p-Nitrophenyl 2-acetamido-2-deoxy-α-D-glucopyranoside (12) crystallized in part (2.7 g) in pure state during O-deacetylation of 5.2 g of its acetate ester (10). Recrystallization from methanol of material recovered from the filtrate yielded additional pure α-glycoside (0.8 g, total yield 91%). The compound had mp 274° dec, $[\alpha]^{23}D$ +273.4° (*c* 0.67, water), unchanged by recrystallization from methanol.

Anal. Calcd for $C_{14}H_{18}N_2O_8$: C, 49.1; H, 5.30; N, 8.19. Found: C, 49.4; H, 5.25; N, 8.15.

Optical Rotations of Nitrophenyl β-Glucosaminides.—These compounds, prepared as described by Leaback and Walker,[2] were purified with some care. *o*-Nitrophenyl 2-acetamido-3,4,6-tri-O-acetyl-2-deoxy-β-D-glucopyranoside (13) had mp 191–191.5°, $[\alpha]^{23}D$ +64.8° (*c* 0.55, chloroform), +2.8° (*c* 0.65, acetone), unchanged by successive recrystallizations from 2-propanol, benzene, and ethyl acetate [lit.[2] mp 196–197°, $[\alpha]^{23}D$ +3.4° (acetone)]. *o*-Nitrophenyl 2-acetamido-2-deoxy-β-D-glucopyranoside had mp 189–190° dec, $[\alpha]^{23}D$ −34.7° (*c* 0.52, water), unchanged by two recrystallizations from methanol [lit.[2] mp 192–194°, $[\alpha]^{20}D$ −33.1° (water)]. *p*-Nitrophenyl 2-acetamido-3,4,6-tri-O-acetyl-2-deoxy-β-D-glucopyranoside (14) had mp 241° dec, $[\alpha]^{23}D$ −26.3° (*c* 0.55, chloroform), −44.2° (*c* 0.53, pyridine), −23.6° (*c* 0.57, acetone), unchanged by three recrystallizations from chloroform–methanol [lit. $[\alpha]^{18}D$ −46.8° (pyridine),[15] $[\alpha]^{18}D$ −46.2° (acetone),[2] $[\alpha]^{20}D$ −40° (acetone)[20]]. *p*-Nitrophenyl 2-acetamido-2-deoxy-β-D-glucopyranoside had mp 215° dec, $[\alpha]^{23}D$ −19.4° (*c* 0.31, water), unchanged by recrystallization from methanol [lit. $[\alpha]^{20}D$ −18.6° (water),[2] −15° (water)[22]].

Anomeric Purity of α-Glycosides.—To test for possible contamination with their β anomers of the α-glycosides prepared in this work, these were subjected to an enzymic test. Solutions of the glycosides in 0.05 *M* sodium citrate buffer of pH 4.3 were incubated for 1 hr at 37° with purified liver β-N-acetylglucosaminidase, present in sufficient quantity per milliliter of digest to liberate 1000 μg of *p*-nitrophenol from *p*-nitrophenyl β-N-acetylglucosaminide.[23] No liberation of aglycon above nonenzymic control levels was detectible with phenyl α-N-acetylglucosaminide (2) at 10 m*M* concentration; phenyl α-N-acetylgalactosaminide (4), 10 m*M*; *o*-nitrophenyl α-N-acetylglucosaminide (11), 5 m*M*; *p*-nitrophenyl α-N-acetylglucosaminide (12), 1 m*M*. When each digest was supplemented with an amount of the corresponding β-glycoside equivalent to 0.5% of the α-glycoside present, enzymic liberation of aglycon was demonstrable.

(22) D. H. Leaback, *Biochem. Prepn.*, **10**, 118 (1963).

(23) B. Weissmann, S. Hadjiioannou, and J. Tornheim, *J. Biol. Chem.*, **239**, 59 (1964).

