atmospheric pressure. The theoretical amount of hydrogen, calculated for saturation of three double bonds and hydrogenolysis of one bromine atom, was absorbed in forty minutes.

3-Bromo-1,3,5-hexatriene (0.3 g.) in 5 ml. of carbon tetrachloride was treated with a solution of bromine in carbon tetrachloride until the bromine color persisted. The reaction medium was then heated on the steam-cone until all solvent had been removed. Petroleum ether (30–60°) was added to the residue and crystals appeared when the mixture was cooled to about −60°. After recrystallization from petroleum ether (30–60°) the solid melted at 87–88°.

Anal. Calcd. for $C_6H_7Br_5$: C, 15.05: H, 1.49; Br, 83.6. Found: C, 15.39; H, 1.66; Br, 84.1.

The ultraviolet absorption spectrum was measured with a Beckmann quartz spectrophotometer in carefully purified cyclohexane. Due to the instability of 3-bromo-1,3,5-hexatriene, no careful weighings were made so only the relation of per cent. transmission to wave length could be obtained. The approximate concentration was 2×10^{-5} mole/liter. Maxima of absorption were observed at 2785, 2675 and 2580 Å. The infrared absorption spectrum determination was kindly done in the laboratory of Dr. Plyler, Radiometry Section of the Bureau of Standards, Washington, D. C.

Summary

1. 3,4-Dibromo-2-ethoxytetrahydropyran has been prepared from 2-ethoxy-Δ^3-dihydropyran.

2. Dehydrohalogenation of 3,4-dibromo-2-ethoxytetrahydropyran yielded 3-bromo-2-ethoxy-Δ^3-dihydropyran.

3. 2-Bromopentadienal was prepared from 3-bromo-2-ethoxy-Δ^3-dihydropyran and treated with methylmagnesium bromide. The product was 3-bromo-3,5-hexadien-2-ol.

4. 3-Bromo-1,3,5-hexatriene was prepared by the catalytic dehydration of 3-bromo-3,5-hexadien-2-ol.

COLLEGE PARK, MD. RECEIVED JUNE 15, 1949

[CONTRIBUTION FROM THE CHANDLER LABORATORY, COLUMBIA UNIVERSITY]

Mechanism of the Decarboxylation of α-Pyridylacetic Acid[1]

BY W. VON E. DOERING* AND VARSENIG ZAMBAK PASTERNAK

The decarboxylation of α-pyridylacetic acid,[2] α-quinolylacetic acid[3] and γ-quinolylacetic acid[4] but not β-pyridylacetic acid[5] occurs with remarkable ease at temperatures below 100°. As a contribution to the elucidation of this decarboxylation, we have synthesized and resolved methylethyl-α-pyridylacetic acid (I) and studied its decarboxylation to α-*s*-butylpyridine (II). As the significance of the study depends both on the optical stability and on a measurably large rotation of the decarboxylation product, II has been resolved and its racemization studied.

The synthesis of II,[6] effected unsatisfactorily (6%) by the reaction of *s*-butylmagnesium bromide and pyridine,[7] is accomplished smoothly (59%) by the reaction[8] of pyridine and *s*-butyllithium. The resolution of II,[9] not realizable through the amorphous *d*-10-camphorsulfonate and *l*-malate salts nor through the crystalline hydrogen *d*-tartrate, is effected by way of the nicely crystalline dibenzoyl-*d*-tartrate, albeit to a substantially complete degree only after a tedious fractional crystallization of twenty steps. The magnitude of the specific rotation ($[\alpha]^{25}D$ −30°) of the most highly resolved II is sufficient to allow facile detection of as little as 0.1% residual optical activity in samples of racemized II.

In racemization attempts (−)-II is optically stable to prolonged refluxing with 1,2-propanediol (b. p. 189°), with concentrated hydrochloric acid, and with ethanolic sodium ethoxide, but is racemized by a solution of potassium in triethylcarbinol rapidly at 142° and more slowly at 100°.[10] The related methiodide (III) of optically active α-*s*-butylpyridine is racemized by boiling in propanediol, but is not affected by boiling in water containing a small amount of acetic acid.

