[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, UNIVERSITY OF TORONTO]

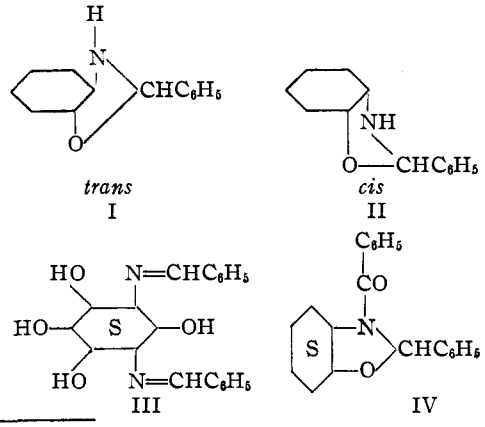
Heterocyclization of Epimeric Aminocyclanols.[1,2] II. Oxazolidines

BY G. E. MCCASLAND AND E. CLYDE HORSWILL

The possible effect of configuration on ease of oxazolidine formation by epimeric 2-aminocyclanols has been investigated *cis*- and *trans*-2-aminocyclohexanol give Schiff bases and not oxazolidines with benzaldehyde. 3-Aminopropanediol-1,2 gives a product consisting primarily of Schiff base, contrary to previous report. These and other Schiff bases containing the grouping C_6H_5—CH=N— are easily recognized by their highly characteristic molar extinction maximum of about 17,000 at 2470 Å. Both *cis*- and *trans*-2-benzylideneaminocyclohexanols on benzoylation are isomerized to N-benzoyloxazolidines

In a previous communication[2a] we suggested that the ease of formation of oxazolidines might serve to distinguish *cis* and *trans* epimers of 2-aminocyclanols, at least in the case of cyclopentane and smaller rings. For such a heterocyclization method[3] to be useful it is desirable that the reaction proceed (with *cis* epimers) in good yield under mild conditions, and that the products should be easily isolated and characterized. We have now investigated this possibility.

Preparation of oxazolidine (I, II) by reaction of benzaldehyde with each of the epimeric 2-aminocyclohexanols was first attempted. The products were characterized by ultraviolet absorption spectra.[4,5,6] Each product showed a curve (Fig. 1) with a molar extinction maximum of about 17,000 at 2470 Å. A survey of the literature revealed that this extinction maximum is highly characteristic[4] (see Table I) of Schiff bases containing the structure C_6H_5–CH=N–. Even the benzylidene derivative of methylamine (oxazolidine structure impossible) gives this value.[7] A striking confirmation is noted in the case of streptamine. The benzaldehyde derivative III of this compound has *two* benzylideneamino groups and gave a molar extinction maximum at 2475 Å. of 34,000—just twice that of the mono-Schiff bases.



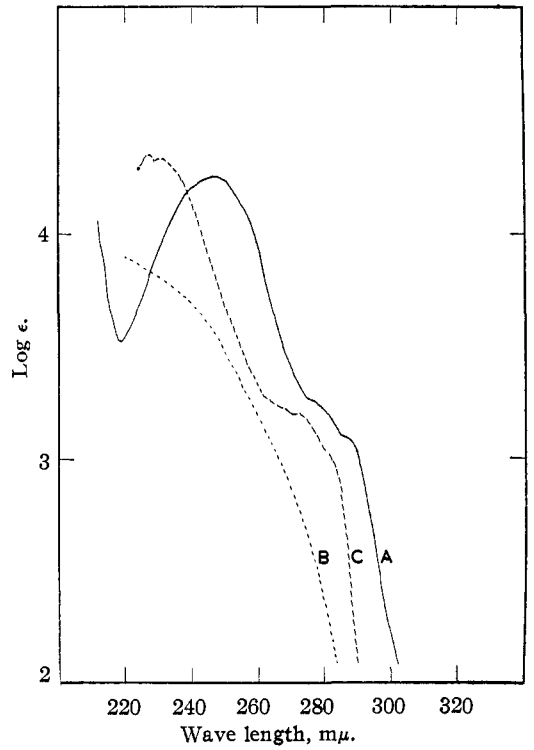


Fig. 1.—Ultraviolet absorption spectra of: (A) *d,l-trans*-2-benzylideneaminocyclohexanol; (B) N-benzoyl-morpholine; (C) *d,l-trans*-2-benzoylaminocyclohexyl benzoate.