The Stereospecific Synthesis of *cis* and *trans* Isomers of Glycidic Esters and Products of the Darzens Synthesis

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The synthesis of *cis* and *trans* isomers of ethyl 2,3-diphenylglycidate and of ethyl 2-methyl-3-phenylglycidate, and *trans* isomers of ethyl and *t*-butyl phenylglycidates by direct epoxidation of the corresponding α,β-unsaturated esters with *m*-chloroperbenzoic acid is described. By comparison of the nmr spectra of the pure isomers with the spectra of products of the Darzens synthesis, the Darzens method is shown to produce both isomers. It is shown also that the Darzens synthesis employing potassium *t*-butoxide in *t*-butyl alcohol results in considerable transesterification.

We have been interested in the question of whether the Darzens synthesis of glycidic esters[1] does not in fact yield both geometrical isomers when their existence is possible.[2] One aspect of the problem involved the synthesis of *cis* and *trans* isomers of several glycidic esters as reference compounds, and we have thus been searching for facile procedures for their preparation.

Various conditions for carrying out epoxidations are described in the literature. Epoxidation of alkenes bearing carbonyl substituents is generally regarded as more difficult than epoxidation of isolated ethylenic functions,[3] but examples of direct epoxidation of α,β-unsaturated carbonyl compounds have appeared.[3-6] Additionally, a method for interconverting geometrical isomers of glycidic esters has been described.[7] Epoxidation with organic peracids is evidently stereospecific.[8]

We have found that direct epoxidation of α,β-unsaturated esters with *m*-chloroperbenzoic acid[8] is satisfactory. By refluxing a solution of an unsaturated ester in methylene chloride with a small excess of the peracid for varying lengths of time, good yields of six glycidic esters (compounds **1–5** and **7**) have been obtained. That all of these compounds are pure stereoisomers is confirmed by their proton magnetic resonance spectra. Table I shows the important features of the nmr spectra of seven glycidic esters and of six corresponding cinnamates.

The spectra were readily correlated with structures on the basis of the known configurations[9] of the ethyl α,β-diphenylglycidates, **1** and **2**, and by noting that chemical shifts of certain proton resonances in the several isomers agree with predictions.[10] All of the compounds prepared carry β-phenyl groups. The effect of this structural feature is to shift the resonance frequency of the ethoxyl protons toward lower values of δ (parts per million) when the phenyl group is moved from a *trans* to a *cis* position relative to the ester group. Models show that the ethoxyl protons are located, part

(1) M. S. Newman and B. J. Magerlein, *Org. Reactions*, **5**, 413 (1949); M. Ballester, *Chem. Rev.*, **55**, 283 (1955).

(2) Evidence for the occurrence of both geometric isomers in the Darzens reaction is found in the following papers, especially d: (a) H. O. House and J. W. Blaker, *J. Am. Chem. Soc.*, **80**, 6389 (1958); (b) E. E. van Tamelen, M. Shamma, A. W. Burgsthaler, J. Wolinsky, R. Tamm, and P. E. Aldrich, *ibid.*, **80**, 5006 (1958); (c) L. Field and C. G. Carlile, *J. Org. Chem.*, **26**, 3170 (1961); (d) C. C. Tung, A. J. Speziale, and H. W. Frazier, *ibid.*, **28**, 1514 (1963); (e) K. Sisido, H. Hirowatari, and T. Isida, *ibid.*, **29**, 2783 (1964).

(3) D. L. MacPeek, P. S. Starcher, and B. Phillips, *J. Am. Chem. Soc.*, **81**, 680 (1959). This paper reviews earlier work with peroxy acids.

(4) G. B. Payne, *J. Org. Chem.*, **26**, 663 (1961); G. B. Payne and P. H. Williams, *ibid.*, **26**, 651 (1961).

(5) P. A. Artamonov, *J. Gen. Chem. USSR*, **28**, 1355 (1958) (p 1414 in Consultants Bureau Translation); *Chem. Abstr.*, **52**, 19932*d* (1958).

