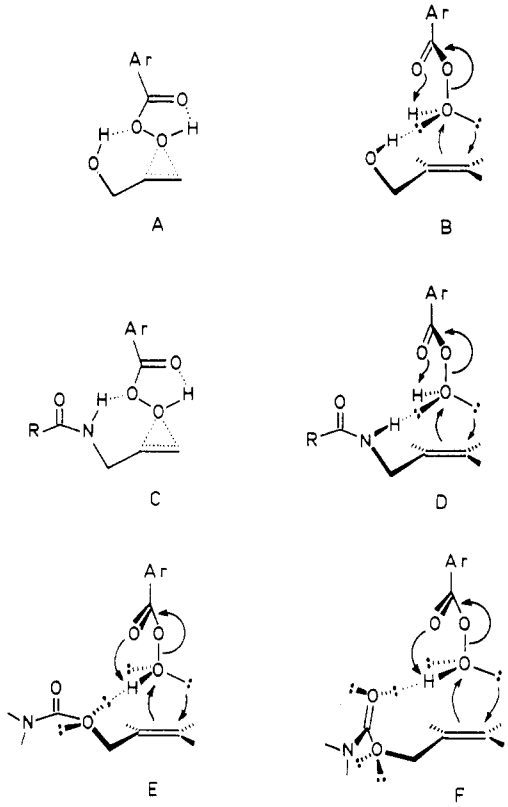
(19) Loughhead, D. G. *J. Org. Chem.* **1985**, *50*, 3931.

(20) Coupling constants of 4-H ($J_{3\alpha,4\alpha} \cong 4$ Hz) in ^1H NMR spectra are diagnostic for the configuration assignment; see: Collins, D. J.; Hobbs, J. J. *Tetrahedron Lett.* **1963**, 623. Moreover, **19** could be obtained from **18** on reaction with BnN=C=O, although in a low yield.

(21) (a) Glotter, E.; Krinsky, P. *J. Chem. Soc., Perkin Trans. 1* **1978**, 408. (b) Weissenberg, M.; Lavie, D.; Glotter, E. *Tetrahedron* **1973**, *29*, 535.

(22) Coupling constants of 1-H, 2-H, and 3-H in the ^1H NMR spectrum of **25** were identical with those in the spectrum of an authentic sample of *trans*-epoxy alcohol **24**, while distinctly different from the coupling pattern in the *cis*-epoxy alcohol **23** (see also ref 21).

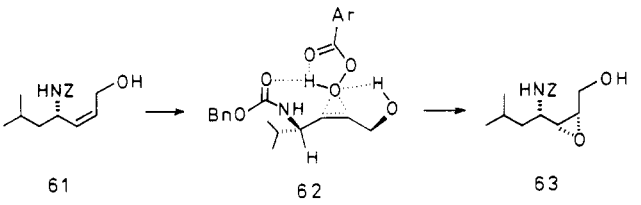
Chart I



noticed that unsaturated N,N'-disubstituted carbamates did not react with MCPBA. The 1,2-unsaturated acetamide **44** afforded mainly β-epoxide **45** (8:1) on reaction with MCPBA. In this case, the acetamido group surpassed hydroxyl (see the related alcohol **21**) in the capability of syn stereocontrol of epoxidation.[23]

The stereocontrolled epoxidation due to the adjacent hydroxy group is not confined to allylic alcohols. A search of literature reveals numerous examples[2i,24] of successful OH-directed epoxidation of homoallylic[25] and bishomoallylic[26] alcohols. Thus, for instance, the homoallylic alcohol **46** (Scheme VII) with hydroxy group sticking above the π-system of 5,6-double bond is known to steer the approaching peroxy acid[27] or t-BuOOH/$(acac)_2VO$[3h] from the β-side, which results in the predominant or exclusive formation of 5β,6β-epoxide **51** (Table I). On the other hand, esterification of the hydroxy group (as in **47**) reverts the steric course of epoxidation back to the sterically favored α-side.[27] We have now found that carbamate **48** and

Scheme VIII



N-benzylcarbamate **49** also ensured the β-face epoxidation producing preferentially the respective 5β,6β-epoxides **53** and **54** (Scheme VII). Note that both the carbamates **48** and **49** furnish a slightly higher cis/trans ratio than does the parent alcohol **46** (Table I). This neighboring group effect is, however, remarkably less manifested with the *N*,*N*-dimethylcarbamate **50**, which affords a 1:1 mixture of epoxides **55** and **60**. Assignment of the configuration again relies on the combination of chemical and spectroscopic methods. Epoxy carbamates **53** and **54** were prepared from the *cis*-epoxy alcohol **51** by derivatization. Moreover, optical rotations for 5β,6β-epoxides are generally much less negative than those for their 5α,6α-diastereoisomers. Since the *N*,*N*-dimethylcarbamate **55** could not be obtained directly from **51**, the configuration was deduced from ^1H NMR spectra: the coupling constant of 6-H in **55** (J = 1.5 Hz) lies in the range for 5β,6β-epoxides (<2.0 Hz) while for **60** (J = 4.0 Hz) corresponds to the values typical for 5α,6α-epoxides (>3.0 Hz). Furthermore, 5β,6β-epoxides exhibit characteristic downfield shift of the signals of 19-H compared to their 5α,6α-counterparts.

Our findings indicate that the carbamate group can serve as an alternative to the hydroxyl in the steric control of epoxidation, although it appears to be slightly weaker. This behavior raises the question as to the mechanism. The steering effect of hydroxy group was attributed by Henbest to the hydrogen bonding between OH and the reagent (A in Chart I)[1] employing O(2) of peroxy acid as the acceptor. Since then this mechanism has been widely accepted.[2d-i] Later, Whitham et al.[11a] suggested alternative OH bonding to the carbonyl oxygen, i.e. to O(3). Finally, detailed analysis of stereoelectronic effects led Sharpless[28] to the formulation of mechanism B, according to which the allylic OH is coordinated to O(1), whose remaining lone pair becomes thus favorably aligned with the π-system of the double bond. Roush et al.[5a] have rationalized the syn epoxidation of allylic amides[4g,5a,6] by analogous NH bonding (C). In light of the Sharpless mechanism B we feel that the Roush scheme can be modified as indicated in D. Our carbamates, however, represent a rather different class of allylic compounds. Although N–H bonding to the reagent can still be assumed for N-unsubstituted (**5**) and *N*-benzyl (**6**) derivatives, the (*N*,*N*-dimethylcarbamoyl)oxy group in **7** or **17** cannot offer any OH or NH. In spite of that the latter group is also capable of controlling the epoxidation in a syn fashion. To account for this behavior we have recently proposed an alternative mechanism assuming the hydrogen bonding in a reversed way, i.e. from the molecule of peroxy acid to the carbamate group of the substrate.[14a] In view of its ambident character, both the ether (E) and the carbonyl oxygen (F) of the carbamoyloxy group can be considered as the acceptor for the hydrogen bonding. Neither the former nor the latter way of steering a peroxy acid is unprecedented. Thus, examples have been reported on epoxidation directed by alkoxy groups[29] and ketone carbonyl.[30] Fur-

(23) For further examples of stronger directive properties of amide group than that of hydroxyl, see refs 4c, 4f.

