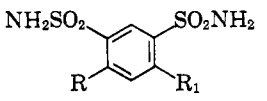
TABLE I



No.	R	R_1	Formula	Yield, %	M.p., °C.	Analysis, % Calcd. C	Calcd. H	Calcd. N	Found C	Found H	Found N
1	Cl	$NHCH_2CH(OC_2H_5)_2$	$C_{12}H_{20}ClN_3O_6S_2$	50	170	35.80	5.02	10.45	35.99	5.17	10.49
2	Cl	$N(CH_3)CH_2CH(OCH_3)_2$	$C_{11}H_{18}ClN_3O_6S_2$	41	200	34.10	4.68	10.83	34.34	5.00	10.31
3	CH_3	$N(CH_3)CH_2CH(OCH_3)_2$	$C_{12}H_{21}N_3O_6S_2$	50	192			11.44			11.39
4	Cl	$N(C_3H_7)CH_2CH(OCH_3)_2$	$C_{13}H_{22}ClN_3O_6S_2$	55	176	37.58	5.33	10.10	37.62	5.54	9.97
5	Cl	$N(CH_2C_6H_5)CH_2CH(OC_2H_5)_2$	$C_{19}H_{26}ClN_3O_6S_2$	32	192 dec.	46.42	5.12	8.58	46.39	5.29	8.08
6	Cl	$NHNH_2$	$C_6H_9ClN_4O_4S_2$	86	230 dec.	23.96	3.02	18.63	23.95	3.20	18.37
7	Cl	NHNHCHO	$C_7H_9ClN_4O_5S_2$	91	260 dec.	25.57	2.76	17.04	25.92	2.89	17.10
8	Cl	$NHNHCOCH_3$	$C_8H_{11}ClN_4O_5S_2$	88	275 dec.	28.03	3.23	16.35	28.25	3.16	16.41
9	CH_3	NHNHCHO	$C_8H_{12}N_4O_5S_2$	90	251 dec.	31.16	3.92	18.55	31.29	4.29	18.17
10	CH_3	$NHNHCOCH_3$	$C_9H_{11}N_4O_5S_2$	85	265 dec.	33.53	4.38	17.38	33.61	4.42	17.05
11	Cl	$NHNHCO(CH_2)_2CO_2H$	$C_{10}H_{13}ClN_4O_7S_2$	32	225 dec.	29.96	3.27	13.98	30.08	3.17	13.95
12	CH_3	$NHNHCOC_2H_5$	$C_{10}H_{16}N_4O_5S_2$	80	285 dec.	35.70	4.79	16.66	36.11	5.26	16.71
13	CH_3	$NHNHCOCH_2C_6H_{11}$	$C_{15}H_{24}N_4O_5S_2$	80	215			13.96			13.94

was obtained in 21% yield, and the 6-methyl derivative (compound B), m.p. 225° was obtained in 28.5% yield.

The infrared spectra of both compounds did not show NH absorption.

Anal. of A. Calcd. for $C_{13}H_{15}ClN_4O_6S_2$: C, 36.92; H, 3.57; N, 13.25. Found: C, 37.02; H, 3.71; N, 13.03.

Anal. of B. Calcd. for $C_{14}H_{18}N_4O_6S_2$: C, 41.78; H, 4.51; N, 13.92. Found: C, 41.61; H, 4.62; N, 13.77.

2,4-Disulfamoyl-N-(β,β-dialkoxyethyl)anilines, Table I, No. 1–5).—A solution of 0.1 mole of the appropriate β,β-dialkoxyethylamine, 0.1 mole of triethylamine and 28.8 g. (0.1 mole) of 5-chloro-2,4-disulfamoylfluorobenzene or 26.8 g. (0.1 mole) of 5-methyl-2,4-disulfamoylfluorobenzene in 80 ml. of ethanol and 20 ml. of dioxane was boiled under reflux for 6 hr. The solution was concentrated, diluted with water and the product allowed to crystallize. The products were purified by recrystallization from dilute alcohol.