These results suggested that many "oxazolidines" in the literature may actually be Schiff bases. One such product which had been prepared by Bergmann, *et al.*,[8] from 3-aminopropanediol-1,2

(1) We wish to thank the Research Council of Ontario for a generous grant in support of this work.

(2) For related publications see: (a) G. E. McCasland and E. C. Horswill, THIS JOURNAL, **73**, 3744 (1951); (b) G. E. McCasland, *ibid.*, **73**, 2293 (1951); (c) G. E. McCasland, *ibid.*, **73**, 2295 (1951); (d) G. E. McCasland and D. A. Smith, *ibid.*, **72**, 2190 (1950); (e) G. E. McCasland, R. K. Clark, Jr., and H. E. Carter, *ibid.*, **71**, 637 (1949); (f) H. E. Carter, R. K. Clark, Jr., Betty Lytle and G. E. McCasland, *J. Biol. Chem.*, **175**, 683 (1948); (g) G. E. McCasland and D. A. Smith (submitted for publication).

(3) W. J. Close (*J. Org. Chem.*, **15**, 1131 (1950)) has recently reported an interesting example of steric specificity in the heterocyclization of epimeric ephedrines with urea. The *trans* ("pseudo")) form gave an oxazolidone, and the *cis* form an imidazolidone. According to Close, this indicates that the functional hydroxy and alkylamino groups are closer in the *trans* form. In this open-chain epimeric pair configuration is significant only by its influence on *conformation*.

(4) Recently L. H. Goodson and Hope Christopher (THIS JOURNAL, **71**, 1117 (1949)) synthesized from ethanolamine and aromatic aldehydes a series of compounds reportedly having extinction maxima of 95000–128,000 at 2450–2550 Å. (A private communication from L. H. Goodson states that the correct extinction maxima were actually one-tenth of those given.) These compounds were proved to be Schiff bases by Daasch and Hanninen[5] using infrared spectra. The values reported by the former authors are characteristic of Schiff bases.

(5) L. W. Daasch and U. E. Hanninen, *ibid.*, **72**, 3673 (1950), used infrared spectra for characterizing such compounds.

(6) Cope and Hancock reported that oxazolidine and Schiff base structures can be distinguished by molar refractivities. Ultraviolet spectra appear to be a better means of characterization, and infrared spectra perhaps still better. See (a) A. C. Cope and E. M. Hancock, *ibid.*, **64**, 1503 (1942); **66**, 1453 (1944); (b) A. C. Cope, C. M. Hofmann, C. Wyckoff and E. Hardenburgh, *ibid.*, **63**, 3452 (1941).

(7) A private communication from L. H. Goodson states that 2-phenyl-3-ethyloxazolidine (Schiff base structure impossible) has an extinction maximum of 945 at 2450 Å.

(8) M. Bergmann, *et al.*, *Ber.*, **54**, 936 (1921). These authors obtained from aminopropanediol and benzaldehyde in near-quantitative yield a product of m.p. 75–79° ("... scheint ein Gemisch von Isomeren zu sein.") which without purification gave C, H and N analyses very close to theoretical values. They regarded this product as an oxazolidine because on benzoylation it gave an N-benzoyloxazolidine.

TABLE I

ULTRAVIOLET ABSORPTION SPECTRA

Substance	Molar extinction ε and wave length, λ (Å.) Low-end λ	Low-end ε	Minimum λ	Minimum ε	Maximum λ	Maximum ε	High-end λ	High-end ε
Benzylidene derivative of								
Methylamine[a]	..	...	..	...	2470	17000	..	..
trans-2-Aminocyclohexanol	2120	11000	2180	3300	2470	17800	3000	160
Streptamine[b]	..	...	..	...	2475	34000	..	..
cis-2-Aminocyclohexanol	2270	5800	..	...	2475	18200	2900	1400
3-Aminopropanediol-1,2[c]	2140	4500	2180	1800	2470	13000	3000	150
Benzoylated benzylidene of								
trans-2-Aminocyclohexanol	2270	9300	None		None		2800	250
3-Aminopropanediol-1,2	2100	20000	2120	18500	2280	24000	2880	200
cis-2-Aminocyclohexanol	2300	5900	None		None		2840	100
Model benzoyl compounds								
N-Benzoylmorpholine	2200	8000	None		None		2800	200
trans-2-Benzoylaminocyclohexanol	2200	11000	None		2280	12000	3000	150
trans-2-Benzoylaminocyclohexyl benzoate	2240	19000	None		2280	22000	2900	100

[a] E. A. Braude, *Ann. Rep. Chem. Soc.*, 126 (45). [b] Bis-benzylidene derivative, calculated by us from the data of R. L. Peck, *et al.*, THIS JOURNAL, **68**, 776 (1946); $E_{1\%}$ = 955 at 2475 Å. [c] Measurements by Dr. J. C. Brantley.

and benzaldehyde was re-examined by us. The ultraviolet spectrum (Table I) indicates that the product consists largely, if not entirely, of Schiff base.