Since the racemization of II is a most sensitive measure of the removal of the α-hydrogen and therefore furnishes information bearing both on condensations of the α-picoline type and on the tautomerization of suitably substituted pyridines to enamines (*e. g.*, IV),[11] it is pertinent to point out that the consistent mechanism of the racemization of II involves the resonating planar carbanion V which is formed by the bimolecular attack of a strong base on the α-hydrogen and not by spontaneous dissociation. Furthermore the

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* Harvard University Ph.D. 1943.

[1] Taken from a dissertation submitted in partial fulfillment of the requirements for the degree of Doctor of Philosophy in the Faculty of Pure Science, Columbia University.

[2] Oparina, *J. Gen. Chem.* (*U. S. S. R.*), **5**, 1699 (1935); *Chem. Zentr.*, **106**, I, 2536 (1935).

[3] Borsche and Manteuffel, *Ann.*, **526**, 22 (1936).

[4] Borsche and Bütschli, *ibid.*, **529**, 266 (1937).

[5] Miescher and Kagi, *Helv. Chim. Acta*, **24**, 1471 (1941), have reported that 2-carboxy-3-pyridineacetic acid at 180° in dimethylaniline is decarboxylated to β-pyridylacetic acid which itself decarboxylates only on heating to higher temperature.

[6] Diels and Alder, *Ann.*, **505**, 103 (1933), have synthesized II from α-acetylpyridine in 24% yield in two steps, addition of ethylmagnesium iodide and reduction with hydrogen iodide and phosphorus.

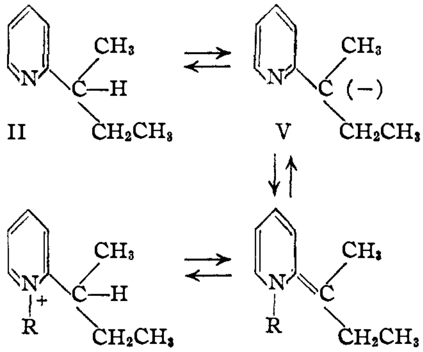
[7] For reactions of this type see Bergstrom and McAllister, THIS JOURNAL, **52**, 2845 (1930).

[8] Ziegler and Zeiser, *Ber.*, **63**, 1847 (1930).

[9] The resolution affords rigorous proof of the *s*-butyl structure of II.

[10] A preliminary kinetic study of the racemization failed to yield results consistent from one experiment to the next, although within a particular run the data may be of sufficient value to allow the inference that the reaction is first order.

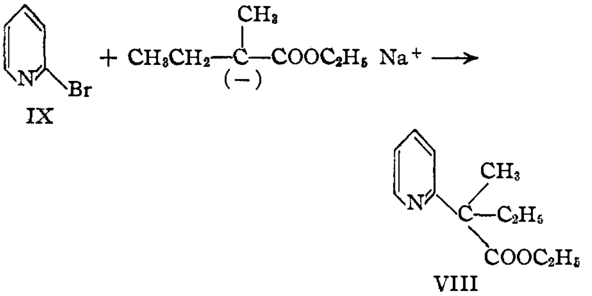
[11] Chichibabin, *Ber.*, **60**, 1607 (1927); *Bull. soc. chim.*, [5] **3**, 1607 (1936); [5] **5**, 429, 436 (1938).