7-Chloro-3-ethoxy-5-methyl-8-sulfamoyl-2,3,4,5-tetrahydro-1,2,5-benzothiadiazepine, VIII, R_1 = CH_3.—Five grams of 5-chloro-2,4-disulfamoyl-N-(β,β-diethoxyethyl)-N-methylaniline was added to 50 ml. of 95% alcohol and 6 ml. of 6N hydrochloric acid. The mixture was warmed on the steam bath. After a few minutes the solid dissolved and the product crystallized from solution. It was recrystallized from dilute alcohol, yield 4 g. (91%), m.p. 205°. The product is much less soluble (*ca.* 3–4 g./l.) than the starting material (*ca.* 15 g./100 ml.) in alcohol, and the melting point of a mixture of the two is depressed below that of either one alone.

Titration of the product in 66% N,N-dimethylformamide showed it to have pK_a' values of 11.4 and 13.0. The molecular weight was observed to be 366.0 (theory 368.5). The assigned structure is consistent with the infrared spectrum, having NH bands at 3.00, 3.09, and 3.22 μ; aryl ring absorption at 6.25 and 6.5 μ; a NH_2 deformation band at 6.32 μ; SO_2 bands at 7.59 and 8.7 μ; and an ether band at 9.26 μ.

Anal. Calcd. for $C_{11}H_{16}ClN_3O_5S_2$: C, 35.78; H, 4.36; N, 11.36; S, 17.35. Found: C, 35.76; H, 4.56; N, 11.36; S, 16.92.

7-Chloro-5-benzyl-3-ethoxy-8-sulfamoyl-2,3,4,5-tetrahydro-1,2,5-benzothiadiazepine, VIII, R_1 = $CH_2C_6H_5$.—Two grams of 5-chloro-2,4-disulfamoyl-N-benzyl-N-(β,β-diethoxyethyl)aniline was treated with 75 ml. of alcohol and 8.5 ml. of 6 *N* hydrochloric acid in the manner described for the preparation of VIII, R_1 = CH_3, yield 1.5 g. (86%), m.p. 198°.

The benzothiadiazepine structure is consistent with the nuclear magnetic resonance data. Maxima for the two *para* protons of the aromatic ring and the three protons of the methyl of the ethoxy group were identified.

Anal. Calcd. for $C_{17}H_{20}ClN_3O_4S_2$: C, 45.60; H, 4.67; N, 9.81; S, 14.38; Cl, 7.95. Found: C, 45.80; H, 4.82; N, 10.05; S, 14.64; Cl, 7.74.

Stereospecific Syntheses of Some Optically Active 5-Substituted 3-Aralkylideneamino-2-oxazolidinones