(6) K. W. Wheeler, M. G. Van Campen, Jr., and R. S. Shelton, *J. Org. Chem.*, **25**, 1021 (1960).

(7) C. C. Tung and A. J. Speziale, *Chem. Ind.* (London), 1985 (1963).

(8) FMC Corp., Inorganic Chemicals Division, New York, 17, N. Y. A technical data bulletin describes the epoxidation of ethyl crotonate in 70% yield.

(9) H. E. Zimmerman and L. Ahramjian, *J. Am. Chem. Soc.*, **82**, 5459 (1960).

(10) L. M. Jackman, "Applications of Nuclear Magnetic Resonance Spectroscopy in Organic Chemistry," Pergamon Press Inc., New York, N. Y., 1959, pp 85, 125.

TABLE I

CHEMICAL SHIFTS IN PARTS PER MILLION FOR GLYCIDIC ESTERS AND RELATED CINNAMATES[a]

$C_6H_5CHC(R)CO_2R'$ (O) $C_6H_5CH{=}C(R)CO_2R'$

Compd, configuration[b]	Compd 1–7: α R	Compd 1–7: β H	Compd 8–13: CH_2CH_3	Compd 8–13: t-C_4H_9	Compd 8–13: J_{AB}
1, *trans*	C_6H_5[c]	4.35	4.09, 1.04[d]		
2, *cis*	C_6H_5	3.85	3.80, 0.93		
3, *trans*	CH_3 1.20	4.12	4.06, 1.26		
4, *cis*	CH_3 1.60	3.75	3.72, 0.85		
5, *trans*	H 3.34 (d)[e]	4.00 (d)[e]	4.17, 1.26		1.5
6, *cis*[f]	H 3.73 (d)[e]	4.16 (d)[e]	3.90, 0.88		5.0
7, *trans*	H 3.03 (d)[e]	3.73 (d)[e]	...	1.43	1.5
8, *trans*	C_6H_5[c]	7.49	4.09, 1.25		
9, *cis*	C_6H_5	6.70	4.04, 1.10		
10, *trans*	CH_3 2.02 (d)	7.35 (q)	4.11, 1.30		1.5
11, *cis*	CH_3 2.00 (d)	6.41 (q)	3.90, 1.03		1.5
12, *trans*	H 6.13 (d)	7.37 (d)	4.05, 1.23		15.8
13, *trans*	H 5.99 (d)	7.19 (d)	...	1.44	15.2

[a] In carbon tetrachloride with TMS as internal standard. Positions reported for doublets (d), quartets (q), or other multiplets are centers of bands. [b] The *trans* configuration is related to *trans*-cinnamic acid. [c] The signals for phenyl protons were near 7 ppm. Two distinct bands appeared in the phenyl region for **1** and **8**. [d] All ethoxyl protons showed the customary splitting with coupling constant J = 7.0 cps for each compound. [e] Assignments tentative. See text. [f] Values given are from ref 7. The chemical shift for ethoxyl CH_3 reported here agrees closely with that observed in a mixture of **5** and **6** prepared by us using the Darzens method.

of the time, directly over the benzene ring in the *cis*-3-phenylglycidates, and are subject to increased shielding due to induced ring currents. Similarly, the α proton in ethyl *trans*-3-phenylglycidate (**5**) is *cis* to the β-phenyl group and is shielded to a greater extent than is the α proton in ethyl *cis*-3-phenylglycidate (**6**). The same comparison may be made of the α-methyl protons in ethyl 2-methyl-*trans*-3-phenylglycidate (**3**) and the epimeric **4**. The shielding effect of the induced ring currents of a suitably placed aryl group has been observed in a number of systems cited by Jackman[10] and also in other phenyl-substituted epoxides and aziranes.[2a,c,7,11]

The epimeric ethyl-3-phenylglycidates **5** and **6** and *t*-butyl *trans*-3-phenylglycidate (**7**) have vicinal α and β protons. The degree of coupling of these protons further confirms our assignments of configuration.