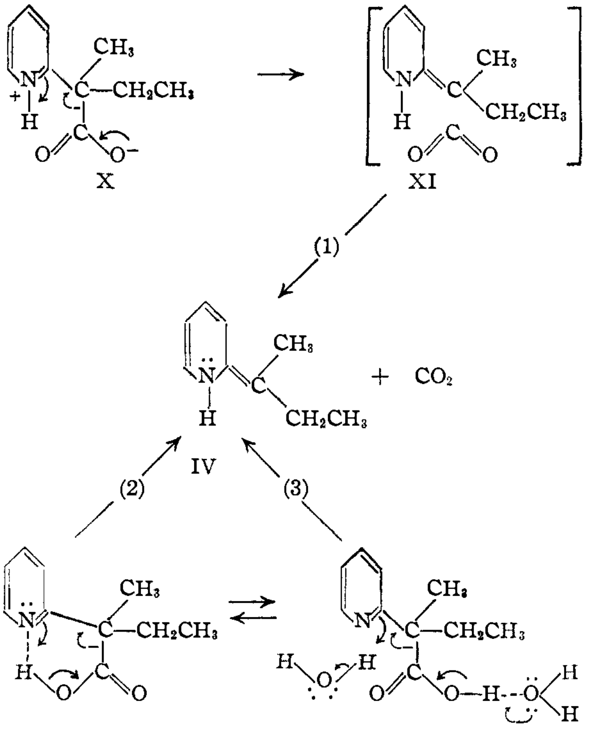
R = H. VI R = H. IV
R = CH₃. III R = CH₃. VII

failure of concentrated hydrochloric acid to racemize II indicates that insufficient labilization of α-hydrogen is furnished in the hydrochloride VI.[12] Pyridinium salts of the α-picoline type are easily converted by treatment with alkali to the neutral enamines which condense with aldehydes and other reactive electrophilic reagents.[13] A hypothetical mechanism for the pyridinium salt–enamine interconversion involves displacement by acid or base of the rapidly and spontaneously-established equilibrium.[14] At least in the case of α-*s*-butylpyridine methiodide (III) unimolecular solvolytic dissociation to the enamine VII does not take place, since III is optically stable in boiling water. Presumably the pyridinium salt–enamine conversion likewise proceeds by the bimolecular attack of a base on the α-hydrogen.

The synthesis of I as its ethyl ester (VIII) has been attempted in several ways. The projected reaction of II with phenyllithium and triphenylmethylsodium followed by treatment with ethyl chloroformate fails.[15] A model experiment involving the reaction of ethyl sodioisobutyrate fails with pyridine but succeeds with α-bromopyridine (IX).[16] Analogously, VIII is prepared in good yield from IX and ethyl sodiomethylethylacetate, the structure being confirmed by hydrolysis and decarboxylation to II.



The partial resolution of VIII, effected by fractional crystallization of the dibenzoyl-*d*-tartrate, gives levorotatory VIII, $[\alpha]^{25}\mathrm{D}\ -0.50^\circ$, and from the mother liquors the dextrorotatory isomer, $[\alpha]^{25}\mathrm{D}\ +0.28^\circ$. When (+)-VIII is hydrolyzed with concentrated hydrochloric acid, crystalline methylethyl-α-pyridylacetic acid (I) hydrochloride, $[\alpha]^{25}\mathrm{D}\ +0.40^\circ$, results. In boiling neutral aqueous solution I decarboxylates smoothly to completely racemic *s*-butylpyridine. This fact can be unequivocally interpreted to establish a symmetrical intermediate in the decarboxylation of I to II. The further observation that I is stable to prolonged boiling both in concentrated hydrochloric acid and in strongly alkaline solution[17] per-



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[12] Quantitative extension of the observations on II to less highly substituted molecules of the α-picoline type is of doubtful value. Quinaldine, for example, exchanges with deutero-ethanol easily [Kharasch, Brown and McNab, *J. Org. Chem.*, **2**, 36 (1937)].

[13] Decker, *Ber.*, **37**, 528 (1904); **38**, 2493 (1905); Mumm and Hingst, *ibid.*, **56**, 2301 (1923); Mumm, *et al.*, *Ann.*, **443**, 272 (1925); Mills and Raper, *J. Chem. Soc.*, **127**, 2466 (1925); Koenigs, Köhler and Blindow, *Ber.*, **58**, 933 (1925); Schneider, Gäertner and Jordon, *ibid.*, **57**, 522 (1928); Chichibabin and Benevolenskaya, *ibid.*, **61**, 547 (1928); Phillips, *J. Org. Chem.*, **12**, 333 (1947).