NICHOLAS D. HARRIS

Eaton Laboratories, Division of The Norwich Pharmacal Company, Norwich, New York

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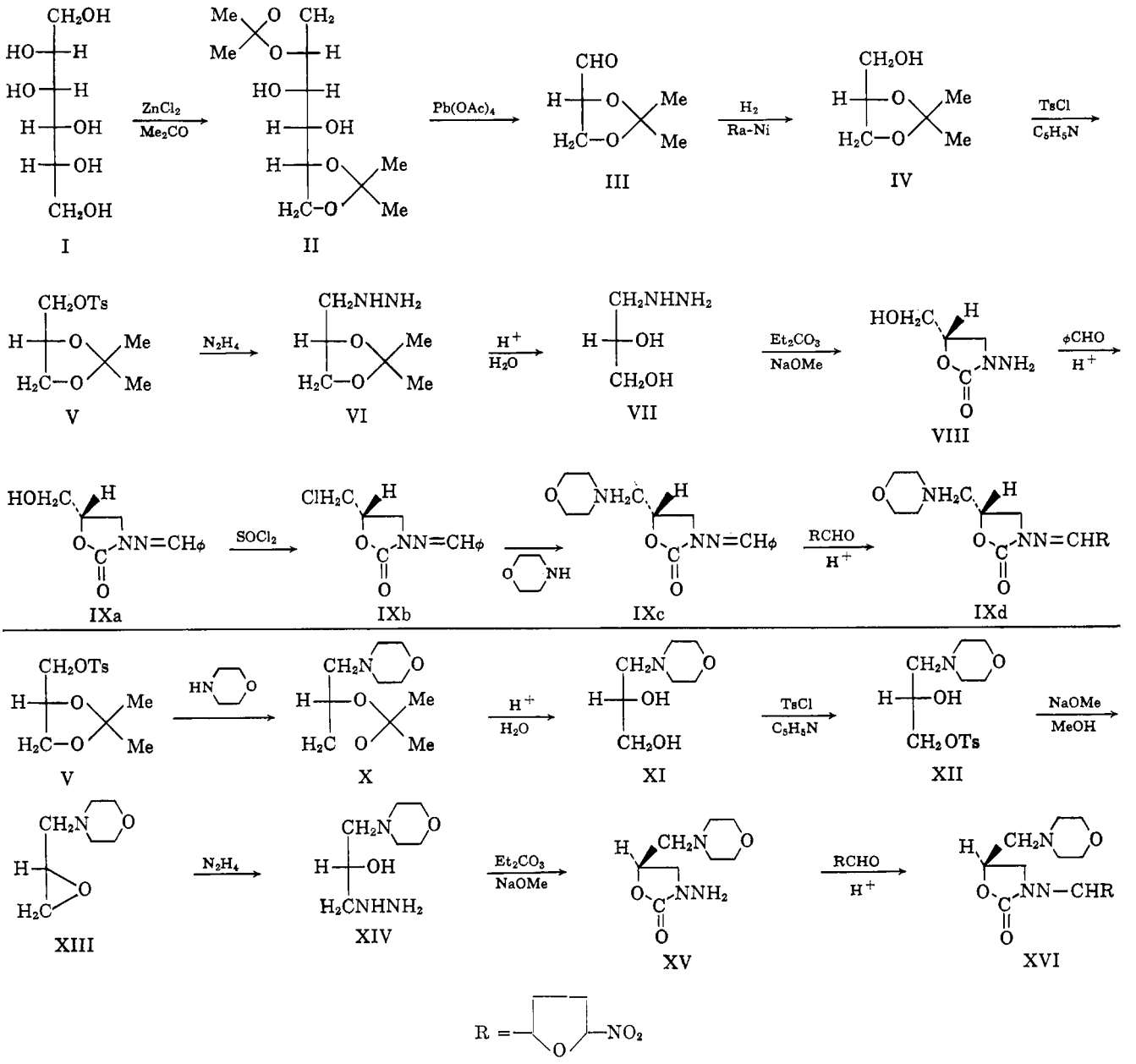
The dextrorotatory 3,5-disubstituted 2-oxazolidinones IXa–d were prepared by a stereospecific synthesis that established their absolute configuration. The enantiomorph of IXd, XVI, was also prepared from the same starting material.

In a study made to determine whether the preparation of (−)-3(5-nitrofurfurylideneamino)-5-morpholinomethyl-2-oxazolidinone[1] from D-mannitol was feasible and to determine its absolute configuration, the compounds reported in this paper were prepared. The syntheses that were used are shown in the Flow Diagram.

The synthetic route V → IX was chosen so that none of the reactions used to make the series of 3,5-disubstituted 2-oxazolidinones, IXa–d, occurred at the asymmetric carbon atom. Thus no choice had to be made between alternate mechanisms in any of the steps and the absolute configuration of the products was elucidated.