Indeed, recent work by others[5] together with our own observation leads us to doubt that any simple oxazolidine (without substituent on nitrogen) of well-established structure and purity is now known. However, when the oxazolidine-nitrogen atom bears an alkyl or acyl group instead of hydrogen rearrangement to Schiff base structure is precluded and thus one possible cause of instability is removed.

We therefore investigated the reaction of 2-alkylaminocyclohexanols with carbonyl compounds. Similar reactions had been reported[9] with acyclic aminoalkanols. The alicyclic compounds, however, did not react under any conditions studied to form the expected N-alkyloxazolidines; in fact no products other than starting materials could be obtained. In the course of this work certain N-alkyl and N-acyl derivatives of the 2-aminocyclohexanols were prepared for the first time, and others characterized more fully than heretofore. The *trans*-N-alkyl derivatives can be obtained conveniently by examination of the oxide; for the *cis* reductive alkylation was used. These methods were found superior to that employing alkylation and detosylation of an N-tosyl derivative.

Formation of N-Acyloxazolidines

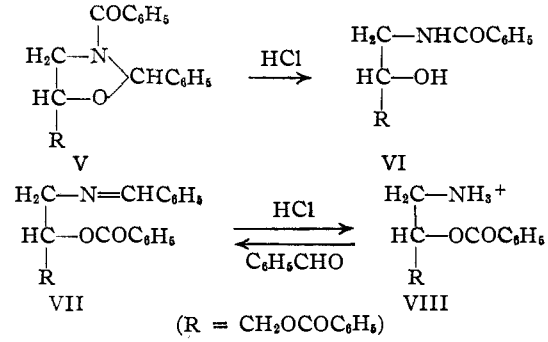
Another possibility investigated was the formation of N-acyloxazolidines such as IV. It is improbable that the reaction of a 2-acylaminoalkanol with a carbonyl compound will yield an acyloxazolidine. However, the experiments of Bergmann, *et al.*,[8] suggested a possible route to such products.

When Bergmann, *et al.*, treated their aminopropanediol derivative mentioned above (now known to consist mainly of the Schiff base) with benzoyl chloride in pyridine–chloroform they obtained a solid product. They reported convincing evidence that this benzoylation product was an N-benzoyloxazolidine (V) and this is now further confirmed by our findings.

It is probable that the Schiff base is isomerized to oxazolidine during this benzoylation, and perhaps under the conditions of various other reactions. This makes questionable any chemical proof of structure for such Schiff bases *alias* oxazolidines. (Another possible mechanism is addition of benzoyl chloride to the C=N bond followed by cyclodehydrohalogenation.)

Bergmann, *et al.*,[8] established the identity of their N-benzoyloxazolidine (V) by the fact that on treatment with aqueous ethereal hydrogen chloride it gave the benzoylaminoalkanol (VI), which would not be the expected product from the O-benzoyl Schiff base (VII). The latter compound was actually prepared[8] from the amino-ester hydrochloride (VIII) by treatment with benzaldehyde and acetic acid and on treatment with hydrochloric acid it reverted to VIII and did not form VI.

First we prepared Bergmann's product V and further established its identity by measuring the saponification equivalent which demonstrated the presence of one O-benzoyl group only. We then attempted the conversion of the epimeric Schiff bases of the 2-aminocyclohexanols to N-benzoyloxazolidines. Solid products were obtained in each case. The products were characterized by their ultraviolet spectra which were closely similar to that of N-benzoylmorpholine (Fig. 1) which has a similar heterocyclic structure. On treatment with aqueous ethereal hydrogen chloride each product gave



(9) M. Senkus, THIS JOURNAL, **67**, 1516 (1945); L. Knorr and H. Matthes, *Ber.*, **34**, 3484 (1901); N. K. Ushenko, *C. A.*, **37**, 4395 (1943); A. I. Kiprianov and B. A. Raschkovan, *J. Gen. Chem. (U. S. S. R.)*, **7**, 1026 (1937); *C. A.*, **31**, 5356 (1937).

the respective 2-benzoylaminocyclanol, and benzaldehyde was liberated. These facts indicate that our compounds have the N-benzoyloxazolidine structure IV.