The assignment of observed peaks in the nmr spectra to specific protons when both α and β hydrogens are present is less certain. In the four α-substituted cinnamates discussed here, the signal due to the β proton is at δ = 7.4–7.5 ppm when it is *cis* to the ester group, and at 6.4–6.7 when it is *trans*. It is therefore reasonable that the signals at δ = 7.37 ppm for ethyl *trans*-cinnamate and at δ = 7.19 ppm for *t*-butyl *trans*-cinnamate are the β protons. Speziale and Tung[12] have made similar assignments for N,N-diethyl *trans*-cinnamides. Their assignments were based on the response of the β protons in four α-bromocinnamates or cinnamides (two epimeric pairs) at δ = 8.16–8.17 ppm.

For the four glycidic esters with α substituents, the same pattern appears for the signals due to β protons as in the case of the cinnamates. When the β proton is *cis* to the ester group (**8** and **10**), its response is at higher field than when it is *trans* (**9** and **11**). This trend is not followed in the case of *cis*- and *trans*-ethyl 3-phenylglycidate (**5** and **6**). If our assignment is correct, the β proton *cis* to the ester group in **5** responds at *lower* field than does the β proton in **6**. We have made our assignment on the grounds that the α proton must respond at higher field in the *trans* ester **5** than in the *cis* ester **6**, because it is more shielded by the β-phenyl group in the former. Also, the assignments made are consistent in that in **5**–**7**, **12**, and **13**, the response of the α proton appears downfield from that of the β proton.

We have compared the nmr spectra of our pure isomers with those of products made by the Darzens reaction in these laboratories several years ago[13] and with a few freshly prepared samples. Even though the old and new materials had been redistilled, their nmr spectra left no doubt that they contained considerable amounts of both geometric isomers. The only exception was ethyl 2,3-diphenylglycidate which apparently contained principally one isomer (see subsequent discussion of transesterification). In one sample of ethyl 3-methyl-3-phenylglycidate prepared by the Darzens reaction, the isomer related to *cis*-cinnamic acid predominated. In most of the preparations, the *trans*-3-phenylglycidate predominated.

The nmr spectra of several of the glycidic esters prepared by Johnson's modification[14] of Darzens method contained sharp, and usually intense, singlets at δ = 1.39–1.44 ppm. The suspicion that the signals were due to *t*-butyl esters arising from transesterification when potassium dissolved in *t*-butyl alcohol was used as condensing agent, was confirmed by synthesis of *t*-butyl *trans*-3-phenylglycidate (**12**) by direct epoxidation. The signal in the spectrum of the latter compound corresponded exactly with the "strange" peak in the product prepared by the modified Darzens method.

The extent of transesterification possible is seen in the relative areas of the C_4H_9 and CH_3 protons in the spectrum of "ethyl" 2,3-diphenylglycidate freshly prepared by the modified Darzens method. In a sample which had been distilled, but not recrystallized, the mole ratio of *t*-butyl–ethyl ester was 2:5. Distillation of several of our mixtures through a 1-m column packed

(11) A. Hassner and C. C. Heathcock, *Tetrahedron Letters*, 1125 (1964).
(12) A. J. Speziale and C. C. Tung, *J. Org. Chem.*, **28**, 1353 (1963).
(13) References to earlier work are found in H. H. Morris, *et al.*, *J. Am. Chem. Soc.*, **79**, 411 (1957), and preceding papers.
(14) W. S. Johnson, J. S. Belew, L. J. Chinn, and R. H. Hunt, *ibid.*, **75**, 4995 (1953).

with a tantalum spiral has not resulted in any appreciable separation of the ethyl and *t*-butyl esters, although separately the compounds have noticeably different boiling points.