(1) The partial resolution of the racemic compound, Furaltadone, was reported in 1960: G. Gever, J. G. Michels, B. F. Stevenson, F. F. Ebetino, E. A. Bellamy, and G. D. Drake, Abstracts of Papers, 137th National Meeting American Chemical Society, Cleveland, Ohio, April, 1960, p. 30 N.



Flow Diagram

The preparation of 1-*O*-(*p*-toluenesulfonyl)-2,3-*O*-isopropylidene-D-glycerol, V, from D-mannitol and its steric relationship to D-glyceraldehyde has been reported by Baer and Fischer.[2]

The reaction of hydrazine with V to form VI retained the base stable acetal group and the mechanism of the displacement on the primary carbon atom did not affect the asymmetric carbon atom as no neighboring group effect could have been operative.

The hydrolysis of the acetal, VI to VII, did not involve the bond between the asymmetric carbon and the oxygen atom but rather the bond between the isopropylidene carbon and the oxygen.[3]

Formation of the 2-oxazolidinone ring, VII → VIII, involved a displacement by either the oxygen of the secondary hydroxyl group or the more nucleophilic nitrogen of the hydrazine moiety on diethyl carbonate and a cyclization. These two reactions whether separate or simultaneous did not involve the asymmetric carbon atom.

The preparation of IXa–d from VIII used no reactions that would change the configuration of the ring and the absolute configuration of the 2-oxazolidinone ring in IX a–d was demonstrated to be as shown in the Flow Diagram.

Reaction route I → IXd did not give the desired levorotatory isomer of Furaltadone[1] which was one of our goals. But an interchange of the morpholino and hydrazino groups did give the optical enantiomorph of IXd.

The reaction of V with morpholine to form X and hydrolysis of X to XI were the obvious first steps and were straightforward reactions and similar to V→VII which are discussed above. Then the hydrazine had to be affixed to the other terminal carbon before cyclization could occur. In addition, the configuration at the asymmetric carbon had to be retained unchanged throughout the remainder of the synthesis.

(2) E. Baer and H. O. L. Fischer, *J. Biol. Chem.*, **128**, 463 (1939); *J. Am. Chem. Soc.*, **70**, 610 (1948).

(3) C. K. Ingold, "Structure and Mechanism in Organic Chemistry," Cornell University Press, Ithaca N. Y., 1953, p. 334.

Although tosyl chloride was not considered a selective reagent for primary alcoholic groups, there was a possibility that the primary alcoholic group of XI would be the one to react to give XIII after treatment with base. Since XVI was the final product it is postulated that tosyl chloride did react on the primary alcoholic group. Reaction on the secondary alcoholic group would have given the enantiomorph of XIII and thus IXd. A mixture of primary and secondary alcoholic tosylates would have led to a racemic product. A ditosylate may also have conceivably been an intermediate. But only an optically active monotosylate, XII, was isolated from the reaction of XI and tosyl chloride which indicates a monotosylate intermediate for the preparation of XII.

Reaction of the epoxide, XIII, with hydrazine occurred as expected to give XIV with the requisite configuration since cyclization of XIV to XV did not affect the asymmetric carbon atom (see discussion of VII → VIII) and the levorotatory isomer, XVI, was obtained.

A satisfactory analysis for XIV, purified by vacuum distillation, was not obtained. The difficulty may have been due to its rapid absorption of carbon dioxide and and water on exposure to the atmosphere.

That IXd and XVI are enantiomorphs was confirmed by comparison of their physical properties. Ultraviolet and infrared absorption and melting points were identical. A mixed melting point showed no depression and they had equal, although opposite, specific rotations.[4,7] Since an elemental analysis of XVI was obtained, the structure of IXd was also established.

The fact that IXd and XVI were prepared from the same optically pure starting material by different routes, IXd by a sequence of reactions none of which occurred at the asymmetric carbon atom, is deemed presumptive evidence for the optical purity of the oxazolidinones and intermediates reported in this paper. A change in specific rotation and m.p. on recrystallization of an optically crude XVI was expected since it exists as a racemic compound in the solid state as evidenced by infrared.