Since both *cis*- and *trans*-acyloxazolidines were obtained in yields of 30–50% it appears that acyloxazolidine formation is not dependent on configuration in the C_6-series, though it might be in the C_5-series.

Each aminocyclanol epimer should yield two of the four diastereomers possible for oxazolidines with three asymmetric ring-atoms; we appear to have isolated only one in each case.[10]

Acknowledgment.—Early experiments in this research were conducted in the laboratory of Dr. H. E. Carter at the University of Illinois, who made helpful suggestions. Dr. R. K. Clark, Jr., helped in some of the preparations.

Experimental

Carbon–hydrogen and Dumas nitrogen microanalyses by Mr. Robert Pyke. All melting and boiling points corrected. M.p.'s were determined on Köfler micro-block.

***d,l*-3-Aminopropanediol-1,2.**—Amination of 80 ml. of *d,l*-3-chloropropanediol-1,2 by the procedure of Bergmann[8] gave 40 g. of colorless liquid, b.p. 153–157° (24 mm.) (reported,[11a] 238–239° (325 mm.)).

N-Benzoylmorpholine.—The crude product of m.p. 71–74° prepared by the method of Knorr[11b] was recrystallized thrice from dry ether. The melting point of the colorless prisms attained a constant sharp value of 73.5–74.0° (reported[11b] 74–75°). For ultraviolet spectrum see Table I and Fig. 1.

***d,l-trans*-2-Benzoylaminocyclohexanol and its Benzoate.**—The two compounds were prepared as previously described.[2d,e] For ultraviolet spectra see Table I and Fig 1.

Reactions with Benzaldehyde. ***d,l-trans*-2-Benzylideneaminocyclohexanol** (A).—A 4.0-g. portion of *trans*-2-aminocyclohexanol was mixed with 4.0 g. of benzaldehyde and 2.0 ml. of ethyl acetate (heat effect). Colorless crystals separated and were recrystallized from ethyl acetate, giving a product of m.p. 80–92°; yield 6.1 g. A Kjeldahl analysis showed 6.83% N (calcd. 6.89). A sample was recrystallized again giving colorless crystals, m.p. 90–92°.

(B).—To a solution of 0.50 g. of *trans*-2-aminocyclohexanol in 6 ml. of dry benzene was added 0.50 g. of freshly distilled benzaldehyde. The mixture was refluxed for 3 hours under a small water separator.[6b] The reaction mixture was allowed to cool to room temperature and the solvent removed under vacuum, leaving 0.88 g. of pale yellow crystalline residue, m.p. 81–85°. Recrystallization from dry petroleum ether (90–100°) and vacuum-drying gave colorless crystals weighing 0.80 g. (91%), m.p. 85–86.5°. A sample was sublimed at 80° (bath) and 1 mm. pressure, recrystallized again and resublimed for analysis, m.p. 90–91°.

Anal. Calcd. for $C_{13}H_{17}NO$: C, 76.81; H, 8.43; N, 6.89. Found: C, 77.31; H, 9.17; N, 7.05 (Kjel.).

The ultraviolet absorption spectrum (Table I and Fig. 1) showed a Schiff base structure. A sample cleaved with acid gave an 88% yield of benzaldehyde, isolated as 2,4-dinitrophenylhydrazone.

***d,l-cis*-2-Benzylideneaminocyclohexanol.**—Treatment of 2.88 g. of *cis*-2-aminocyclohexanol by the same procedure as above gave a viscous, pale yellow oil which crystallized upon seeding (seeding is unnecessary if oil is distilled first, b.p. 122–123° (1 mm.)), weight 4.80 g. (94%), m.p. 44–47°. A sample for analysis was recrystallized from dry isopentane, filtered at 0°, and then sublimed at 40° (bath) (0.002 mm.) to give colorless crystals, m.p. 46–47°.

Anal. Calcd. for $C_{13}H_{17}NO$: C, 76.81; H, 8.43; N, 6.89. Found: C, 76.96; H, 8.31; N, 6.36.