Experimental Section

Melting points, with one exception noted, were determined by the usual capillary method in an electrically heated, stirred bath and all are corrected. Column chromatography purifications were made on neutral alumina, Brockmann activity I, obtained from the Fisher Scientific Co. Thin layer chromatographic examinations were made on E. Merck silica gel G from Brinkmann Instruments, Inc. The proton magnetic resonance spectra were obtained by Dr. Ralph Hill of this laboratory on a Varian Associates Model A-60 instrument. Elemental analyses were by Dr. A. Bernhardt, Mülheim, Germany, or by Midwest Microlabs. Infrared spectra of all the compounds in the table and of the related cinnamic acids except **6** and **11** have been recorded.[15]

Ethyl α-Phenyl-*trans*-cinnamate.—α-Phenyl-*trans*-cinnamic acid,[16] 28 g, was esterified in the usual manner with 800 ml of absolute ethanol and 24 ml of concentrated sulfuric acid. The mixture was kept at reflux overnight. After obtaining the product in solution in dry ether, an equal volume of hexane was added and the solution was chilled. A 75% yield of long colorless needles, mp 31–32°, was obtained. Reported melting points are 28 and 33–34°.[17]

Ethyl α-Phenyl-*cis*-cinnamate.—Following the method of Buckles and Mock,[18] 10 g (0.045 mole) of the corresponding acid and 4 g of anhydrous potassium carbonate were heated with 275 ml of absolute ethanol at reflux temperature for 1 hr. The mixture was cooled, 4.9 ml (0.06 mole) of ethyl iodide was added, and the system was kept at reflux temperature and protected from atmospheric moisture for 1 week. After about 100 ml of ethanol was removed by distillation, the residue was washed once with water, the aqueous layer was extracted with ether, and the ether extract was combined with the main organic layer. The product was then washed with 10% aqueous sodium bisulfite and dilute silver nitrate to remove any remaining iodide ion, treated with solid sodium chloride, then dried over sodium sulfate.

Evaporation of ether from the dried solution in a rotary evaporator left 7.8 g, or 68% yield, of a light yellow oil. This material was distilled in a short-path distillation apparatus at about 0.01 torr and an oven temperature of 130° to give a colorless oil having $n^{25}D$ 1.6059.

Anal. Calcd for $C_{17}H_{16}O_2$: C, 80.92; H, 6.39. Found: C, 80.93; H, 6.28.

An attempt to prepare the ester by way of the acid chloride, following the procedure of Riemschneider and Kampfer,[19] resulted in very poor yield, but the product had an infrared spectrum identical with that of the ester prepared as described above.

Ethyl 2,*trans*-3-Diphenylglycidate.—To a solution of 2.5 g (0.01 mole) of ethyl α-phenyl-*trans*-cinnamate in 10 ml of CH_2Cl_2 was added 2.04 g (0.01 mole) of 85% *m*-chloroperbenzoic acid dissolved in 10 ml of CH_2Cl_2. The mixture was refluxed gently for 56 hr, cooled, and shaken with a 10% solution of sodium sulfite to destroy any excess peroxide. The organic layer then was shaken with 5% aqueous $NaHCO_3$ to remove *m*-chlorobenzoic acid and dried over anhydrous sodium sulfate. The solvent was evaporated from the dried solution and the residue was taken up in ether, chilled in an ice bath, and diluted with an equal volume of hexane. Crystals soon separated which melted at 59–60° after a single recrystallization, and showed no depression of the melting point when mixed with a sample of the product prepared by the Darzens reaction. The infrared and nmr spectra of the two products were identical. The yield was only 1.0 g or 37% of theory but no attempt was made in this case to work out the best conditions. In later epoxidations an excess of peracid was used with much better results.

Ethyl 2,*cis*-3-Diphenylglycidate.—To 4.0 g (0.016 mole) of ethyl α-phenyl-*cis*-cinnamate in 30 ml of methylene chloride was added 3.9 g (0.02 mole) of 85% *m*-chloroperbenzoic acid dissolved in 20 ml of warm methylene chloride. Most of the peracid had disappeared at the end of 3 days at reflux temperature, as shown by treating an aliquot of the reaction mixture with solution of potassium iodide and titration of the liberated iodine with sodium thiosulfate. The mixture was worked up as described above. The residual oil, 2.76 g (65% of theory), was then chromatographed over neutral alumina, using benzene–hexane (1:1) as eluent. Examination of the product by thin layer chromatography indicated only one component.