(24) Arcoria, A.; Ballstreri, F. P.; Tomaselli, G. A.; DiFuria, F.; Modena, G. *J. Org. Chem.* **1986**, *51*, 2375.

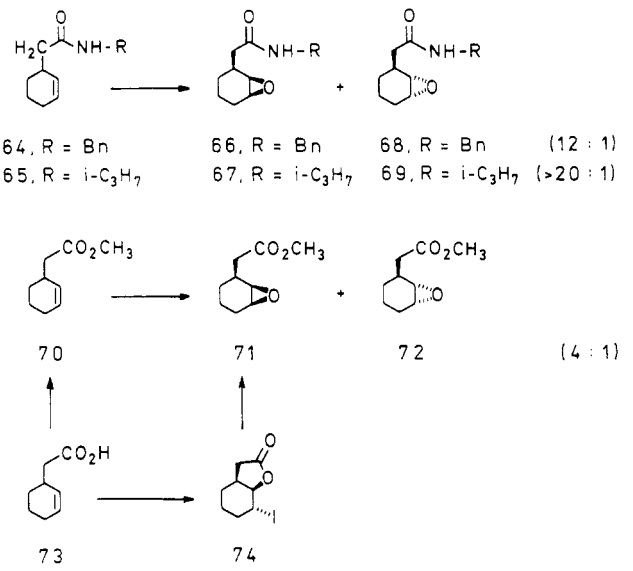
(25) (a) Michelich, E. D.; Daniels, K.; Eickhoff, D. J. *J. Am. Chem. Soc.* **1981**, *103*, 7690. (b) Rossiter, B. E.; Sharpless, K. B. *J. Org. Chem.* **1984**, *49*, 3707. (c) Miyashita, M.; Suzuki, T.; Yoshikoshi, A. *J. Org. Chem.* **1985**, *50*, 3377. (d) Roush, W. R.; Michaelides, M. R. *Tetrahedron Lett.* **1986**, *27*, 3353. (e) Hanamoto, T.; Katsuki, T.; Yamaguchi, M. *Tetrahedron Lett.* **1987**, *28*, 6191. (f) Barrish, J. C.; Lee, H. L.; Mitt, T.; Pizzolato, G.; Baggiolini, E. G.; Uskokovic, M. R. *J. Org. Chem.* **1988**, *53*, 4282. (g) Braish, T. F.; Saddler, J. C.; Fuchs, P. L. *J. Org. Chem.* **1988**, *53*, 3647. (h) Lipshutz, B. H.; Barton, J. C. *J. Org. Chem.* **1988**, *53*, 4495.

(26) (a) Fukuyama, T.; Vranesic, B.; Negri, D. P.; Kishi, Y. *Tetrahedron Lett.* **1978**, 2741. (b) Itoh, T.; Jitsukawa, K.; Kaneda, K.; Teranishi, S. *J. Am. Chem. Soc.* **1979**, *101*, 159. (c) Hashimoto, M.; Kan, T.; Nozaki, K.; Yanagiya, M.; Shirahama, H.; Matsumoto, T. *Tetrahedron Lett.* **1988**, *29*, 1143.

(27) (a) Fraser, R. R.; Kaufman, M.; Morand, P.; Govil, G. *Can. J. Chem.* **1969**, *47*, 403. (b) Joska, J.; Fajkoš, J. *Collect. Czech. Chem. Commun.* **1978**, *43*, 3433. (c) Mousseron-Canet, M.; Labeeuw, B.; Lanet, J. C. *Bull. Soc. Chim. Fr.* **1968**, 2125.

(28) Sharpless, K. B.; Verhoeven, T. R. *Aldrichimica Acta* **1979**, *12*, 63.

Scheme IX

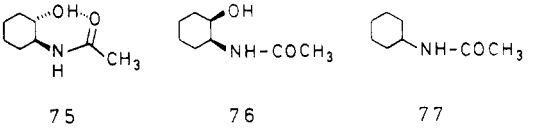


thermore, cooperative effect[31] of a carbonyl group was postulated by Kogen and Nishi[5b] to account for the high diastereoselectivity of epoxidation of the unsaturated hydroxy carbamate **61** (Scheme VIII). It was therefore desirable to bring further experimental material in order to address the question as to which of the two oxygen centers in the carbamoyloxy group acts as the proton acceptor and steers the approach of peroxy acid.

Amide **64** can be considered as the "carba" analogue for the carbamate **6** and should provide the desired evidence. If the carbonyl oxygen in **6** were responsible for the steering effect (F), amide **64** should also afford the *cis*-epoxide as the major product. On the other hand, if the steering in **6** were due to the ether oxygen (E), we could anticipate predominant formation of a *trans*-epoxide in this case or a nonstereoselective reaction.

Amide **64** was prepared from the known[32] acid **73** by standard amidation with benzylamine using *N,N'*-dicyclohexylcarbodiimide (DCC) and 1-hydroxybenzotriazole. On treatment with MCPBA the amide **64** produced a mixture of two epoxides in a 12:1 ratio.[33a] Similarly, ester **70** afforded two epoxides in a 4:1 ratio.[33b] Since the configuration of the products could not be unequivocally assessed from the NMR spectra, a chemical correlation was required. The acid **73** was converted to iodo lactone **74**, which on reaction with sodium methoxide gave *cis*-epoxide **71** as a pure product (Scheme IX). The latter compound turned out to be identical with the major product from the epoxidation of methyl ester **70**. Comparison of the high-field ^1H NMR and ^{13}C NMR spectra of **71**, whose cis configuration was ascertained by the chemistry of its formation, with the spectra of the two epoxy amides arising from **64**, revealed close analogies in the spectra of the major product, while the spectra of the minor isomer were considerably different: the diagnostic coupling constant between 2'-H and 3'-H in **71** (2.2 Hz) correlate well with the coupling in the major product (2.5 Hz). Also the shifts in ^{13}C NMR spectra are similar in these two compounds. The major isomer thus can be assigned cis configuration (**66**), while the minor product should be the *trans*-epoxide **68**.

