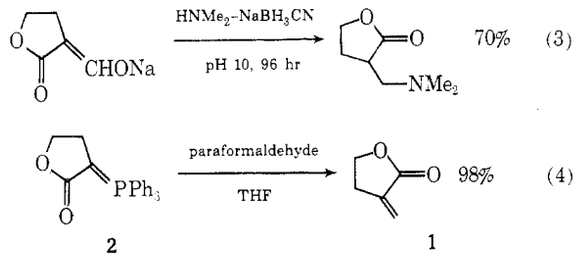
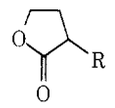


2 1

These approaches either suffer from low yields or require tedious, long chemical operations.[7] We wish to report a practical synthesis of α-methylene-γ-butyrolactone which employs as the key step a previously unreported method for the introduction of the α-methylene unit. We have observed that γ-butyrolactonylidene triphenylphosphorane (2) reacts with paraformaldehyde in refluxing anhydrous tetrahydrofuran, providing a near-quantitative yield of α-methylene-γ-butyrolactone (1) (eq 4).[8,9]

The required phosphorane 2 is readily available from the corresponding phosphonium bromide 3c in yields of 85–95% (crystalline) upon treatment of 3c with sodium carbonate in aqueous methanol.[10] The phosphonium salt 3c is obtained by treatment of α-bromo-γ-butyrolactone (3b) with triphenylphosphine in refluxing tetrahydrofuran.[10] Yields for this reaction are 40–50% of crystalline material. Attempts to brominate[11] the lithium enolate[12] of 3a at low temperature have resulted in disappointingly low yields (20–30%) of 3b. However, the classical method of Price and Judge[13] provides reproducible yields (55%) of 3b which can be carried out on a very large scale.



3a, R = H
b, R = Br
c, R = $\overset{+}{P}Ph_3Br^-$

The synthesis of 1 *via* readily available crystalline intermediates represents the most convenient route to 1 in comparison with previously reported syntheses. Furthermore, it permits large-scale production and facile isotopic labeling of the α-methylene unit for biochemical studies. We believe that the present method offers some obvious advantages over the existing methods for the preparation of α-methylene-γ-butyrolactone.

Experimental Section[14]

α-Methylene-γ-butyrolactone. A suspension of 3.46 g (0.01 mol) of α-(γ-butyrolactonylidene)triphenylphosphorane[10] and 0.6 g (0.02 mol) of paraformaldehyde in 150 ml of freshly distilled tetrahydrofuran under an atmosphere of nitrogen was heated at gentle reflux. After 2.5 hr, the contents of the flask were cooled to room temperature and the solvent was removed on a rotary evaporator, reducing the total volume of the reaction mixture by two-thirds. After addition of pentane, the contents of the flask were passed through a very short column of silica gel to remove triphenylphosphine oxide. After removal of the solvent *in vacuo*, there was obtained 974 mg of α-methylene-γ-butyrolactone (98% yield) which was pure by nmr analysis. Vacuum distillation afforded an analytical sample of 1: bp 60–53° (0.45 mm); ir ($CHCl_3$) 1765 (C=O) and 1670 cm^{-1} (=CH_2); nmr (CCl_4) 6.08 (t, J = 3 Hz, 1 H), 5.63 (t, J = 3 Hz, 1 H), 4.30 (t, J = 7 Hz, 2 H), 2.97 (m, 2 H); M^+ m/e 98. Ir and nmr spectra of 1 were identical with those previously reported for the natural product.[1,2] *Anal.* Calcd for $C_5H_6O_2$: C, 61.21; H, 6.17. Found: C, 61.09; H, 6.10.

Acknowledgment. We thank Professor Paul Dowd for a generous gift of α-bromo-γ-butyrolactone. We thank the National Cancer Institute (Public Health Service Research Grant R01 CA 13689-02) and Eli Lilly and Co. for generous support of this research.

Registry No.—1, 547-65-9; 2, 34932-07-5.