Following the removal of as much solvent as possible by evaporation *in vacuo*, the material was distilled at 0.005 torr and an oven temperature of 120° to yield a colorless oil having $n^{25}D$ 1.5561. The product has been prepared previously.[9]

Anal. Calcd for $C_{17}H_{16}O_3$: C, 76.10; H, 6.01. Found: C, 76.21; H, 5.89.

Ethyl α-Methyl-*cis*-cinnamate.—The acid was prepared following the method of Stoermer and Voht.[20] We irradiated 10 g of α-methyl-*trans*-cinnamic acid (Aldrich Chemical Co.), mp 81–82°, from hexane, in 150 ml of benzene for 5 hr with light from a high-pressure mercury arc. After the benzene was removed at reduced pressure, the remaining solid was taken up in hexane. Slow evaporation at room temperature of the hexane in an evaporating dish produced two distinct types of crystals. Hand separation of the mass of large, stout crystals in the center of the dish, and subsequent rinsing with, then recrystallization from hexane, produced 2.5 g of α-methyl-*cis*-cinnamic acid, mp 91–92°.

A mixture of 2.0 g (0.0123 mole) of α-methyl-*cis*-cinnamic acid, 1.0 g of anhydrous potassium carbonate, and 150 ml of absolute ethanol was heated for 30 min, cooled, and 1.5 ml (0.0185 mole) of ethyl iodide was added. The mixture was heated at reflux for 4 days, then worked up as described for ethyl α-phenyl-*cis*-cinnamate. The product, a light brown oil, was purified by chromatography over alumina using benzene as eluent. The yield was 2.04 g (87%) of a yellowish oil which was used for epoxidation.

Ethyl 2-Methyl-*trans*-3-phenylglycidate.—Ethyl α-methyl-*trans*-cinnamic acid was esterified in the usual manner using absolute ethanol and sulfuric acid, as already described, and was purified by chromatography over neutral alumina using benzene–hexane (1:1).

A solution of 3.0 g (0.016 mole) of ethyl α-methyl-*trans*-cinnamate in 30 ml of methylene chloride was mixed with 10 ml of methylene chloride containing 3.9 g (0.021 mole) of 85% *m*-chloroperbenzoic acid. The color of the solution changed from pale to dark yellow at the time of mixing, but no rise in temperature was noted. After 4.5 days at reflux, the now colorless solution was dissolved in ether and worked up as described for previous epoxidations. Examination of the product, a light brown oil, by thin layer chromatography disclosed the presence of at least two substances. The mixture was then purified by chromatography over neutral alumina using benzene as eluent. The infrared spectrum of the resulting light yellow oil was markedly different from that of the crude material. Yield of purified product was 3.0 g (92%). This was further purified, to remove solvent, by short-path distillation at a pressure of 0.01 torr using an oven temperature of 130°. The refractive index of the colorless distillate was $n^{25}D$ 1.4997.[21] The infrared and nmr spectra compared with those of the *cis* isomer and of the same substance prepared by the Darzens method left no doubt as to the identity of the product.

Ethyl 2-Methyl-*cis*-3-phenylglycidate.—Ethyl α-methyl-*cis*-cinnamate (2 g, 0.01 mole) was dissolved in 30 ml of methylene chloride, and a solution of 2.6 g (0.014 mole) of 85% *m*-chloroperbenzoic acid in methylene chloride was added. The mixture was refluxed for 4 days and worked up as described for previous epoxidations. The yield of product, after chromatography over neutral alumina and removal of solvent, was 1.8 g (87%) of a pale yellow oil. Short-path distillation at 0.01 torr and an oven temperature of about 130° afforded a colorless liquid, $n^{25}D$ 1.5015.