Experimental[5]

(+)-3-Benzylideneamino-5-hydroxymethyl-2-oxazolidinone (IXa).—1-*O*-(*p*-Toluenesulfonyl)-2,3-*O*-isopropylidene-D-glycerol (100 g., 0.35 mole) prepared by the method of Baer and Fischer[2] ($n^{22}D$ 1.5054, $[\alpha]^{25}D$ −7.96°, neat) and 100% hydrazine hydrate (300 g., 6 moles) were heated on the steam bath for 2 hr. The reaction mixture was cooled and extracted with ether. The ether extracts were washed with 50% aqueous potassium hydroxide solution, dried, and the ether was evaporated from the extracts under vacuum. The residue was heated at reflux 2 hr. with dilute sulfuric acid; the solution was cooled and the sulfate was precipitated with barium hydroxide octahydrate and the mixture was filtered. The filtrate was evaporated under vacuum to a brown oil.

The residual oil, diethyl carbonate (42 g., 0.36 mole) and sodium methoxide (3.8 g., 0.07 mole) dissolved in 10 ml. of methanol were heated at 75–86° for 1 hr., cooled and acidified with 46 ml. of 25% aqueous sulfuric acid. Benzaldehyde (25 g., 0.24 mole) dissolved in 46 ml. of 95% ethanol was added to the mixture and, at steam bath temperatures, enough water was added to develop a cloudiness, then the reaction mixture was evaporated to one quarter its volume and cooled.

The lower oily layer was isolated and was treated with a small amount of an absolute ethanol–ether mixture. On standing 5.8 g. of solid, m.p. 128–132°, was collected.

Two recrystallizations from absolute ethanol elevated the melting point to 138–138.5°, $[\alpha]^{24}D$ +103.20°, 5% dimethylformamide (DMF) solution.

Anal. Calcd. for $C_{11}H_{12}N_2O_3$: C, 59.99%; H, 5.49%; N, 12.72%. Found: C, 60.08%; H, 5.63%; N, 12.74%.

(+)-3-Benzylideneamino-5-chloromethyl-2-oxazolidinone (IXb).—Crude (+)-3-benzylideneamino-5-hydroxymethyl-2-oxazolidinone (4.7 g., 0.02 mole), 105 ml. of chloroform, 5.3 ml. of dry pyridine and thionyl chloride (17.5 ml., 28.7 g., 0.24 mole) were heated at reflux 2 hr. then allowed to stand at room temperature overnight.

The reaction mixture was poured into 500 g. of ice–water and the chloroform layer was separated. The water layer was extracted with four 50-ml. portions of chloroform and the chloroform was evaporated from the combined chloroform extracts.

An oil remained which crystallized on standing. One recrystallization from 95% ethanol gave 3.9 g. of solid, m.p. 116–118°.

Three more recrystallizations from 95% ethanol elevated the melting point to 117.5–118°, $[\alpha]^{24}D$ +90.0°, 2% DMF solution.

Anal. Calcd. for $C_{11}H_{11}ClN_2O_2$: C, 55.35%; H, 4.65%; Cl, 14.86%; N, 11.74%. Found: C, 55.47%; H, 4.71%; Cl, 14.91%; N, 11.67%.

(+)-3-Benzylideneamino-5-morpholinomethyl-2-oxazolidinone (IXc).—Once recrystallized (+)-3-benzylideneamino-5-chloromethyl-2-oxazolidinone[6] (2.5 g., 0.01 mole) and morpholine (11 ml., 11 g., 0.13 mole) were heated at reflux 4.5 hr. Then enough water was added to the hot solution to produce a slight haziness. The mixture was cooled and 2 g. of solid was collected, m.p. 169–171°. Two recrystallizations from 95% ethanol elevated the melting point to 169.5–170.5°, $[\alpha]^{23}D$ +98.50°, 4% in 25% aqueous acetic acid.