References and Notes

(1) C. J. Cavallito and T. H. Haskell, *J. Amer. Chem. Soc.*, **68**, 2332 (1946).
(2) U. W. Brongersma-Oosterhoff, *Recl. Trav. Chim. Pays-Bas*, **86**, 705 (1967); B. H. H. Bergman, J. C. M. Beijersbergen, J. C. Overeem, and A. Kaars Sijpesteijn, *ibid.*, **86**, 709 (1967).
(3) S. M. Kupchan, *Trans. N. Y. Acad. Sci.*, **32**, 85 (1970); G. A. W. Verspyck Mijnssen, *Brit. J. Dermatol.*, **81**, 737 (1969); K.-H. Lee, E.-S. Huang, C. Piantidosi, J. S. Pagno, and T. A. Geissman, *Cancer Res.*, **31**, 1649 (1971).
(4) For recent methods of introducing the α-methylene unit from lactone precursors see (a) P. A. Grieco and K. Hiroi, *J. Chem. Soc., Chem. Commun.*, 1317 (1972); (b) P. A. Grieco and K. Hiroi, *Tetrahedron Lett.*, 1831 (1973); (c) P. A. Grieco and K. Hiroi, *J. Chem. Soc., Chem. Commun.*, 500 (1973); (d) P. A. Grieco and M. Miyashita, *J. Org. Chem.*, **39**, 120 (1974); (e) P. A. Grieco and J. J. Reap, *Tetrahedron Lett.*, 1097 (1974); (f) A. D. Harmon and C. R. Hutchinson, *ibid.*, 1293 (1973); (g) R. C. Ronald, *ibid.*, 3831 (1973); (h) A. E. Greene, J. C. Muller, and G. Ourisson, *ibid.*, 2489, 3375 (1972).
(5) E. R. H. Jones, T. Y. Shen, and M. C. Whitting, *J. Chem. Soc.*, 230 (1950).
(6) P. F. Hudrlik, L. R. Rudnick, and S. H. Korzeniowski, *J. Amer. Chem. Soc.*, **95**, 6848 (1973).
(7) A report concerning the reductive (H_2/EtOH/Raney Ni, 100 atm) elimination (alumina, 340–350°) of α-formyl-γ-butyrolactone to 1 has also appeared: W. J. McGraw, U. S. Patent 2,624,723 (1953); *Chem. Abstr.*, **47**, 11232*h* (1953).
(8) A similar route to substituted α-benzylidene-γ-butyrolactones has been described: H. Zimmer and T. Pampalone, *J. Heterocycl. Chem.*, **2**, 95 (1965).
(9) Professor P. F. Hudrlik has informed us of his independent efforts to introduce the α-methylene unit of 1 *via* an *in situ* generation of 2.
(10) S. Fliszar, R. F. Hudson, and G. Salvadori, *Helv. Chim. Acta*, **46**, 1580 (1963).
(11) We have observed the direct bromination of lactone enolates (*e.g.*, i and ii) (prepared from lithium diisopropylamide in tetrahydrofuran

i ii

at −78°) with bromine in 60–70% isolated yields: P. A. Grieco and J. J. Reap, unpublished results.
(12) We have demonstrated that lactone enolates undergo high-yield α-hydroxymethylation,[4a,b] α-carboxylation,[4c] α-phenylselenenylation,[4d] and α-phenylsulfenylation.[4e]
(13) C. C. Price and J. M. Judge, *Org. Syn.*, **45**, 22 (1965).
(14) The following spectrometers were used: nmr, Varian A-60D, T-60; ir, Perkin-Elmer Model 347; mass spectrum, LKB-9.