Chart II



When this work was in progress a paper by Mohamadi and Spees appeared,[34] dealing with the stereochemistry of closely related isopropyl amide **65**. In consonance with our findings, they also observed the MCPBA epoxidation occurring mostly in a syn fashion (>20:1).[34,35]

These observations strongly support the mechanism F according to which the carbonyl oxygen of the carbamoyloxy and amido group serves as the acceptor for bonding the molecule of peroxy acid and is thus responsible for the pronounced syn steering. Lower syn/anti ratio in the epoxidation of ester **70** may be attributed to the lower basicity (and nucleophilicity[16a,36]) of the carbonyl oxygen in ester group. It appears that the increased coordination capability of the carbonyl oxygen in carbamates and amides stems from the strong donation by nitrogen, as reflected in general increase of the nucleophilicity of carbamate vs ester groups in other reactions.[5g,16a] There are two possible acceptor sites at the carbonyl oxygen for hydrogen bonding, namely π-electrons and 2p orbital. In view of the fact that, e.g., IR spectra of hydroxy carbonyl compounds indicate much higher basicity of the 2p orbital,[37] we believe that the latter is responsible also for coordination of the molecule of peroxy acid. Participation of the nitrogen lone pair in coordination does not seem probable in light of the general reactivity of carbamate and amide groups[16a] and in view of the similar syn directive effect of the ester group. Further evidence for the preferential C=O participation can be inferred from IR spectrum of vicinal acetamidocyclohexanol **75** (Chart II).[38] The spectrum of **75** shows ν_{OH} = 3598 cm^{-1}, indicating strong intramolecular bonding, ν_{NH} = 3443 cm^{-1}, and a shifted carbonyl frequency ν_{CO} = 1670 cm^{-1}. Reference compounds **76** and **77**, where no OH bonding is encountered, exhibit ν_{CO} = 1677 cm^{-1} (both **76** and **77**) and ν_{NH} = 3445 cm^{-1} (**76**) and ν_{NH} = 3446 cm^{-1} (**77**), while only the free OH group is seen in the spectrum of **76** (ν_{OH} = 3629

(29) (a) McKittrick, B. A.; Ganem, B. *Tetrahedron Lett.* **1985**, *26*, 4895. (b) Černý, V.; Kočovský, P. *Collect. Czech. Chem. Commun.* **1982**, *47*, 3062. For discussion of the steric course of epoxidation of allylic alkoxy derivatives, see ref 11a and: (c) Barili, P. L.; Bellucci, G.; Berti, G.; Golfarini, M.; Marioni, F.; Scartoni, V. *Gazz. Chim. Ital.* **1974**, *104*, 107. (d) Cahn, S. D.; Pau, C. F.; Chamberlin, A. R.; Hehre, W. J. *J. Am. Chem. Soc.* **1987**, *109*, 650. (e) Kahn, S. D.; Hehre, W. J. *J. Am. Chem. Soc.* **1987**, *109*, 666. (f) Chamberlin, A. R.; Mullholland, R. J., Jr.; Kahn, S. D.; Hehre, W. J. *J. Am. Chem. Soc.* **1987**, *109*, 672.

(30) (a) Takeda, K.; Hamamoto, K.; Sasaki, K.; Maezono, N.; Murabayashi, A. *Steroids* **1963**, *2*, 27. (b) Černý, V.; Buděšínský, M.; Ryba, M.; Tureček, F. *Collect. Czech. Chem. Commun.* **1988**, *53*, 1549.

(31) Johnson, M. R.; Kishi, Y. *Tetrahedron Lett.* **1979**, 4347.

(32) (a) Youssef, A. A.; Sharaf, S. M. *J. Org. Chem.* **1968**, *33*, 2581. (b) Tureček, F. *Collect. Czech. Chem. Commun.* **1982**, *47*, 858.

(33) (a) Determined by ^1H NMR measurement of the crude mixture. Preparative chromatographic separation gave a 9:1 ratio. (b) Determined by ^1H NMR measurement of the crude mixture.

(34) Mohamadi, F.; Spees, M. M. *Tetrahedron Lett.* **1989**, *30*, 1309.

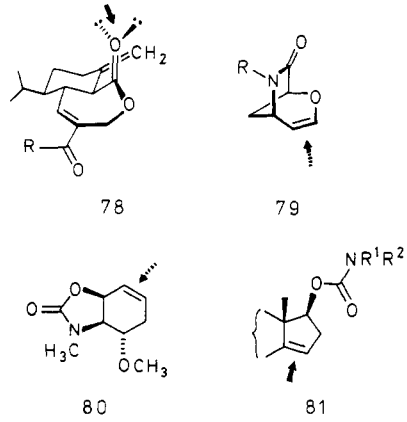
(35) Similarly, isopropyl ester of **73** afforded ca 3:1 mixture of *cis*- and *trans*-epoxides.[34]

(36) For further comparison of the effective nucleophilicity of various groups in the intramolecular reactions, see e.g.: (a) Kočovský, P.; Tureček, F. *Tetrahedron* **1983**, *21*, 3621. (b) Kurth, M. J.; Beard, R. L.; Olmstead, M.; Macmillan, J. G. *J. Am. Chem. Soc.* **1989**, *111*, 3712. For discussion of hydrogen bonding to the carbonyl oxygen, see: (c) Murray-Rust, P.; Glusker, J. P. *J. Am. Chem. Soc.* **1984**, *106*, 1018 and references cited therein.

(37) (a) Suga, T.; Imamura, K.; von Rudolf, E. *J. Chem. Soc., Perkin Trans. 1* **1972**, 962. For discussion, see: (b) Golfier, M. In *Stereochemistry*; Kagan, H. B., Ed.; Thieme: Stuttgart, 1977; Vol. 1, p 39. (c) Tichý, M. *Adv. Org. Chem.* **1965**, *5*, 115. (d) For the ab initio calculation of hydrogen bonding to formamide, see: Jaisen, P. G.; Stevens, W. J. *J. Chem. Phys.* **1986**, *84*, 3271.

(38) (a) Staněk, J., Jr. Thesis, Charles University, Prague, 1974. (b) Smolíková, J.; Vítek, A.; Bláha, K. *Collect. Czech. Chem. Commun.* **1973**, *38*, 548.