Anal. Calcd for $C_{12}H_{14}O_3$: C, 69.88; H, 6.84. Found: C, 69.13; H, 6.83.

(15) V. R. Valente, M.S. Thesis, University of Maine, Orono, Maine, 1964. The spectra of **1–4** and **8–11** are reported on pp 41–64.

(16) L. F. Fieser, "Experiments in Organic Chemistry," 3rd ed, D. C. Heath and Co., Boston, Mass., 1955, p 182. Our nomenclature differs from that of Fieser.

(17) (a) K. Auwers and F. Eisenlohr, *J. Prakt. Chem.*, [2] **84**, 87 (1912), cited in F. K. Beilstein, Vol. 9, 1st Suppl., 4th ed, 1932, p 299; (b) J. v. Braun and G. Manz, *Ann.*, **468**, 258 (1928).

(18) R. Buckles and G. Mock, *J. Org. Chem.*, **15**, 680 (1950).

(19) R. Riemschneider and H. Kampfer, *Monatsh.*, **90**, 518 (1959).

(20) R. Stoermer and G. Voht, *Ann.*, **409**, 36 (1915).

(21) G. Richard, *Compt. Rend.*, **199**, 71 (1934); *Chem. Abstr.*, **28**, 5812 (1934).

Ethyl *trans*-3-Phenylglycidate.—A solution of 8.8 g (0.05 mole) of distilled ethyl cinnamate was mixed with a solution of 13 g (0.064 mole) of *m*-chloroperbenzoic acid in 100 ml of methylene chloride and treated as has already been described, except that the product was passed rapidly through a column of alumina, using benzene as solvent. The product from this treatment contained a trace of impurity, shown by thin layer chromatography, but after solvent was removed and the epoxide was subjected to short-path distillation, only the signals associated with the glycidic ester were observed in the nmr spectrum. Yield, after chromatography and distillation, was 4.5 g (47%), bp 115° at 1.1 torr, $n^{25}D$ 1.5159.

***t*-Butyl *trans*-3-Phenylglycidate.**—Cinnamoyl chloride was prepared as a slightly yellow solid having bp 130° at aspirator pressure (about 14 torr) in 82% yield from *trans*-cinnamic acid and thionyl chloride. The acid chloride was then converted to the *t*-butyl ester, bp 117–119° at 2.7–3.0 torr, in 59% yield by following a published procedure.[22]

To 50 ml of methylene chloride containing 6.14 g (0.030 mole) of *t*-butyl *trans*-cinnamate was added a solution of 7.60 g (0.037 mole) of 85% *m*-chloroperbenzoic acid in 60 ml of methylene chloride. An additional 10 ml of solvent was used for rinsing. After 48 hr at reflux, when about 90% of the initial amount of peracid had disappeared, the mixture was washed, successively, with dilute solutions of sodium sulfite and sodium bicarbonate, water, then with saturated sodium chloride to break an emulsion. After the organic layer was dried over sodium sulfate, it was stripped of solvent at aspirator pressure, and distilled in a simple Claissen-type apparatus, bp 135–138° at 3.5 torr. The distillate was barely colored and solidified shortly after distillation. Thin layer chromatography with 50% (vv) hexane–benzene, indicated complete conversion to glycidic ester (R_f values were 0.38 for the cinnamate, 0.15 for the glycidate). A satisfactorily sharp melting point has not been obtained. The distillate, air dried, melted at 64–66° on a Kofler block with prior sintering. A sample which had been chromatographed over neutral alumina, then air dried, melted at 65–66°, again with prior sintering. The product showed a tendency to sublime when it was distilled in a short-path distillation apparatus, and sublimed crystals used for elemental analysis did not have an improved melting point.

Anal. Calcd for $C_{13}H_{16}O_3$: C, 70.88; H, 7.32. Found: C, 70.77; H, 7.21, 7.36.

(22) B. Abramovitch, J. C. Shiver, B. E. Hudson, and C. R. Hauser, *J. Am. Chem. Soc.*, **65**, 986 (1943).