New Routes for the Degradation of the Lanosterol Side Chain

Marcel Fetizon,* Frederic J. Kakis, and Valentine Ignatiadou-Ragoussis

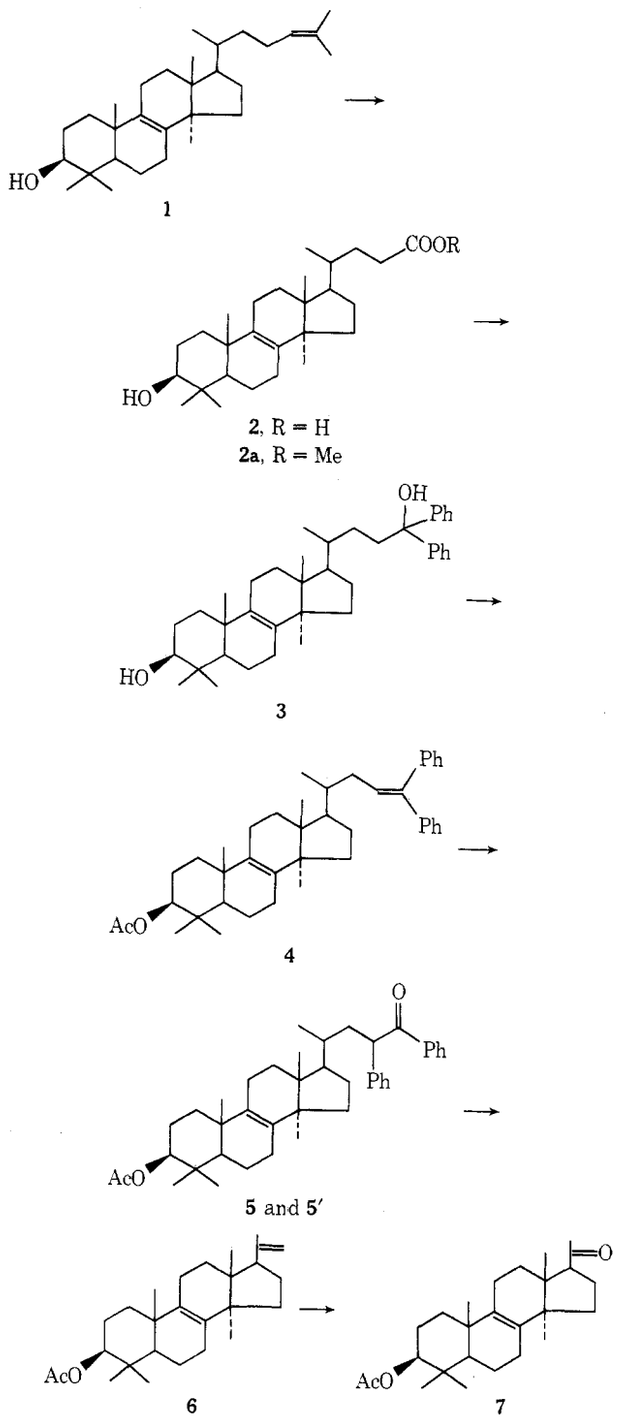
Stereochemistry Laboratory, University of Paris, 11, 91415 Orsay, France[1]

Received January 23, 1974

Recent reports[2,3a] describe the degradation of the lanosterol side chain with overall yields of approximately 4–10%. Other steroid side-chain degradations have also been reported,[4,5] but none of them seem to give particularly attractive yields. In view of this, we decided that it would be of considerable interest to apply a newly developed method of degradation[6] to these substrates, in the hope of improving the yields. This method, originally applied to the side-chain degradation of cholic acids,[6] utilizes as the key step a Norrish type II photoelimination reaction of a phenyl ketone which is easily obtained by means of an established rearrangement procedure.[7] Application of this photoelimination method[6] to lanosterol (Scheme I) resulted in a 23% overall yield.

Similarly, the modification of the original Briggs procedure[2] (Scheme II) gave a 15% overall yield, *i.e.*, approximately three times that obtained by the original method. Thus it appears that the photolysis of ketonic in-

Scheme I



termediates shows considerable promise as an alternative to currently used degradation schemes for the interconversion of natural products.

Experimental Section

General. Melting points were taken on a Kofler apparatus and are uncorrected. Infrared spectra were recorded on a Perkin-Elmer Model 257 spectrophotometer. Nmr spectra were determined on a Joel Model C60H spectrometer using tetramethylsilane as internal standard and are reported in parts per million. Optical rotations were measured with the aid of a Perkin-Elmer Model 141 polarimeter. Irradiations were performed with a Hanau TQ 150-W medium-pressure mercury lamp contained in a quartz immersion well. The 3130-Å line was isolated with 1-cm path of 0.002 *M* potassium chromate in a 5% aqueous solution of potassium carbonate. The required cooling was achieved by the circulation of this solution. For column chromatography Merck silica (0.063–0.2 mm) was always used. Microanalyses were performed by the microanalysis service of Centre national de la Recherche scientifique at the Gif sur Yvette laboratories in France.

Methyl 3β-Hydroxy-4,4,14α-trimethyl-5α-cholan-8-ene-24-methanoate (2a). A sample (4.7 g) of crude trisnorlanostenolic acid (**2**), obtained from the ozonolysis of commercial grade lanosterol[8] by the method of Curtis and Silbermann,[9,10] was esterified in the usual way by simple reflux with methanol (250 ml) and 12 *N* hydrochloric acid (10 ml). The crude ester was isolated by extraction with ether and purified by column chromatography over silica using a pentane–ether (2:1) mixture as the eluent. The product was further purified by recrystallizations from methanol. The pure (mp 154–156°) ester gave the following spectral data: ir (CS_2) 3630 and 1740 cm^{-1}; nmr ($CDCl_3$) δ 0.7 (3 H, singlet), 0.795 (3 H, singlet), 0.875 (6 H, singlet), 0.98 (6 H, singlet), 3.7 (3 H, singlet, $-COOCH_3$ protons).