Chart III



cm^{-1}). Thus the frequency of C=O in **75** is significantly shifted, while its NH appears roughly in the same region as observed with **76** and **77**. These results can be interpreted as more evidence for the higher basicity of the carbonyl oxygen vs the nitrogen lone pair in an amido group and hence the higher propensity of the former to coordinate the molecule of peroxy acid by OH bonding.

Another mechanism can involve Coulombic interaction of the electrophile with the nucleophilic allylic center, where the negative electrostatic potential in the most reactive conformation[29d-f] is created by the π-system of the double bond and the carbonyl oxygen. Further experiments involving other electrophiles will be needed to shed light onto this issue.

Our results are, however, in conflict with the observation by Julia and Fürer,[5g] who have reported that *N*-phenylcarbamate derived from **15** (R = C_6H_5NHCO) gave preferentially the 4α,5α-epoxide on peroxy acid oxidation. The opposite stereochemistry of epoxidation in this case and the absence of syn control could be rationalized, by assuming that aromatic conjugation will result in decreasing the propensity of carbonyl oxygen to coordinate the reagent. The steric course of epoxidation will then be controlled by normal steric bias of the skeleton.[39]

Additional support for operating of the carbonyl steering of the peroxy acid approach can be found by analyzing the literature data. Thus, for instance, ester **78** (Chart III) is approached by MCPBA from β-side (syn to the ester carbonyl), while the Mo(0)-catalyzed epoxidation with t-BuOOH proceeds from α-side.[40] Although other effects can operate in this instance,[41] it is not unreasonable to consider hydrogen bonding of the peroxy acid molecule to the carbonyl oxygen, which is very close to the π-system of the double bond. On the other hand, in rigid structures of amide **79**[42] and carbamate **80**[43] where the carbonyl oxygen (and particularly the p orbital) is remote from the double bond, epoxidation is apparently directed by ordinary steric effects, which prefer epoxidation from the concave side of the respective molecules. In contrast, homoallylic carbamate **81** with a flexible steering group adheres again to the syn epoxidation[15] in spite of the large steric hindrance imposed by the angular methyl group.

Regardless of the detailed mechanism of the above epoxidation, carbamoyloxy epoxides in general are useful intermediates for organic synthesis, both in aliphatic and alicyclic series.[5,44] In principle, they can be prepared in a reversed way, i.e. by epoxidation of allylic or homoallylic alcohols followed by derivatization with the corresponding isocyantes. Although this method seems reasonably reliable and has found numerous applications to the synthesis of natural products, there are examples where it fails, as some epoxy alcohols do not cleanly react with isocyanates (particularly **18**). Furthermore, preparation of (*N*,*N*-dimethylcarbamoyl)oxy epoxides **10**, **20**, **30**, **32**, **36**, **38**, **55**, and **60** from the corresponding epoxy alcohols would require drastic conditions (Me_2NCOCl + BuLi)[14a,45] that are not compatible with this sensitive functionality. Our stereoselective epoxidation of carbamates thus seems to be a useful alternative to the classical approach. Since the carbamate groups have been frequently employed to control opening of the oxirane ring,[44] we believe that our stereocontrolled epoxidation could also find synthetic application.[46] On top of it, the carbonyl-directed epoxidation of amides of γ,δ-unsaturated carboxylic acids seems particularly promising.

Conclusion

We have found a syn stereodirecting effect of allylic and of certain homoallylic carbamate groups in peroxy acid epoxidation, similar to that of hydroxyl, although slightly weaker. We have presented a mechanism based on our experimental data which favors coordination of the reagent to the carbonyl oxygen (F) rather than the ether oxygen of this ambident neighboring group. Accordingly, epoxidation of γ,δ-unsaturated amides also occurs in a syn fashion.

Experimental Section

Materials and Equipment. Melting points (uncorrected) were obtained on a Kofler block. Optical rotations were measured in $CHCl_3$ with an error of +3 °C. The infrared spectra were obtained on a Perkin-Elmer 621 instrument in CCl_4. ^1H NMR spectra were measured on Varian VXR 400, Varian XL-200, and Tesla BS 476 (60 MHz) instruments in $CDCl_3$ at 25 °C. Chemical shifts are given in δ values (ppm) relative to the signal of tetramethylsilane (δ = 0.00). Apparent coupling constants were obtained from the first-order analysis. Standard workup of an ethereal solution means washing with 5% HCl (aqueous), water, and 5% $KHCO_3$ (aqueous), drying with Na_2SO_4, and evaporation of the solvent in vacuo. Petroleum ether refers to the fraction boiling in the range 40–60 °C. The identity of samples prepared by different routes was checked by mixed melting point determination, TLC, and IR and NMR spectra. Yields are given in milligrams of isolated product showing one spot on chromatographic plate and no trace of impurities detectable in the NMR spectrum. Product ratios in epoxidation reactions were determined from ^1H NMR spectra of the crude reaction mixtures.

General Procedure for Epoxidation with *m*-Chloroperoxybenzoic Acid. The unsaturated carbamate (0.5 mmol) was dissolved in chloroform or dichloromethane (5 mL) and treated with *m*-chloroperoxybenzoic acid (0.6 mmol) at 0 °C for 30 min to 2 h (depending on the reactivity). The mixture was diluted

(39) Another example of the stereoselective epoxidation of an unsaturated amide was rationalized by intervention of other functional group (MeO) in the molecule rather than by the direct effect of amide group: Bucourt, R.; Clapier, P.; Guénard, D.; Thal, C. *Tetrahedron Lett.* **1989**, *30*, 3973 and references given therein.

(40) Danishefsky, S. J.; Mantlo, N. *J. Am. Chem. Soc.* **1988**, *110*, 8129.

(41) (a) Sevin, A.; Cense, J.-M. *Bull. Soc. Chim. Fr.* **1974**, 963. (b) Carlson, R. G.; Behn, N. S. *J. Org. Chem.* **1967**, *32*, 1363. See also discussion in ref 40.

(42) Knapp, S.; Levorse, A. T.; Potenza, J. A. *J. Org. Chem.* **1988**, *53*, 4773.

(43) Knapp, S.; Sebastian, M. J.; Ramanathan, H. *J. Org. Chem.* **1983**, *48*, 4788.