Anal. Calcd. for $C_{15}H_{19}N_3O_3$: C, 62.26%; H, 6.62%; N, 14.52%. Found: C, 62.28%; H, 6.63%; N, 14.64%.

(+)-3-(5-Nitrofurfurylideneamino)-5-morpholinomethyl-2-oxazolidinone (IXd).—(+)-3-Benzylideneamino-5-morpholinomethyl-2-oxazolidinone, m.p. 169–171°, (1 g., 3.5 mmoles), 10 ml. of concentrated hydrochloric acid and 5-nitro-2-furfural (0.7 g., 5 mmoles) were heated on the steam bath for 5 min., then cooled. The mixture was extracted with ether and the aqueous layer was neutralized with concentrated aqueous ammonia. A yellow solid precipitated and was collected, m.p. 207–209°. A mixed melting point with XVI showed no depression,[7] $[\alpha]^{23}D$ +49.9°, 3.97% solution in 25% aqueous acetic acid.

The infrared absorption curves of IXd and XVI were identical as were the ultraviolet absorption curves.

(+)-3-Morpholino-1,2-*O*-isopropylidene-1,2-propanediol (X).—Crude 1-*O*-(*p*-toluenesulfonyl)-2,3-*O*-isopropylidene-D-glycerol (113 g., 0.4 mole) and morpholine (181 g., 2.1 moles) were heated at reflux 4 hr. The reaction mixture was evaporated under vacuum on the steam bath to 179 g. of solid residue. The residue was extracted with four 150-ml. portions of ether and the ether was evaporated from the extract under vacuum. The residue (86.9 g.) was distilled under vacuum. There was collected 63.2 g. of liquid (77.5% yield), b.p. 98–101° at 3.5 mm.

A redistilled sample was used for the physical data, b.p. 100–100.5° at 3.6 mm., $[\alpha]^{26}D$ +30.10°, neat, $n^{25}D$ 1.45881.

(4) Dr. Julian Michels (unpublished work) derived the following equation for the change of specific rotation with concentration for (+)- or (−)-3-(5-nitro-2-furfurylideneamino)-5-morpholinomethyl-2-oxazolidinone: $|SR_5| = |SR_c| + 2.69\,(C - 5)$, where SR_5 = specific rotation of a 5% solution SR_c = specific rotation of a C% solution. Calculation of the specific rotations for 5% solutions with this equation for IXd and XVI gave values of +47.1° and −47.9°, respectively.

(5) All melting points were taken on a Fisher–Johns Block and are uncorrected. The infrared curves were obtained with a Perkin–Elmer Infracord spectrophotometer, Model #137. The ultraviolet spectra were obtained with a Perkin–Elmer spectrophotometer, Model #350. The refractive indices were determined with a Bausch and Lomb precision refractometer. Optical rotations were measured with an O. C. Rudolph precision polarimeter, Model #70.

(6) Use of the benzylidene derivative in this reaction was suggested by Dr. E. Watson of Eaton Laboratories after a preliminary experiment had indicated that the 5-nitro-2-furfurylidene derivative would not react with morpholine.

(7) The author is indebted to one of the referees who pointed out that this fact would have been significant only if the mixed m.p. had shown a change. That no change was observed in the mixed m.p. indicates that no racemic compound was formed when the enantiomorphs were mixed or, fortuitously, the right proportions were mixed.

Anal. Calcd. for $C_{10}H_{19}NO_3$: C, 59.66%; H, 9.53%; N, 6.96%. Found: C, 59.63%; H, 9.86%; N, 7.39%.

(−)-3-Morpholino-1,2-propanediol (XI).—(+)-3-Morpholino-1,2-*O*-isopropylidene-1,2-propanediol (63.2 g., 0.31 mole), 4060 ml. of water and concentrated sulfuric acid (16.5 ml., 30.4 g., 0.30 mole) were heated at reflux for 3 hr. then cooled. Barium hydroxide octahydrate (98 g., 031 mole) was added to the solution and the white precipitate filtered.