3β,24-Dihydroxy-4,4,14α-trimethyl-24,24-diphenyl-5α-cholan-8-ene (3). This compound was prepared from a sample (7.2 g, 0.0167 mol) of pure (mp 154–156°) ester **2a** by the standard addition of phenylmagnesium bromide (25 g, 0.138 mol) in anhydrous tetrahydrofuran. The mixture was refluxed for 15 hr and then decomposed with a saturated solution of ammonium chloride. Ether extraction of the hydrolyzed mixture followed by drying and removal of the solvents afforded a crude, oily product mixture, which contained an excess of the usual Grignard coupling products. Crystallization of the diol **3** was achieved by treating the oil with hexane. Thus 6.8 of the diol **3** was obtained.

Column chromatography of the mother liquors over silica with pentane–ether (2:1) followed by recrystallization from methanol afforded another 2.2 g of the pure (mp 172–173°) diol **3**, bringing the total yield to 9 g (97%): ir (CS_2) 3610, 3090, 3060, 3030, and 700 cm^{-1}; nmr ($CDCl_3$) δ 0.57 (3 H, singlet), 0.77, 0.85, 0.92, 0.95 (15 H, singlet), 7.1–7.6 (10 H, multiplet, aromatic protons).

3β-Acetoxy-4,4,14α-trimethyl-24,24-diphenyl-5α-cholane-8,23-diene (4). The dehydration of the alcohol at C_{23} and the acetylation of the C_3 hydroxyl group were simultaneously achieved by refluxing a sample (9.2 g) of the diol **3** with a mixture of acetic anhydride–acetic acid (60 ml, 5:1) for a period of 5 hr. After the usual work-up and recrystallization of the crude product from acetone, 6.5 g of pure (mp 196–199°) diene **4** was obtained. Chromatography of the mother liquors over silica with pentane–ether (5:1) afforded another 2.4 g of pure product, bringing the total yield of the diene **4** to 8.9 g (93%): ir (CS_2) 3090, 3060, 3030, 1735, 1240, and 700 cm^{-1}; nmr ($CDCl_3$) δ 0.62 (3 H, singlet), 0.77, 0.85, 0.90, 0.95 (15 H, singlets), 2.0 (3 H, singlet, acetoxy protons), 4.47 (1 H, multiplet, 3α proton), 6.075 (1 H, triplet, ethylenic proton, J = 7.5 Hz), 6.95–7.5 (10 H, multiplet, aromatic protons).

Anal. Calcd for $C_{41}H_{54}O_2$: C, 85.07; H, 9.40; O, 5.53. Found: C, 84.83; H, 9.24; O, 5.59.

3β-Acetoxy-4,4,14α-trimethyl-23,24-diphenyl-5α-cholan-8-en-24-one (5 and 5′). The rearrangement of compound **4** above (1.156 g, 0.002 mol) to the mixture of ketones **5** and **5′** was achieved by the Kakis method,[7] except that a stoichiometric amount of bromine (5.5–6 ml of a 2% Br_2 solution in chloroform corresponding to *ca.* 0.32 g, 0.002 mol) had to be used to avoid the bromination of the $\Delta^{8,9}$ double bond.