(44) (a) Minami, M.; Ko, S. S.; Kishi, Y. *J. Am. Chem. Soc.* **1982**, *104*, 1109. (b) Roush, W. R.; Di Mare, M. *J. Org. Chem.* **1983**, *48*, 5083. (c) Roush, W. R.; Brown, W. R. *J. Org. Chem.* **1983**, *48*, 5093. (d) Roush, W. R.; Adam, M. A. *J. Org. Chem.* **1985**, *50*, 3752.

(45) Overman, L. E.; Campbell, C. B.; Knoll, F. M. *J. Am. Chem. Soc.* **1978**, *100*, 4822.

(46) Attempted epoxidation of **5–7**, **48**, and **49** with $(acac)_2VO$ and TBHP or $Mo(CO)_6$ and TBHP in CH_2Cl_2 or C_6H_6 either at room temperature or at reflux gave no reaction, whereas the use of $(i\text{-}PrO)_4Ti$ and TBHP at elevated temperature led to complex mixtures of products.

with dichloromethane, washed with 5% $KHCO_3$ (aqueous), 5% $Na_2S_2O_3$ (aqueous), and water, and dried with Na_2SO_4, and the solvent was evaporated. The residue was chromatographed on a column of silica gel (10 g) with a benzene–ether mixture (97:3) as eluant or on three preparative silica gel plates (20 × 20 cm) using a petroleum ether–ether–acetone mixture (80:10:10 or 75:15:10) as developer. The yields of pure products are given in the text. The physical and analytical data for new compounds are listed below.

General Procedure for Preparation of Carbamoyloxy Epoxides from Epoxy Alcohols. To a solution of epoxy alcohol (0.5 mmol) in dry benzene or CH_2Cl_2 (4 mL) was added trichloroacetyl isocyanate (0.6 mmol) in benzene (1 mL) under argon atmosphere, and the mixture was stirred at 0 °C for 30 min. The solution was then soaked into a pad of aluminum oxide (neutral, activity II, Brockmann), and after 5 min the product was washed using a mixture of C_6H_6–CH_2Cl_2 (2:1) as eluant. The filtrate was evaporated in vacuo to give pure carbamates **8** (84%) **53** (70%), and **58** (41%), respectively.

General Procedure for Preparation of (*N*-Benzylcarbamoyl)oxy Epoxides from Epoxy Alcohols. To a solution of epoxy alcohol (0.5 mmol) in benzene or CH_2Cl_2 (5 mL) was added *N*-benzyl isocyanate (0.7 mmol) in benzene (1 mL), and the mixture was set aside under argon atmosphere at room temperature for 2 days. The mixture was then concentrated on rotary evaporator and filtered through a pad of aluminum oxide. The residue was chromatographed on two preparative plates of silica (20 × 20 cm) using petroleum ether–ether–acetone mixture (80:10:10) as developer. Zones containing the desired products were collected, the products were eluted with ether, and the ethereal solutions were evaporated to afford pure *N*-benzylcarbamates **9** (59%), **14** (64%), **19** (26%), and **54** (31%).

(1*R,2*S**,3*S**)-1-(Carbamoyloxy)-2,3-epoxycyclohexane (8)**: mp 132–133 °C; ^1H NMR 3.32 (br s, 2 H, 2-H and 3-H), 4.92 (m, $W/2$ = 22 Hz, 2 H, NH_2), 5.05 (m, $W/2$ = 18 Hz, 1 H, 1-H).

Anal. Calcd for $C_7H_{11}NO_3$: C, 53.49; H, 7.05; N, 8.91. Found: C, 53.27; H, 7.18; N, 8.75.

(1*R,2*S**,3*S**)-1-((*N*-Benzylcarbamoyl)oxy)-2,3-epoxycyclohexane (9)**: mp 87–89 °C; ^1H NMR 3.28 (d, J = 1.5 Hz, 2 H, 2-H and 3-H), 4.33 (d, J = 6 Hz, 2 H, CH_2NH), 5.08 (m, $W/2$ = 17 Hz, 1-H and NH), 7.25 (br s, 5 H, C_6H_5).

Anal. Calcd for $C_{13}H_{15}NO_3$: C, 66.94; H, 6.48; N, 6.00. Found: C, 66.63; H, 6.72; N, 5.81.

(1*R,2*S**,3*S**)-1-((*N*,*N*-Dimethylcarbamoyl)oxy)-2,3-epoxycyclohexane (10)**: ^1H NMR 2.90 (s, 6 H, Me_2N), 3.28 (d, J = 1.5 Hz, 2 H, 2-H and 3-H), 5.03 (t, J = 6.5 Hz, 1 H, 1-H).

Anal. Calcd for $C_9H_{15}NO_3$: C, 58.36; H, 8.16; N, 7.56. Found: C, 58.14; H, 8.30; N, 7.41.

(1*R,2*S**,3*S**)-1-((*N*-Benzylcarbamoyl)oxy)-2-methyl-2,3-epoxycyclopentane (14)**: mp 75–77 °C; ^1H NMR 1.28 (s, 3 H, CH_3), 3.28 (br s, 1 H, 3-H), 4.37 (d, J = 6 Hz, 2 H, CH_2NH), 5.05 (m, W = 25 Hz, 2 H, 1-H and NH), 7.28 (s, 5 H, C_6H_5).

Anal. Calcd for $C_{13}H_{15}NO_3$: C, 66.94; H, 6.48; N, 6.00. Found: C, 66.78; H, 6.32; N, 5.82.

3β-((*N*-Benzylcarbamoyl)oxy)-4β,5-epoxy-5β-cholestane (19): $[\alpha]_D$ +7° (*c* 3.0); ^1H NMR 0.66 (s, 3 H, 18-H), 1.04 (s, 3 H, 19-H), 3.21 (d, J = 3.5 Hz, 1 H, 4α-H), 4.37 (d, J = 6 Hz, 2 H, CH_2NH), 4.94 (m, W = 30 Hz, 1 H, 3α-H), 5.14 (m, $W/2$ = 14 Hz, 1 H, NH), 7.30 (s, 5 H, C_6H_5).

Anal. Calcd for $C_{35}H_{53}NO_3$: C, 78.46; H, 9.97; N, 2.61. Found: C, 78.69; H, 10.20; N, 2.35.

3β-((*N*,*N*-Dimethylcarbamoyl)oxy)-4β,5-epoxy-5β-cholestane (20): mp 89–91 °C; $[\alpha]_D$ +2° (*c* 2.0); ^1H NMR 0.68 (s, 3 H, 18-H), 1.03 (s, 3 H, 19-H), 2.91 (s, 6 H, Me_2N), 3.17 (d, J = 3.0 Hz, 1 H, 4α-H), 5.00 (m, W = 22 Hz, 1 H, 3α-H).