[14] *Cf.* König, *Ber.*, **55**, 3293 (1922). For a brief discussion of these and related problems, see Bergstrom, *Chem. Revs.*, **35**, 125 (1944).

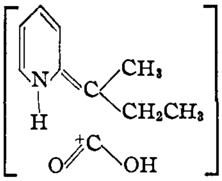
[15] The facts that unracemized II is recovered from the treatment of (+)-II with phenyllithium in ether for seventy-five minutes at room temperature and that the red color of triphenylmethylsodium is never discharged allow the unequivocal conclusion that the condensation fails because the α-hydrogen is not removed under these conditions. When forced by boiling in benzene, phenyllithium gives 6(?)-phenyl-2-*s*-butylpyridine; that is, the Ziegler addition reaction rather than proton abstraction is favored [*cf.* Gilman and Broadbent, This Journal, **70**, 2809 (1948)].

[16] Walter and McElvain, *ibid.*, **57**, 1891 (1935), have treated α-bromopyridine with diethyl sodioethylmalonate, the displacement being electronically of the *p*-nitrohalobenzene type.

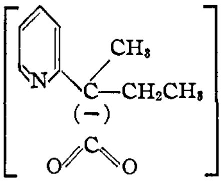
[17] *Cf.* the hot alkaline hydrolysis of α-pyridylacetamide [Pattison and Carmack, *ibid.*, **68**, 2033 (1946)], alkaline hydrolysis of γ-pyridylacetamide and the isolation of γ-pyridylacetic acid hydrochloride [Malan and Dean, *ibid.*, **69**, 1797 (1947)] and our observations on the stability of α-pyridylacetic acid under both acidic and alkaline conditions.

mits the conclusion that the neutral molecule decarboxylates with much greater ease than either the pyridinium salt or the carboxylate-ion.

One of the consistent mechanisms of the decarboxylation (1) is initiated from the inner salt X, proceeds by way of a transition state in which much stabilization is derived from the incipient formation of carbon dioxide and IV (resonance structure XI), and leads to the stable, symmetrical, intermediate enamine IV. The resistance to decarboxylation shown by I-hydrochloride and the sodium salt of I is due hypothetically to the lower energy of the pyridinium salt and the carboxylate ion as well as to the higher energy of the respective transition states. Thus the transition state in the decarboxylation of pyridinium salt is represented among others by the resonance structure XII (compare the positive carboxyl group with carbon dioxide in XI) while the transition state in the decarboxylation of the carboxylate ion is in part represented by structure XIII (compare the higher energy of the incipient carbanion V with the neutral enamine in XI). This hypothetical mechanism is consistent with the resistance β-pyridylacetic acid to decarboxylation (no contribution in the transition state from a structure of stability comparable to that of IV) and readily accommodates the ease of decarboxylating acids of the γ-pyridylacetic acid type.[4,18] The mechanism is not presently experimentally distinguishable from two alternative mechanisms (2) and (3) which are initiated from the cyclic hydrogen-bonded tautomers XIV or from the externally hydrogen-bonded form XV rather than from the inner salt X.[19]



XII



XIII

Experimental[20]

α-*s*-Butylpyridine (II). (a) **Grignard.**—After the addition of 79.1 g. of dry pyridine to an ethereal solution of *s*-butylmagnesium bromide (from 24 g. of magnesium and 137 g. of *s*-butyl bromide), the ether was removed and the residue was heated for four hours at 150–160°. The product was treated with 70 g. of ammonium chloride in 600 cc. of water and extracted with large volumes of ether. The concentrated ether solution was distilled *in vacuo* to give 7.87 g. (5.8%) of II, b. p. (17 mm.) 72–73°, and 4.51 g. of γ-*s*-butylpyridine, b. p. (18 mm.) 100–106°, identified as the picrate, m. p. 142° (reported,[11] m. p. 142°).