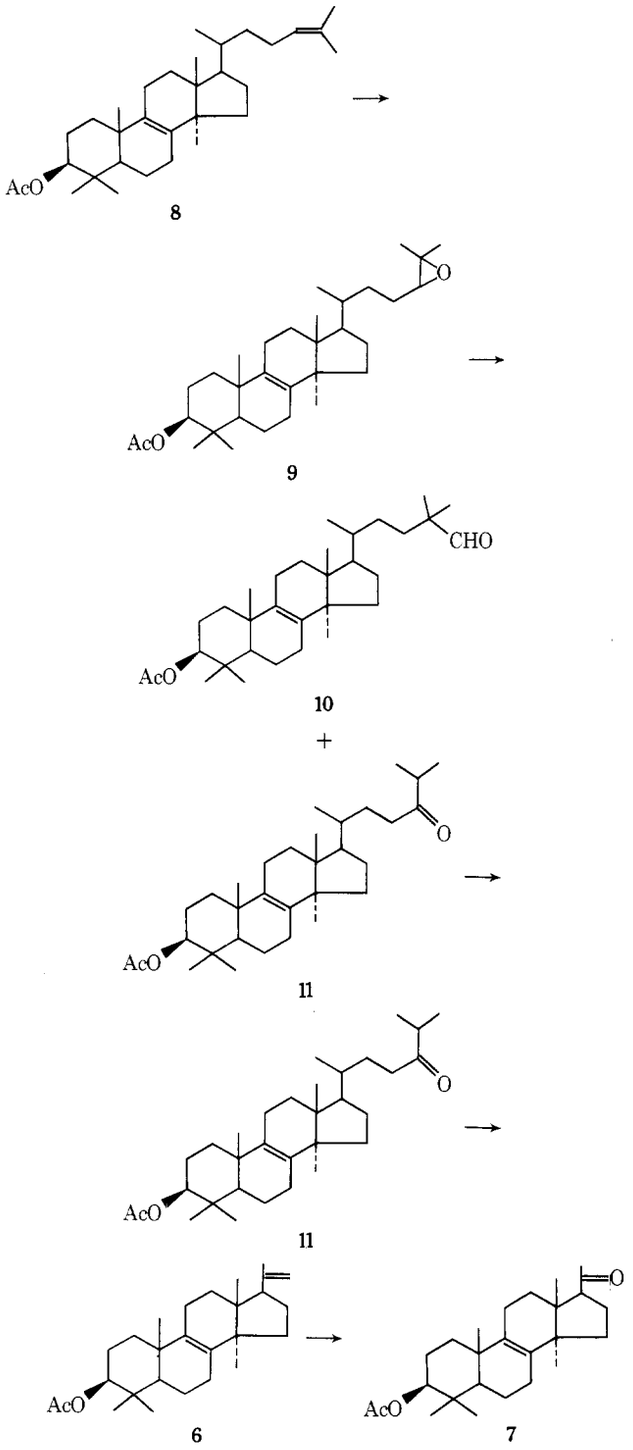
The crude mixture (1.4 g) of the diastereomeric ketones **5** and **5′** obtained from this rearrangement was purified by recrystallization from a mixture of ethanol and methylene chloride. Thus a pure sample (950 mg) of the ketones **5** and **5′** was obtained. By chromatographing the mother liquors another 70 mg of pure ketones were obtained, bringing the total yield of ketones to 1.020 g (87%): ir (CS_2) 3080, 3060, 3030, 1735, 1685, 1245, 910, 740, and 700 cm^{-1}.

Anal. Calcd for $C_{41}H_{54}O_3$: C, 82.78; H, 9.15; O, 8.07. Found: C, 82.54; H, 8.99; O, 8.17.

The separation of the two diastereomeric ketones **5** and **5′**, which was attempted on a small sample of the mixture, proved to be quite laborious. Separation was finally achieved by thin layer chromatography on fluorescent silica using several successive elutions with pentane–ether (10:1). Each isomer was subsequently recrystallized from a mixture of ethanol and methylene chloride.

The least polar isomer (**5**) gave needles (mp 187–189°), whereas the more polar isomer (**5′**) gave hexagonal plates (mp 229–232°). In addition the following physical data were obtained: compound **5**, $[\alpha]_D$ ($CHCl_3$) −36°; nmr ($CDCl_3$) δ 0.55 (3 H, singlet), 0.8 (9 H, singlet), 0.9 (6 H, singlet), 1.93 (3 H, singlet, acetoxy protons), 4.5 (2 H, multiplet, 3α and C_{23} protons), 6.9–8 (10 H, multiplet, aromatic protons); compound **5′**, $[\alpha]_D$ ($CHCl_3$) +108.5°; nmr ($CDCl_3$) δ 0.45 (3 H, singlet), 0.79 (9 H, singlet), 0.85 (6 H, singlet), 1.95 (3 H, singlet, acetoxy protons), 4.45 (2 H, multiplet, 3α

Scheme II



and C_{23} protons), 6.95–8.05 (10 H, multiplet, aromatic protons).