The filtrate was evaporated under vacuum then re-evaporated twice with 100 ml. of absolute ethanol to 51.5 g. of pale yellow oil.

This pale yellow oil was distilled under vacuum and a colorless liquid (39.3 g.) was collected, b.p. 124–127° at 1.1 mm.

A redistilled sample was used for the physical data, b.p. 120–121° at 0.9 mm., $[\alpha]^{26}D$ −19.4°, 10.04% in water.

Anal. Calcd. for $C_7H_{15}NO_3$: C, 52.16%; H, 9.38%; N, 8.69%; Found: C, 52.07%; H, 9.50%; N, 8.68%.

(+)-3-Morpholino-1-*O*-(*p*-toluenesulfonyl)-1,2-propanediol (XII).—To (−)-3-morpholino-1,2-propanediol (19 g., 0.15 mole) dissolved in 60 ml. of dry pyridine was added *p*-toluenesulfonyl chloride (28 g., 0.15 mole) with ice-bath cooling. The reaction mixture was allowed to stand at room temperature for 2 days. Water (100 ml.) was added and the mixture was extracted with ether.

The ether extract was washed with water then dried and the ether was evaporated under vacuum. The crude residual solid was recrystallized twice from 2-propanol to recover 6.7 g. of white solid, m.p. 134–143°. Two recrystallizations from benzene–absolute ethanol elevated the melting point to 146–147°, $[\alpha]^{23}D$ +0.80°, 5% in 95% EtOH.

Anal. Calcd. for $C_{14}H_{21}NO_5S$: C, 53.31%; H, 6.71%; N, 4.44%; S, 10.17%. Found: C, 53.50%; H, 6.61%; N, 4.17%; S, 10.24%.

(−)-N-Glycidylmorpholine (XIII).—To (−)-3-morpholino-1,2-propanediol (47 g., 0.29 mole) dissolved in 100 ml. of dry pyridine was added, with cooling, *p*-toluenesulfonyl chloride (57 g., 0.30 mole). The reaction mixture was allowed to stand at room temperature 2 days.

Methanol (100 ml.) was added to the reaction mixture and, at 0°, added sodium (14.8 g., 0.64 g.-atom) dissolved in 370 ml. of methanol. After 14 hr. at 0–6°, the mixture was filtered and the filtrate was evaporated under vacuum. Carbon tetrachloride was added to the residue and the mixture was filtered. The carbon tetrachloride was distilled under vacuum and the residue was fractionated under vacuum. A colorless liquid (10.3 g.) was collected, b.p. 77–86° at 2.0–2.3 mm. Redistillation of an aliquot gave a colorless liquid, b.p. 65° at 1.8 mm., for determination of the physical data, $[\alpha]^{24}D$ −20.56°, 5.012% in water.

Anal. Calcd. for $C_7H_{13}NO_2$: C, 58.72%; H, 9.15%; N, 9.78%. Found: C, 58.86%; H, 9.01%; N, 9.70%.

(−)-3-(5-Nitrofurfurylideneamino)-5-morpholinomethyl-2-oxazolidinone (XVI).—To *N*-(−)-glycidylmorpholine, b.p. 71–75° at 2.1–2.2 mm., (2 g., 0.014 mole) was added 85% hydrazine hydrate (9 g., 0.15 mole) with ice-bath cooling. The mixture was kept at ice bath temperature an additional hour and allowed to stand at room temperature for 24 hr. The solution was heated to 50° for 0.5 hr. and the excess hydrazine and water were removed under vacuum.

Diethyl carbonate (5 g., 0.042 mole) and sodium methoxide (0.2 g., 3.7 mmoles) dissolved in 0.7 ml. of methanol were added to the residue (2.3 g.) and the mixture was heated at reflux 30 min.