Anal. Calcd for $C_{30}H_{51}NO_3$: C, 76.06; H, 10.85; N, 2.96. Found: C, 75.91; H, 10.97; N, 3.15.

3β-((*N*-Benzylcarbamoyl)oxy)-1α,2α-epoxy-5α-cholestane (25): mp 137–139 °C; $[\alpha]_D$ +18° (*c* 2.8); ^1H NMR 0.66 (s, 3 H, 18-H), 0.93 (s, 3 H, 19-H), 3.07 (s, 2 H, 1β-H and 2β-H), 4.37 (d, J = 6 Hz, 2 H, CH_2NH), 5.00 (m, W = 40 Hz, 2 H, 3α-H and NH), 7.30 (s, 5 H, C_6H_5).

Anal. Calcd for $C_{35}H_{53}NO_3$: C, 78.46; H, 9.97; N, 2.61. Found: C, 78.19; H, 10.25; N, 2.49.

5α-Cholestane-1α,2β,3β-triol 2,3-carbonate (26): mp 173–174 °C; $[\alpha]_D$ +17° (*c* 2.2); ^1H NMR 0.66 (s, 3 H, 18-H), 0.92 (s, 3 H, 19-H), 4.10 (d, J = 1.8 Hz, 1 H, 1β-H), 4.66 (dd, J = 6.5 and 1.8 Hz, 1 H, 2α-H), 4.79 (m, W = 30 Hz, 1 H, 3α-H); IR 1808, 3625 cm^{-1}.

Anal. Calcd for $C_{28}H_{46}O_4$: C, 75.29; H, 10.38. Found: C, 75.03; H, 10.57.

2β-((*N*,*N*-Dimethylcarbamoyl)oxy)-3α,4α-epoxy-5α-cholestane (30): mp 102–105 °C; $[\alpha]_D$ +2° (*c* 2.8); ^1H NMR 0.65 (s, 3 H, 18-H), 0.91 (s, 3 H, 19-H), 2.81 (d, J = 3.5 Hz, 1 H, 4β-H), 2.93 (s, 6 H, Me_2N), 3.16 (d, J = 3.5 Hz, 1 H, 3β-H), 5.27 (d, J = 5.5 Hz, 1 H, 2α-H).

Anal. Calcd for $C_{30}H_{51}NO_3$: C, 76.06; H, 10.85; N, 2.96. Found: C, 75.77; H, 10.94; N, 2.70.

2β-((*N*,*N*-Dimethylcarbamoyl)oxy)-3α-bromo-5α-cholestan-4β-ol (31): mp 165–167 °C; ^1H NMR 0.65 (s, 3 H, 18-H), 1.20 (s, 3 H, 19-H), 2.91 (s, 6 H, Me_2N), 3.97 (m, $W/2$ = 6 Hz, 1 H, 4α-H), 4.35 (m, $W/2$ = 5.5 Hz, 1 H, 3β-H), 5.20 (m, $W/2$ = 8.5 Hz, 1 H, 2α-H); IR 1193, 1695, 3440 (OH, intramol bond), 3622 cm^{-1}.

Anal. Calcd for $C_{30}H_{52}NO_3$: C, 64.96; H, 9.45; Br, 14.41. Found: C, 64.69; H, 9.68; Br, 14.72.

2β-((*N*,*N*-Dimethylcarbamoyl)oxy)-3β,4β-epoxy-5α-cholestane (32): mp 170–171 °C; ^1H NMR 0.63 (s, 3 H, 18-H), 1.10 (s, 3 H, 19-H), 2.93 (s, 6 H, Me_2N), 3.06 (d, J = 4 Hz, 1 H, 4α-H), 3.39 (t, J = 4 Hz, 1 H, 3α-H), 5.23 (m, W = 18 Hz, 1 H, 2α-H).

Anal. Calcd for $C_{30}H_{51}NO_3$: C, 76.06; H, 10.85; N, 2.96. Found: C, 75.83; H, 10.99; N, 2.76.

4β-((*N*,*N*-Dimethylcarbamoyl)oxy)-2α,3α-epoxy-5α-cholestane (36): mp 110–112 °C; $[\alpha]_D$ +34° (*c* 3.0); ^1H NMR 0.64 (s, 3 H, 18-H), 0.97 (s, 3 H, 19-H), 2.94 (s, 6 H, Me_2N), 3.20 (d, J = 3 Hz, 2 H, 2β-H and 3β-H), 5.18 (m, $W/2$ = 6 Hz, 1 H, 4α-H).

Anal. Calcd for $C_{30}H_{51}NO_3$: C, 76.06; H, 10.85; N, 2.96. Found: C, 75.89; H, 11.02; N, 2.71.

3α-Bromo-4β-((*N*,*N*-dimethylcarbamoyl)oxy)-5α-cholestan-2β-ol (37): mp 174–175 °C, $[\alpha]_D$ +13° (*c* 3.0); ^1H NMR 0.66 (s, 3 H, 18-H), 1.23 (s, 3 H, 19-H), 2.92 (s, 6 H, Me_2N), 4.22 (q, J = 4 Hz, 1 H, 2α-H), 4.36 (t, J = 3 Hz, 1 H, 3β-H), 5.07 (t, J = 3 Hz, 1 H, 4α-H); IR 1687, 1709, 3583 (OH, intramol bond), 3620 cm^{-1}.

Anal. Calcd for $C_{30}H_{52}BrNO_3$: C, 64.96; H, 9.45; Br, 14.41. Found: C, 64.70; H, 9.68; Br, 14.62.

4β-((*N*,*N*-Dimethylcarbamoyl)oxy)-2β,3β-epoxy-5α-cholestane (38): mp 115–117 °C; $[\alpha]_D$ +68° (*c* 2.6); ^1H NMR 0.63 (s, 3 H, 18-H), 1.05 (s, 3 H, 19-H), 2.93 (s, 6 H, Me_2N), 3.25 (m, $W/2$ = 5.5 Hz, 1 H, 2α-H), 3.48 (dd, J = 4 and 5 Hz, 1 H, 3α-H), 5.03 (t, J = 5 Hz, 1 H, 4α-H).

Anal. Calcd for $C_{30}H_{51}NO_3$: C, 76.06; H, 10.85; N, 2.96. Found: C, 75.81; H, 11.06; N, 3.28.