The ultraviolet absorption spectrum (Table I) was almost identical with that of the *trans* compound, indicating a Schiff base structure. A sample cleaved with acid gave a 98% yield of benzaldehyde, isolated as 2,4-dinitrophenylhydrazone.

***d,l*-3-Benzylideneaminopropanediol-1,2.**—A 3.0-g. portion of 3-aminopropanediol-1,2 was treated by the procedure of Bergmann.[8] Recrystallization from ethyl acetate gave 3.8 g. of colorless crystals, m.p. 72–78° (reported[8] m.p. 75–79°).

Anal. Calcd. for $C_{10}H_{13}NO_2$: N, 7.82. Found: N, 7.78 (Kjel.).

The ultraviolet spectrum (Table I) was similar to that of the *trans* Schiff base (above) and indicates that the product contains a large amount of Schiff base, which may be in equilibrium with oxazolidine.

Benzoylation of Benzylidene Derivatives. Benzoylation of *trans*-2-Benzylideneaminocyclohexanol.—A solution of 0.71 g. of the *trans*-benzylidene derivative and 0.54 g. of benzoyl chloride in 1.0 ml. of dry chloroform–pyridine (2:1) was left at 25° overnight. To the solidified reaction mixture was added 5 ml. of water and 10 ml. of ether. The ether phase was separated and the aqueous layer extracted with three 5-ml. portions of ether. The combined ether extracts were washed successively with 10% sodium bicarbonate solution and water and dried over anhydrous magnesium sulfate. The residue after removal of solvent was a colorless crystalline powder weighing 0.35 g., m.p. 125–144°. A 150-mg. sample of this material after recrystallization from ethyl acetate–petroleum ether (1:1) and then thrice from benzene appeared as colorless needles, weight 44 mg., m.p. 150–151°.

Anal. Calcd. for $C_{20}H_{21}NO_2$: C, 78.14; H, 6.89; N, 4.56. Found: C, 77.51; H, 6.51; N, 4.39 (Dumas), 4.61 (Kjel.). (The calculated analysis for the O,N-dibenzoyl derivative ($C_{20}H_{21}NO_3$) would be C, 74.28; H, 6.55; N, 4.33; a mixed m.p. with this compound was depressed.)

The ultraviolet absorption spectrum (Table I) showed that a Schiff base structure was no longer present. The spectrum is virtually identical with that of N-benzoylmorpholine (Fig. 1). The product of m.p. 150–151° appears to be ***d,l-cis*-(2?,4)-2-phenyl-3-benzoyl-4,5-cyclohexanoöxazolidine.**[12] The crude yield (0.35 g.) would then be 33%.

Cleavage of the product with aqueous ethereal hydrogen chloride gave 91% of *trans*-2-benzoylaminocyclohexanol, with liberation of benzaldehyde. A saponification analysis on the acyloxazolidine for O-benzoyl was negative (a control analysis on *trans*-2-benzoylaminocyclohexyl benzoate gave a correct result).

From the first benzene mother liquors above, a low yield of purified *trans*-2-benzoylaminocyclohexyl benzoate (identified by mixed m.p.) was recovered by recrystallization of the dried residue from 95% ethanol. This may indicate a small amount of free aminocyclanol as impurity in the Schiff base, or that a small fraction of the latter is cleaved during acylation.

Benzoylation of *cis*-2-Benzylideneaminocyclohexanol.—When 1.01 g. of *cis*-2-benzylideneaminocyclohexanol was benzoylated by the preceding method the product was a colorless oil which slowly crystallized after scratching or seeding to a white solid weighing 1.01 g. (67%), m.p. 70–82°. Recrystallization from hexane–cyclohexane (2:1) gave 0.67 g. (45%) of tiny prismatic needles, m.p. 80–85°.

A sample recrystallized further for analysis had a m.p. 86–87°.

Anal. Calcd. for $C_{20}H_{21}NO_2$: C, 78.14; H, 6.89; N, 4.56. Found: C, 77.87; H, 6.63; N, 4.45 (Dumas), 4.69 (Kjel.).

The ultraviolet absorption spectrum (Table I) shows no Schiff base peak at 2470 Å. and is almost coincident with those of both N-benzoylmorpholine (Fig. 1) and the corresponding *trans* compound. The product is believed to be ***d,l-cis*-(2?,4,5)-2-phenyl-3-benzoyl-4,5-cyclohexanoöxazolidine.**[12]

When treated with ether and concentrated hydrochloric acid the material gave 92% of *cis*-2-benzoylaminocyclohexanol, and benzaldehyde was liberated.