The reaction mixture was cooled and 2 ml. of 2-propanol, 10 ml. of water, 5 *N* sulfuric acid to pH 2 and 5-nitro-2-furfural (3 g., 0.02 mole) dissolved in 10 ml. of 2-propanol were added. The mixture was heated on the steam bath 15 min., cooled, and filtered.

The filtrate was extracted with ether and the aqueous layer was neutralized with concentrated aqueous ammonia. The solid which precipitated was collected (1.5 g.), m.p. 208–209°C., $[\alpha]^{27}D$ −54.50°, 2% in 25% aqueous acetic acid.

After three recrystallizations an isopropyl alcohol-nitromethane mixture there was recovered 0.39 g. of solid, m.p. 208–209°. No change in the specific rotation was observed, $[\alpha]^{24}D$ −56.0°, 2% in 25% aqueous acetic acid, since the 1-1/2° difference in the specific rotation is within the experimental error of the determination.

Anal. Calcd. for $C_{13}H_{16}N_4O_6$: C, 48.15%; H, 4.97%; N, 17.28%. Found: C, 48.24%; H, 5.09%; N, 17.24%.

Acknowledgment.—The author gratefully acknowledges the invaluable services of Dr. Julian G. Michels, Messrs. Gordon B. Ginther and Grant Gustin, and associates of the Eaton Laboratories Physical and Analytical Section who obtained the elementary analyses and the ultraviolet and infrared curves. The author also wishes to thank Mr. Frank F. Ebetino and Dr. Edward Watson for the many helpful discussions during the course of this work.

An Approach to the Total Synthesis of Steroids[1a]

MICHAEL CHAYKOVSKY[1b] AND ROBERT E. IRELAND

Department of Chemistry, The University of Michigan, Ann Arbor, Michigan

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The construction of 1-carbomethoxy-8β-methyl-$\Delta^{4(9)}$-tetrahydroindanone-5 (15) is described and its conversion to a tricyclic steroid intermediate was investigated.

Since the mythical barrier to the synthesis of the nonaromatic steroids was first breached independently by Robinson[2] and Woodward,[3] this once formidable obstacle has been overcome by numerous scientists with more or less finesse. In general, this effort has not only led to highly stereoselective and short syntheses of these complex molecules, but also to a much more thorough understanding of polycyclic systems and their construction.[4] While the former result may, in the final analysis, be quite temporal in character, the latter information transcends the immediate goal at hand and is of incalculable value to the science as a whole. It is with the hope that some small portion of the work we record here may fall into this latter category that prompts the description of yet another approach to the synthesis of the steroid nucleus.

The plan that was envisaged for this work was the CD → B → A approach, whereby the keto ester **1** could be condensed with ethyl vinyl ketone to form ring B and the resulting tricyclic keto ester **2** with methyl vinyl ketone to add ring A and form the steroid nucleus **3**. By a sequence of hydrolysis, decarboxyla-

(1) (a) Taken from the Ph.D. dissertation of M. Chaykovsky, University of Michigan, 1961. (b) National Institutes of Health Predoctoral Research Fellow, 1959–1961.

(2) H. M. E. Cardwell, J. W. Cornforth, S. R. Duff, H. Holtermann, and R. Robinson, *J. Chem. Soc.*, 361 (1953).

(3) R. B. Woodward, F. Sondheimer, D. Taub, K. Heusler, and W. M. MacLamore, *J. Am. Chem. Soc.*, **74**, 4223 (1952).

(4) W. S. Johnson, D. S. Allen, Jr., R. R. Hindersinn, G. N. Sausen, and R. Pappo, *ibid.*, **84**, 2181 (1962); L. H. Sarett, G. E. Arth, R. M. Lukes, R. E. Beyler, G. I. Poos, W. F. Johns, and J. M. Constantin, *ibid.*, **74**, 4974 (1952).