3β-(Carbethoxyamino)-4β,5-epoxy-5β-cholestane (42): $[\alpha]_D$ +4° (*c* 3.9); ^1H NMR 0.67 (s, 3 H, 18-H), 1.00 (s, 3 H, 19-H), 1.23 (t, J = 7 Hz, 3 H, CH_3CH_2O), 3.05 (d, J = 4 Hz, 1 H, 4α-H), 4.11 (q, J = 7 Hz, 2 H, CH_3CH_2O), 5.15 and 5.28 (2 m, W = 7 Hz each, 1 H in total, NH).

Anal. Calcd for $C_{30}H_{51}NO_3$: C, 76.06; H, 10.85; N, 2.96. Found: C, 75.82; H, 11.06; N, 3.05.

3β-Acetamido-1β,2β-epoxy-5α-cholestane (45): mp 196–198 °C; $[\alpha]_D$ +40° (c 2.8); ^1H NMR 0.68 (s, 3 H, 18-H), 0.89 (s, 3 H, 19-H), 2.01 (s, 3 H, CH_3CO), 3.21 (br s, 2 H, 1α-H and 2α-H), 4.38 (m, W = 30 Hz, 1 H, 3α-H), 5.75 (m, W = 22 Hz, 1 H, NH).

Anal. Calcd for $C_{29}H_{49}NO_2$: C, 78.50; H, 11.13; N, 3.16. Found: C, 78.26; H, 11.29; N, 3.04.

19-(Carbamoyloxy)-5,6β-epoxy-5β-cholestan-3β-yl 3-acetate (53): mp 192–194 °C; $[\alpha]_D$ −7° (*c* 2.4); ^1H NMR 0.65 (s, 3 H, 18-H), 2.02 (s, 3 H, CH_3CO_2), 2.97 (br d, J = 2.0 Hz, 1 H, 6α-H), 4.14 and 4.39 (AB system, J = 11.3 Hz, 2 H, 19-H), 4.74 (br s, 2 H, NH_2), 4.83 (m, W = 30 Hz, 1 H, 3α-H); IR 1250, 1728, 3433, 3550 cm^{-1}.

Anal. Calcd for $C_{30}H_{49}NO_5$: C, 71.53; H, 9.80; N, 2.78. Found: C, 71.36; H, 10.03; N, 2.50.

19-((*N*-Benzylcarbamoyl)oxy)-5,6β-epoxy-5β-cholestan-3β-yl 3-acetate (54): $[\alpha]_D$ −6° (*c* 2.8); ^1H NMR 0.62 (s, 3 H, 18-H), 2.01 (s, 3 H, CH_3CO_2), 2.98 (d, J =2 Hz, 1 H, 6α-H), 4.22 and 4.40 (AB system, J = 12 Hz, 2 H, 19-H), 4.41 (d, J = 6 Hz, 2 H, CH_2NH), 4.82 (m, W = 30 Hz, 1 H, 3α-H), 5.07 (m, W = 15 Hz, 1 H, NH), 7.31 (s, 5 H, C_6H_5).

Anal. Calcd for $C_{37}H_{57}NO_5$: C, 74.58; H, 9.64; N, 2.35. Found: C, 74.15; H, 9.87; N, 2.21.

19-((*N*,*N*-Dimethylcarbamoyl)oxy)-5,6β-epoxy-5β-cholestan-3β-yl 3-acetate (55): ^{1}H NMR (in admixture with **60**) 0.63 (s, 3 H, 18-H), 2.00 (s, 3 H, CH_3CO_2), 2.90 (d, J = 1.5 Hz, 1 H, 6α-H), 2.95 (s, 6 H, Me_2N), 4.29 and 4.41 (AB system, J = 12.2 Hz, 2-H, 19-H), 4.83 (m, W = 30 Hz, 1 H, 3α-H).

19-(Carbamoyloxy)-5,6α-epoxy-5α-cholestan-3β-yl 3-acetate (58): $[\alpha]_D$ −45° (c 2.1); ^{1}H NMR 0.63 (s, 3 H, 18-H), 2.02 (s, 3 H, CH_3CO_2), 2.98 (d, J = 3 Hz, 1 H, 6β-H), 4.38 (br s, 2 H, 19-H), 4.75 (m, $W/2$ = 7.5 Hz, 2 H, NH_2), 5.08 (m, W = 30 Hz, 1 H, 3α-H).

Anal. Calcd for $C_{30}H_{49}NO_5$: C, 71.53; H, 9.80; N, 2.78. Found: C, 71.28; H, 9.97; N, 2.54.

19-((*N*,*N*-Dimethylcarbamoyl)oxy)-5,6α-epoxy-5α-cholestan-3β-yl 3-acetate (60): ^{1}H NMR (in admixture with **55**) 0.61 (s, 3 H, 18-H), 2.02 (s, 3 H, CH_3CO_2), 2.95 (s, 6 H, CH_3N), 2.99 (d, J = 4.0 Hz, 1 H, 6β-H), 4.20 and 4.30 (AB system, J = 11.6 Hz, 2 H, 19-H), 5.00 (m, W = 30 Hz, 1 H, 3α-H).

***N*-Benzyl-2-(3-cyclohexenyl)acetamide (64)**: To a solution cyclohexenylacetic acid **73** (200 mg, 1.43 mmol) and benzylamine (170 μL, 1.56 mmol) in *N*,*N*-dimethylformamide (4 mL) was added 1-hydroxybenzotriazole (225 mg, 1.57 mmol), and the mixture was stirred at room temperature for 2 min. *N*,*N*'-Dicyclohexylcarbodiimide (325 mg, 1.58 mmol) in *N*,*N*-diethylformamide (2 mL) was added, and the mixture was stirred at room temperature overnight (12 h). Precipitated *N*,*N*'-dicyclohexylurea was filtered off and washed with ether. The filtrate was concentrated on a rotary evaporator, and the residue was partitioned between saturated $(NH_4)_2SO_4$ (aqueous) and ether. The ethereal extract was washed successively with 5% HCl (aqueous), saturated NaCl (aqueous), and 5% $KHCO_3$ (aqueous), dried with $MgSO_4$, and evaporated. The residue was dissolved in a benzene–chloroform mixture (3:1) and filtered through a pad of aluminum oxide, and the filtrate was evaporated to afford pure *N*-benzylamide **64** (241 mg): mp 212–217 °C (with sublimation); IR 1497 (arom), 1550 (NH), 1645 (C=O), 3290 and 3450 (NH) cm^{-1}; ^{1}H NMR 1.06–2.12 (m, 6 H, 3 CH_2), 2.18 (d, J = 8 Hz, 2 H, CH_2CON), 2.64 (m, W = 42 Hz, 1 H, $CHCH_2CO$), 4.44 (d, J = 6 Hz, 2 H, CH_2NH), 5.54 and 5.73 (AB system, J = 11 Hz, 2 H, HC=CH), 5.86 (m, W = 36 Hz, 1 H, NH), 7.18–7.44 (m, 5 H, arom).