(b) **Lithium.**—To a solution of *s*-butyllithium, prepared from 14.5 g. of lithium and 93 g. of *s*-butyl chloride in *ca.* 1 l. of purified petroleum ether (b. p. 20–40°) under an atmosphere of nitrogen, there was added slowly a solution of 162 cc. of dry pyridine in 700 cc. of purified ligroin (b. p. 75–115°). After distillation of the low-boiling solvent, the solution was stirred and refluxed for six hours under nitrogen. The reaction mixture was treated with ice-water, and extracted with ether. Distillation of the dried extract gave 79 g. (58.5%) of II, b. p. 63° (11 mm.), 74° (18 mm.), 93° (26 mm.). The chloroplatinate of II was crystallized from ethanol; m. p. 163–167° (reported,[1] m. p. 166°).

α-*s*-Butylpyridine picrate, m. p. 91°, was crystallized from ethanol.

Anal. Calcd. for $C_{15}H_{16}N_4O_7$: C, 49.45; H, 4.42; N, 15.37. Found: C, 50.05; H, 4.56; N, 14.54.

For analysis II was regenerated from purified picrate.

Anal. Calcd. for $C_9H_{13}N$: C, 79.95; H, 9.69. Found: C, 80.01; H, 9.74.

Resolution of α-*s*-Butylpyridine (II).—In a preliminary experiment on the resolution of II by dibenzoyl-*d*-tartaric acid it was found that the regeneration of the mother liquors gave II of wide boiling range (73–95° (15 mm.)) so that in subsequent resolutions II purified over the picrate was employed.

Mixing a solution of 111 g. of dibenzoyl-*d*-tartaric acid monohydrate,[21] m. p. 90–91°, in 350 cc. of absolute ethanol with 38.5 g. of purified II gave **α-*s*-butylpyridine hydrogen dibenzoyl-*d*-tartrate,** m. p. 140°.

Anal. Calcd. for $C_{27}H_{27}NO_8$: N, 2.84. Found: N, 2.79.

The resolution, pursued by fractional crystallization from absolute ethanol, progressed slowly as illustrated by the following properties of the head fractions, numbers 1, 5, 10 and 20: % yield, 77, 38, 10, —; m. p. of salt, 140°, 147°, 148°, 149.5°: $[\alpha]^{25}$D of salt, −83.7°, −85.1°, −87.6°, —; $[\alpha]^{25}$D of free base, —, −9.9°, −22.8°, −29.7°. Regeneration of mother liquors from which no more crystalline material could be forced gave II of $[\alpha]^{25}$D + 14.3°. While this (+)-base formed a nicely crystalline salt with dibenzoyl-*l*-tartaric acid, m. p. 138°, $[\alpha]^{25}$D + 88.8°, the resolution of the (+)-enantiomer was not pursued.

Racemization Experiments with α-*s*-Butylpyridine. (a) **Propanediol-1,2.**—II, $[\alpha]^{25}$D −7.3° (c = 7.00, ethanol), was refluxed for twenty-four hours in propanediol-1,2 (b. p. 189°). Recovered by distribution between water and ether, the base. still slightly contaminated with propanediol, had $[\alpha]^{27}$D −6.1° (c = 10.46. ethanol).

(b) **Hydrochloric Acid.**—A solution of 1.438 g. of II, $[\alpha]^{25}$D −9.91° (neat): in 25 cc. of 2 *N* hydrochloric acid, $[\alpha]^{25}$D −6.5°, was refluxed for four hours. Upon remaking the volume to 25 cc., the specific rotation was unchanged. In a similar experiment in which the same quantity of II was refluxed for twenty-six hours with concentrated hydrochloric acid, the rotation of the solution made up to 25 cc. was unchanged (−6.5°).