(10) One would expect that an oxazolidine could be obtained in better yield by use of a symmetric carbonyl reagent which would give a single diastereomer. However trials of such reagents gave poor results.

(11) (a) L. Knorr and A. Knorr, *Ber.*, **32**, 750 (1899); (b) L. Knorr, *Ann.*, **301**, 7 (1898).

(12) The prefixes "*cis*-(2?,4,5)-" and "*cis*-(2?,4)" indicate that the respective diastereomers have 4,5-*cis*- and 4,5-*trans*-configurations while both position-2 configurations are unknown.

Benzoylation of 3-Benzylideneaminopropanediol-1,2.—A 3.0-g. portion of the benzylidene compound was benzoylated by a similar procedure. Recrystallization from ethyl acetate–petroleum ether gave 5.0 g. of colorless crystals, m.p. 126–140°. These were recrystallized again giving 4.2 g., m.p. 120–133° (reported[8,13] 116–126°).

Anal. Calcd. for $C_{24}H_{21}NO_4$: N, 3.62; sapon. equiv. (one O-benzoyl group), 387. Found: N, 3.86; sapon. equiv., 405.

The ultraviolet spectrum (Table I) is strongly affected by the presence of an O-benzoyl group, and in fact was quite similar to that of 2-benzoylaminocyclohexyl benzoate (Fig. 1).

Ultraviolet Absorption Spectra.—Each sample was dissolved in 95% ethanol and diluted to 80–200 micro-molar concentration for examination with a Beckman model DU quartz spectrophotometer, using a 1-cm. quartz cell. The results are given in Table I and Fig. 1.

Preparation of 2-Alkylamino and 2-Tosylaminocyclohexanols. *d,l-trans*-2-Ethylaminocyclohexanol.—By the method of Brunel[14] a 62% yield of colorless crystals, b.p. 93° (8 mm.), m.p. 50.5–51°, was obtained (reported[14] m.p. 44–45°).

d,l-trans-2-Butylaminocyclohexanol.—Cyclohexene oxide (0.98 g.) was heated with 1.10 g. of dry 1-aminobutane for 12 hours at 150–160° (sealed tube). On vacuum distillation the desired product was obtained at 115° (7 mm.), and it crystallized in the receiver, m.p. 39.0–40.5° (yield 84%). A sample was sublimed at 1 mm. for analysis, m.p. unchanged.

Anal. Calcd. for $C_{10}H_{21}NO$: C, 70.12; H, 12.36. Found: C, 70.17; H, 12.28.

(13) Bergmann[8] reported the separation of the mixture of benzoyloxazolidines from aminopropanediol into two diastereomers of m.p. 118° and 143° by a treatment with alcoholic hydrogen chloride at 0°.

(14) L. Brunel, *Ann. chim. phys.*, [8] **6**, 257 (1905).

The compound was also prepared by reductive alkylation, in slightly lower yield.

With dry ethereal hydrogen chloride, an amine hydrochloride of m.p. 232–233.5° (dec.) was obtained.

d,l-cis-2-Butylaminocyclohexanol.—To a solution of 1.80 g. of *cis*-2-aminocyclohexanol in 50 ml. of absolute ethanol was added a 10% excess of freshly distilled butanal. The mixture was hydrogenated for four hours at 3 atm. (25°), using Raney nickel catalyst. Filtration and vacuum distillation gave a residue of 2.26 g., colorless needles, m.p. 49–54°. Sublimation at 1 mm. gave 1.90 g. of colorless silky needles, m.p. 59–60°. Resublimation for analysis caused no change in m.p.

Anal. Calcd. for $C_{10}H_{21}NO$: C, 70.12; H, 12.36. Found: C, 69.95; H, 12.22.

d,l-trans-2-*p*-Toluenesulfonylaminocyclohexanol.—A solution of 0.231 g. of the aminocyclanol hydrochloride in water was treated with the sulfonyl chloride in acetone[15] in the presence of sodium bicarbonate. There was obtained 0.344 g. (83%) of colorless crystals, m.p. 129–130° (reported[16] m.p. 128°). A sample vacuum distilled for analysis showed no change in m.p.