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Microbiological Dehydrogenation of Racemic 13β-Alkylgonanes[1a]

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Microbiological dehydrogenations of racemic 13β-ethyl- and 13β-propyl-17β-hydroxygon-4-en-3-one with *Corynebacterium simplex* and with *C. hoagii* and of racemic 13β-ethyl-3-methoxygona-1,3,5(10)-trien-17β-ol with *C. simplex* and with *Flavobacterium dehydrogenans* gave *d* and *l*, as well as racemic, transformation products.

In an earlier paper[1a] we detailed our experience in the preparation of some 13β-alkylgonane derivatives of unnatural configuration *via* microbiological means. The present report deals with an extension of this work in the preparation of 13β-alkylgonane derivatives primarily of natural *d* configuration.[2]

Microbiological oxidation–reduction reactions at C-17 have been successfully utilized in select cases for resolution of racemic steroids obtained by total synthesis,[3] and a variety of microorganisms are available for such transformations.[4]

Our study of oxidation–reduction reactions of the C-17 ketone–alcohol system generally did not afford satisfactory results. Reduction of the 17-ketone group of select racemic 13β-alkylgonan-17-ones (specifically IIa) by yeast did not occur, and bacterial oxidation of the 17β-hydroxy group of racemic IIIc was effected in poor yield. Although oxidation of IIIc by *Flavobacterium dehydrogenans* gave the 17β-ketone IIc, the product was racemic. The transformation with *Corynebacterium simplex* afforded in low yield a resolved 17-ketone IIc and unoxidized substrate. These poor results appeared to be a consequence of the additional steric hindrance of the 13β-ethyl group in comparison with estrane derivatives.

Our attention was diverted to microbiological dehydrogenation of the A ring of 13β-alkylgon-4-en-3-one derivatives in anticipation of better transformations. Such dehydrogenations of 19-nor steroids with *C. simplex*[5] or other bacteria[6] are accompanied by aromatization, and indeed *C. simplex* attack on racemic Ia gave a product mixture of two phenols, recognized as the 17-ketone IIa and the 17β-alcohol IIIa. Attack by *C. simplex* on the 13β-propyl derivative Ib gave mainly the phenol IIb with traces of IIIb.

Methylation of the 17-ketone IIa gave the 3-methyl ether IIc, which was reduced by sodium borohydride to the 17β-alcohol IIIc, which in turn was reduced by lithium metal and liquid ammonia and hydrolyzed to the Δ^4-3-ketone Ia. A similar sequence employing the 13β-propyl derivative IIb led to Ib.

(1) (a) Paper IX in the series "Totally Synthetic Steroid Hormones." For Part VIII, see L. L. Smith, G. Greenspan, R. Rees, and T. Foell, *J. Am. Chem. Soc.*, **88**, 3120 (1966). (b) To whom correspondence should be addressed: Department of Biochemistry and Nutrition, University of Texas Medical Branch, Galveston, Texas 77550.

(2) The nomenclature convention of L. F. Fieser and M. Fieser ["Steroids," Reinhold Publishing Corp., New York, N. Y., 1959, p 336] is used throughout.

(3) (a) E. Vischer, J. Schmidlin, and A. Wettstein, *Experientia*, **12**, 50 (1956); (b) A. Wettstein, E. Vischer, and C. Meystre, U. S. Patent 2,844,513 (July 22, 1958); (c) W. S. Johnson, W. A. Vredenburgh, and J. E. Pike, *J. Am. Chem. Soc.*, **82**, 3409 (1960); (d) K. V. Yorka, W. L. Truett, and W. S. Johnson, *J. Org. Chem.*, **27**, 4580 (1962).

(4) See the recent reviews by T. H. Stoudt, *Advan. Appl. Microbiol.*, **2**, 183 (1960); S. H. Eppstein, P. D. Meister, H. C. Murray, and D. H. Peterson, *Vitamins Hormones*, **14**, 359 (1956).

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