3β-Acetoxy-4,4,14α-trimethyl-5α-pregna-8,20-diene (6). A. From 5 and 5′. A sample (1 g) of the ketone mixture (5 and 5′) was dissolved in pure anhydrous benzene and irradiated for about 2 hr. Evaporation of the solvents afforded a yellow oil (1.09 g). The isolation of the diene 6 from the mixture of photolysis products was achieved by thin layer chromatography over fluorescent silica which contained 8% silver nitrate, using a mixture of pentane–ether (4:1) as the eluent. Thus a pure sample (0.3 g, 45%) of the diene 6 was obtained. Recrystallization from ethanol afforded an analytical sample: mp 168–170°; ir (CS_2) 3080, 1735, 1240, and 890 cm^{-1}; nmr ($CDCl_3$) δ 0.5 (3 H, singlet), 0.8, 0.85, 0.9 (12 H, singlets), 1.67 (C_{21} protons), 1.97 (3 H, singlet, acetoxy protons), 4.65 and 4.77 (3 H, two singlets and a multiplet, terminal methylene and 3α protons); $[\alpha]D$ ($CHCl_3$) +47.5°.

Anal. Calcd for $C_{27}H_{42}O_2$: C, 81.35; H, 10.62; O, 8.03. Found: C, 80.50; H, 10.41; O, 8.04.

B. From 11. A sample (500 mg) of the isopropyl ketone 11 was subjected to photoelimination by a procedure identical with that described for the irradiation of the mixture of phenyl ketones (5 and 5′). Complete disappearance of the ketone in this case required over 9 hr of irradiation. Following the same isolation and purification procedure used for the photolysis products of compounds 5 and 5′, a pure sample (215 mg, 52%) of compound 6 was obtained. The physical constants and spectra of this product were identical with those obtained for the product isolated from the photolysis of the phenyl ketones 5 and 5′ in part A above.

3β-Acetoxy-4,4,14α-trimethyl-5α-pregn-8-en-20-one (7). A sample of compound 6 (250 mg, 0.63 mmol) was dissolved in a mixture of pyridine (5 ml) and benzene (2 ml). The resulting solution was then treated with osmium tetroxide (160 mg, 0.63 mmol). The mixture became black-red. After the mixture was stirred for 1 hr at room temperature, a mixture of pyridine (2 ml), water (2 ml), and sodium bisulfite solution (2 ml) was added to the reaction flask. The stirring was continued for another hour, after which the mixture was diluted with water and extracted with methylene chloride. The organic phase was then washed successively with aqueous sulfuric acid (10%), a sodium bicarbonate solution (10%), and distilled water. Drying of the solvents, followed by evaporation, afforded 280 mg of crude 3β-acetoxy-4,4,14α-trimethyl-5α-pregn-8-ene-20,22-diol: ir (CS_2) 3630, 3580, 1735, and 1240 cm^{-1}. This intermediate, without purification, was dissolved in tetrahydrofuran and treated gradually with a mixture of H_5IO_6 (150 mg) in tetrahydrofuran. The reaction was instantaneous. Extraction of the reaction mixture followed by the usual work-up afforded a sample (265 mg) of product 7. Purification was achieved by thin layer chromatography over fluorescent silica with a pentane–ether (4:1) mixture as the eluent followed by recrystallization from methanol. Thus 165 mg of the pure (mp 167–169°) product 7 was obtained (66% yield based on compound 6): ir (CS_2) 1735, 1710, and 1240 cm^{-1}; nmr ($CDCl_3$) δ 0.57 (3 H, singlet), 0.85, 0.92, 0.96 (12 H, singlets), 2.03 (3 H, singlet, C_{21} protons), 2.1 (3 H, singlet, acetoxy protons). $[\alpha]D$ ($CHCl_3$), +115°; Mass spec. gave molecular ion peak at m/e 400.

3β-Acetoxylanosta-8,24-diene (8). Treatment of a commercial lanosterol sample[8] with acetic anhydride in pyridine led to a mixture of the corresponding acetates. Separation was achieved by column chromatography over silica impregnated with silver nitrate (10%), using a pentane–ether mixture (30:1) as the eluent. The weight ratio of column packing to mixture was 100:1. Thus a pure (mp 129–130°) sample of compound 8 was obtained (lit.[11] mp 127–128°).

3β-Acetoxylanost-8-en-24-one (11). This ketone was prepared from compound 8 by the same series of reactions used by Briggs.[2] The total yield of ketone 11 from compound 8 was 42%. All the physical constants and spectra were in agreement with the previously reported[2] values.

Acknowledgments. The participation of Dr. F. J. Kakis in this project was made possible through a grant by the Research Corporation. We are grateful for this assistance. We would also like to thank the Centre national de la Recherche scientifique for their generous support of this work.