Anal. Calcd. for $C_{13}H_{19}NO_3S$: C, 57.96; H, 7.11; N, 5.20. Found: C, 57.42; H, 7.12; N, 5.25.

d,l-cis-2-*p*-Toluenesulfonylaminocyclohexanol.—By treatment of 0.210 g. of the *cis*-aminocyclanol hydrochloride in the same manner as above, there was obtained 0.359 g. (96%) of colorless crystals, m.p. 158.5–159.5 (reported[16] m.p. 152–154°).

Anal. Calcd. for $C_{13}H_{19}NO_3S$: C, 57.96; H, 7.11. Found: C, 57.83; H, 6.76.

(15) The method is similar to that used by I. S. Shupe, *J. Assn. Off. Agr. Chem.*, **24**, 755 (1941), with ethanolamine.

(16) G. Fodor and J. Kiss (THIS JOURNAL, **72**, 3495 (1950)) carried out only nitrogen analyses on their N-tosyl products. The procedures now reported give somewhat higher yields.

TORONTO, CANADA RECEIVED FEBRUARY 12, 1951

[CONTRIBUTION FROM THE CHEMICAL DIVISION OF THE PROCTER & GAMBLE COMPANY]

Directed Interesterification in Glycerides. III. The Synthesis of Single-Fatty Acid 1,3-Diglycerides[1]

BY FRED J. BAUR AND WILLY LANGE

A method for the synthesis of single-fatty acid symmetrical diglycerides has been described. The process involves the use of low-temperature directed interesterification in which symmetrical diglycerides are preferentially crystallized from statistically distributed catalyzed single-fatty acid triglyceride–triacetin–glycerol mixtures. The method is useful in the preparation of symmetrical diglycerides derived from single fatty acids with melting points above 20°. A new diglyceride, 1,3-dibehenin, has been prepared.

The classical methods for the synthesis of symmetrical diglycerides involve the use of glycerol derivatives containing two free and one temporarily blocked hydroxyl group.[2] Pure diglycerides also may be obtained by direct esterification of 1-monoglycerides with either fatty acids or acid chlorides[3a] and separation from unreacted monoglyceride by solvent crystallization. A similar method, just reported,[3b] involves the direct esterification of glycidyl fatty acid esters with fatty acids.

Eckey's process of low-temperature directed interesterification of fats[4] has been modified recently by Eckey and Formo[5] to include simultaneous alcoholysis as well as ester–ester interchange. In the modified process, in the presence of catalysts, melted fats and glycerol interesterify to produce an equilibrium mixture of monoglycerides, diglycerides, triglycerides and free glycerol. Crystallization of high melting monoglycerides or diglycerides takes place when the temperature of the liquid product is lowered sufficiently. This lowering of the temperature and subsequent crystallization of a component from the liquid phase disturbs the equilibrium, re-establishment of which is promoted continuously by the rearrangement catalyst. The desired glyceride continues to crystallize out until the supply of its constituent groups is no longer suf-

(1) The papers by E. W. Eckey (ref. 4) and E. W. Eckey and M. W. Formo (ref. 5) are designated as I and II of this series, respectively.

(2) E. Fischer, M. Bergmann and H. Barwind, *Ber.*, **53**, 1589 (1920); E. Fischer, *ibid.*, **53**, 1621 (1920); D. T. Jackson and C. G. King, THIS JOURNAL, **55**, 678 (1933); B. F. Daubert and C. G. King, *ibid.*, **61**, 3328 (1939); P. E. Verkade, J. van der Lee and W. Meerburg, *Rec. trav. chim.*, **51**, 850 (1932); **54**, 716 (1935); P. E. Verkade and J. van der Lee, *ibid.*, **55**, 267 (1936); F. L. Jackson, B. F. Daubert, C. G. King and H. E. Longenecker, THIS JOURNAL, **66**, 289 (1944).

(3) (a) T. Malkin, M. R. el Shurbagy and M. L. Meara, *J. Chem. Soc.*, 1409 (1937); M. G. R. Carter and T. Malkin, *ibid.*, 554 (1947); (b) E. B. Kester (to the U. S. Dept. of Agriculture), U. S. Patent 2,523,309 (1950).

(4) E. W. Eckey (to The Procter & Gamble Company), U. S. Patent 2,442,531 (1948); E. W. Eckey, *Ind. Eng. Chem.*, **40**, 1183 (1948).

(5) E. W. Eckey and M. W. Formo, *J. Am. Oil Chem. Soc.*, **23**, 207 (1949).