Anal. Calcd for $C_{15}H_{19}NO$: C, 78.56; H, 8.35; N, 6.11. Found: C, 78.71; H, 8.21; 5.84.

(1*S,2*R**,3*S**)-*N*-Benzyl-2-[3-(1,2-epoxycyclohexanyl)]-acetamide (66)**: mp 98–99 °C; IR 1497, 1509, 1538, 1605, 1658, 1674, 3444 cm^{-1}; ^{1}H NMR 2.22 (dd, J = 13.3 and 6.8 Hz, 1 H, 2-H_a), 2.44 (dd, J = 13.3 and 8.0 Hz, 2-H_b), 2.49 (m, 1 H, 3'-H), 3.12 (dd, J = 4.1 and 2.5 Hz, 1 H, 2'-H), 3.20 (ddd, J = 4.1, 4.1, and 1.3 Hz, 1 H, 1'-H), 4.43 (dd, J = 14.7 and 5.6 Hz, 1 H, CH_2NH), 4.48 (dd, J = 14.7 and 5.9 Hz, 1 H, CH_2NH), 5.99 (br s, 1 H, NH), 7.25–7.35 (m, 5 H, C_6H_5); ^{13}C NMR 19.33, 23.70, 25.21, 32.07, 40.29, 43.67, 53.56, 55.13.

Anal. Calcd for $C_{15}H_{19}NO_2$: C, 73.44; H, 7.81; N, 5.71. Found: C, 73.10; H, 7.98; N, 5.53.

(1*R,2*S**,3*S**)-*N*-Benzyl-2-[3-(1,2-epoxycyclohexanyl)]-acetamide (68)**: mp 128–129 °C; ^{13}C NMR 24.39, 24.82, 30.00, 30.33, 43.66, 43.74, 51.56, 52.32.

Anal. Calcd for $C_{15}H_{19}NO_2$: C, 73.44; H, 7.81; N, 5.71. Found: C, 73.19; H, 8.06; N, 5.44.

Methyl (1*S,2*R**,3*S**)-2-[3-(1,2-epoxycyclohexanyl)]-acetate (71)**: ^{1}H NMR 2.35 (dd, J = 17.9 and 6.9 Hz, 1 H, 2-H_a), 2.37 (m, 1 H, 3'-H), 2.59 (dd, J = 17.9 and 9.6 Hz, 1 H, 2-H_b), 3.16 (dddd, J = 4.1, 2.2, 0.7, and 0.6 Hz, 1 H, 2'-H), 3.28 (dddd, J = 4.1, 4.1, 1.2, and 0.6 Hz, 1 H, 1'-H), 3.70 (s, 3 H, CO_2CH_3); ^{13}C NMR 19.48, 23.52, 25.01, 31.88, 37.55, 51.58, 53.20, 54.95.

Anal. Calcd for $C_9H_{14}O_3$: C, 63.51; H, 8.29. Found: C, 63.29; H, 8.05.

Methyl (1*R,2*S**,3*S**)-2-[3-(1,2-epoxycyclohexanyl)]-acetate (72)**: ^{13}C NMR (taken in a mixture with **71**) 16.88, 24.40, 26.69, 31.32, 38.16, 51.74, 52.52, 55.39.

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Registry No. 1, 62860-38-2; *cis*-**2**, 120522-60-3; *trans*-**2**, 126059-76-5; **5**, 125972-95-4; **6**, 125972-96-5; **7**, 125972-97-6; ***cis*-8**, 126059-77-6; *trans*-**8**, 126059-78-7; *cis*-**9**, 126059-79-8; *trans*-**9**, 126059-80-1; *cis*-**10**, 126059-82-3; *trans*-**10**, 126059-82-3; **11**, 108297-40-1; **12**, 125972-98-7; *cis*-**13**, 126059-83-4; *trans*-**13**, 126059-84-5; *cis*-**14**, 126059-85-6; *trans*-**14**, 126059-86-7; **15**, 517-10-2; **16**, 119449-86-4; **17**, 119449-87-5; **18**, 20220-27-3; *cis*-19, 119449-88-6; *trans*-**19**, 125995-55-3; *cis*-**20**, 119449-89-7; *trans*-**20**, 125972-99-8; **21**, 17808-78-5; **22**, 125973-00-4; **23**, 6656-45-7; **24**, 41000-54-8; **25**, 125973-01-5; **26**, 125973-02-6; **27**, 126059-87-8; **28**, 125973-03-7; *cis*-**29**, 125973-04-8; *trans*-**29**, 126059-88-9; **30**, 125973-06-0; **31**, 125973-07-1; **32**, 125973-05-9; **33**, 76026-06-7; **34**, 125973-08-2; **35**, 125973-09-3; **36**, 125973-11-7; **37**, 125973-12-8; **38**, 125973-10-6; **39**, 125973-13-9; **40**, 66500-89-8; **41**, 125973-14-0; *cis*-**42**, 125973-15-1; *trans*-**42**, 125973-16-2; **43**, 16356-56-2; **44**, 13901-13-8; *cis*-**45**, 125973-17-3; *trans*-**45**, 125973-18-4; **46**, 750-59-4; **47**, 67308-53-6; **48**, 112383-60-5; **49**, 119449-90-0; **50**, 119449-91-1; **51**, 21072-77-5; **52**, 70633-16-8; **53**, 112402-97-8; **54**, 119449-92-2; **55**, 119449-94-4; **56**, 21072-78-6; **57**, 70632-92-7; **58**, 112383-58-1; **59**, 125973-19-5; **60**, 119449-95-5; **64**, 125973-20-8; **65**, 125973-21-9; **66**, 125973-22-0; **67**, 125973-23-1; **68**, 126059-89-0; **69**, 126059-90-3; **70**, 112052-21-8; **71**, 126059-91-4; **72**, 126059-92-5; **73**, 125973-24-2; benzylamine, 100-46-9; benzyl isocyanate, 3173-56-6.