Registry No.—**1**, 79-63-0; **2**, 51348-64-2; **2a**, 51348-65-3; **3**, 51270-47-4; **4**, 51270-48-5; **5**, 51270-49-6; **5′**, 51270-50-9; **6**, 49810-38-0; **7**, 27868-09-3; **11**, 13553-26-9.

References and Notes

(1) Equipe de Recherche Associee au Centre national de la Recherche scientifique, 070395 ERA 01.
(2) (a) L. H. Briggs, J. P. Bartley, and P. S. Rutledge, *Tetrahedron Lett.*, **15**, 1237 (1970); (b) *J. Chem. Soc.*, 806 (1973).
(3) (a) G. Habermehl and G. Volkwein, *Justus Liebigs Ann. Chem.*, **742**, 145 (1970). (b) We are indebted to Professor Habermehl for supplying us with the infrared and nmr spectra of his degradation product. When we compared these spectra to those of our own product (7) we found them superimposable.
(4) W. Voser, M. V. Mijović, O. Jeger, and L. Ruzicka, *Helv. Chim. Acta*, **34**, 1585 (1951).
(5) D. Rosenthal, P. Grabowich, E. F. Sabo, and J. Fried. *J. Amer. Chem. Soc.*, **85**, 3971 (1963).
(6) M. Fetizon, F. J. Kakis, and V. Ignatiadou-Ragoussis, *J. Org. Chem.*, **38**, 4308 (1973).
(7) F. J. Kakis, D. Brase, and A. Oshima, *J. Org. Chem.*, **36**, 4117 (1971).
(8) (a) Aldrich Chemical Co. Inc., Milwaukee, Wis. (b) A mixture of Δ^8-lanostenol and $\Delta^{8,24}$-lanostadienol.
(9) R. G. Curtis and M. Silbermann, *J. Chem. Soc.*, 1187 (1952).

(10) During the course of our investigation, the oxidation method of Habermehl (ref 4) was also tried in our laboratory and found to give better yields of the acid **2**.
(11) J. D. Johnston, F. Gautschi, and K. Block, *J. Biol. Chem.*, **224**, 185 (1957).

Electrophilic Additions and Substitutions of *tert*-Butyl Hypochlorite Catalyzed by Boron Trifluoride[1]

Cheves Walling* and Roger T. Clark

Department of Chemistry, University of Utah, Salt Lake City, Utah 84112

Received January 29, 1974

In nonpolar solvents with light or radical initiators, *tert*-butyl hypochlorite reacts with olefins to give allylic chlorides in good yield by a radical chain process.[2] On the other hand, Anbar and Ginsberg, in their comprehensive review,[3] report that, in polar solvents, addition occurs to yield β-chloro ethers *via* electrophilic addition where R′ is either *tert*-butyl or, in an alcohol solvent, the corresponding alcohol residue. Since we had need of such products for another study,[4] and since yields and procedures were ill-defined in the original papers cited by Anbar, we have reexamined this polar addition, and find that the success of the reaction depends markedly upon reaction conditions but proceeds particularly smoothly simply by adding the hypochlorite to cold olefin–alcohol mixture containing a few drops of boron trifluoride etherate. Yields are 50–90% and, of particular interest, β-chloro-*tert*-alkyl ethers can be produced which are difficulty accessible by other means. Typical results are shown in Table I, and we assume that reaction occurs *via* a typical "chloronium ion" intermediate which then reacts with solvent as the predominant nucleophile. Although the preparation appears general for simple olefins, it fails with negatively substituted olefins such as 1,1- and *cis*-1,2-dichloro- and trichloroethylene.

$$t\text{-BuOCl} + CH_2{=}CHR \rightarrow ClCH_2CH(OR')R$$

We were also unable to observe any cyclized product on attempting to prepare the hypochlorite from 4-penten-1-ol *in situ* and then carrying out the addition, although others have reported accomplishing the cyclization *via* a radical path.[5]

Anbar[3] also reports a few examples of acid-catalyzed electrophilic aromatic substitution by *tert*-butyl hypochlorite, and such reactions have occasionally been noted as complications in attempted radical chlorination of alkylbenzenes with strong electron-supplying groups and in the reactions of complex hypochlorites containing reactive aromatic nuclei.[4] We find that the *tert*-butyl hypochlorite–boron trifluoride technique leads to smooth chlorination of benzene, chlorobenzene, and toluene at room temperature, although the reaction fails with more negatively substituted aromatics. With toluene we obtain an isomer distribution of 70.2% ortho and 29.8% para and, in competition, toluene is 21 times as reactive as benzene. For Cl_2 in acetic acid the isomer distribution is reported as 59.8% ortho, 0.5% meta, and 39.7% para with toluene 344 times as reactive as benzene,[6] while with hypochlorous acid in water the isomer distribution is 74.6% ortho, 2.2% meta, and 23.2% para with a total reactivity 60 times that of benzene.[7] Our results are much closer to the latter, and indicate that the electrophilic species is indeed a *tert*-butyl hypochlorite–boron trifluoride complex, rather than traces of adventitious Cl_2 which might be formed during the reaction. With *tert*-butylbenzene we obtain a mixture of 53% ortho and 47% *p*-chloro substitution.

In summary, our results show that a variety of electrophilic addition and substitution reactions of *tert*-butyl hypochlorite (and presumably other alkyl hypochlorites) can be carried out in good yield under very mild conditions using small amounts of boron trifluoride catalyst. The reaction provides a simple, efficient synthesis of β-chloro ethers and a convenient laboratory alternative to gaseous Cl_2 for the chlorination of suitable aromatic nuclei.

Experimental Section

β-Chloro Ethers. The preparation of 2-chlorocyclohexyl isopropyl ether is typical. Anhydrous isopropyl alcohol (0.1 mol), cyclohexene (0.1 mol), and a few drops of boron trifluoride etherate were placed in a 25-ml flask cooled in ice water. *tert*-Butyl hypochlorite (0.03 mol) was added dropwise with stirring. Each drop apparently reacted immediately. The solvent was removed *in vacuo* and the product was distilled, yield 2.3 g (43.2%), bp 48° (0.1 mm). Analysis and nmr spectra were consistent with the assigned structure and vpc indicated a single isomer, assumed to have the trans structure. Other reactions were carried out similarly, using equimolar quantities of alcohol and olefin, except that addition to isobutylene was made at −78°. Yields were determined either by vpc or actual isolation as indicated in Table I.

Table I
Preparation of β-Chloro Ethers

Olefin	Registry no.	Product	Registry no.	Yield, % Vpc	Yield, % Isolated
Cyclohexene	110-83-8	*trans*-2-Chlorocyclohexyl *tert*-butyl ether	51286-79-4	49	49
Cyclohexene		*trans*-2-Chlorocyclohexyl isopropyl ether	51286-80-7	57	43
Cyclohexene		*trans*-2-Chlorocyclohexyl *n*-propyl ether	51286-81-8	96	66
Isobutylene	115-11-7	Chloro-*tert*-butyl *n*-propyl ether	51286-82-9	67	

Aromatic substitution reactions were carried out by adding hypochlorite at or below room temperature to an excess of the appropriate aromatic (or mixture) in the presence of a small amount of boron trifluoride etherate but no added solvent. The yellow color of the hypochlorite disappeared within 0.5 hr, and total yields (essentially quantitative) and product distributions were determined by vpc using known standards. The spread of analytical results indicated that the isomer distributions reported are reliable to ±1–2%.

Registry No.—*tert*-butyl hypochlorite, 507-40-4; boron trifluoride, 7637-07-2.

References and Notes

(1) Taken from the Ph.D. Thesis of Roger T. Clark, University of Utah, 1973. Support of this work by a grant from the National Science Foundation is gratefully acknowledged.
(2) C. Walling and W. Thaler, *J. Amer. Chem. Soc.*, **83**, 3877 (1961).
(3) M. Anbar and D. Ginsberg, *Chem. Rev.*, **54**, 925 (1954).
(4) C. Walling and R. T. Clark, *J. Amer. Chem. Soc.*, in press. Under more vigorous conditions ($AlCl_3$), *tert*-butyl hypochlorite is reported to convert benzene to *tert*-butylbenzene: N. Berman and A. Lowy, *ibid.*, **60**, 2596 (1938).
(5) J. M. Surzur, P. Cozzone, H. P. Bertrand, and M. A. Normant, *C. R. Acad. Sci.*, **267**, 908 (1968).
(6) H. C. Brown and L. M. Stock, *J. Amer. Chem. Soc.*, **79**, 5175 (1957).
(7) P. B. de la Mare, J. T. Harvey, M. Hassen, and S. Varma, *J. Chem. Soc.*, 2750 (1958).