(c) **Sodium Ethoxide.**—A solution of 1.52 g. of II in absolute ethanol containing 2 equivalents of sodium ethoxide, $[\alpha]^{25}$D −7.5° (c = 6.08), showed no change in rotation after two hours at room temperature. After being refluxed in a similar solution for forty-eight hours, substantially unracemized II was recovered, $[\alpha]^{25}$D −7.0° (c = 8.72. ethanol).

(d) **Potassium Salt of Triethylcarbinol.**—Into a solution of 1.0 g. of potassium in 25 cc. of dry triethylcarbinol, boiling under nitrogen, there was introduced by means of a hypodermic syringe and rubber nipple 2.7 g. of II, $[\alpha]^{24}$D −13.9° (neat). After twenty minutes only 2% of the original activity remained.

The results of two similar experiments at 99.6°, the first involving 0.35 g. of potassium, 20 cc. of triethylcarbinol and 2 cc. of II, $[\alpha]^{24}$D −13.9°, and the second involving

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[18] Pannizon. *Helv. Chim. Acta.* **27**. 1748 (1944): Gebauer. German Patent 644,193 (1937).

[19] It is entirely thinkable that the free energies of activation of paths (1). (2) and (3) are so nearly equal that the decarboxylation occurs simultaneously by all paths. But on the grounds that path (3) introduces complications of no apparent value and that path (2) cannot encompass decarboxylation of the γ-pyridylacetic acid type we favor (1).

[20] We are indebted to the Misses Lathrope Baker and Lois May for the microanalyses. All melting points are corrected.

[21] Prepared according to Butler and Cretcher, THIS JOURNAL, **55**, 2605 (1933).

0.40 g. of potassium, 22 cc. of triethylcarbinol and 1.6 cc. of II (−13.9°), are shown in Table I.

Table I

α, deg.	Time, sec.	$k_1 \times 10^4$
−0.76	55	
− .63	430	5.01
− .43	1210	4.90
− .32	1810	4.60
− .59	45	
− .48	3600	0.581
− .44	6000	.362
− .32	10800	.664
− .24	17100	.457

(−)-Methyl-*α*-*s*-butylpyridinium Iodide (III).—Treatment of (−)-II, $[\alpha]^{25}\mathrm{D}$ −9.91° (neat), with excess methyliodide gave crystalline methiodide (III) which melted at 107–108° after two crystallizations from acetone–ether.

Anal. Calcd. for $C_{10}H_{16}NI$: C, 43.32; H, 5.82; N, 5.05; I, 45.78. Found: C, 43.03; H, 5.89; N, 4.96; I, 46.10.

A solution of III in 1,2-propanediol, b. p. 189°, containing a few drops of acetic acid, $[\alpha]^{30}\mathrm{D}$ −3.3° (c = 8.25), was refluxed, considerable racemization being observed after three hours and total racemization after eight hours.

In a similar experiment in which boiling water containing a few drops of acetic acid was solvent, no racemization was observed after twelve hours.

***α*-Pyridylacetic Acid.**—The solution obtained by allowing 0.5 mole of phenyllithium in pentane solution to react with 0.5 mole of *α*-picoline for one hour, was forced under nitrogen into a flask containing 4 lb. of Dry Ice. Evaporation of the solvent and washing with ether gave the unstable lithium *α*-pyridylacetate. A portion of this salt was treated for twelve hours with dry alcoholic hydrogen chloride. The solution was then neutralized with an aqueous paste of potassium carbonate and distilled *in vacuo* to give 14.5 g. of ethyl *α*-pyridylacetate, b. p. 122–123° (13 mm.); reported,[2] b. p. 123° (12 mm.).

A solution of 2.5 g. of ethyl *α*-pyridylacetate was hydrolyzed by 10 cc. of concentrated hydrochloric acid in twelve hours. Evaporation to dryness *in vacuo* gave crystalline *α*-pyridylacetic acid hydrochloride (1.1 g.) which was recrystallized from water-acetone, m. p. 131°.

α-Pyridylacetic acid was obtained from the hydrochloride by treating with freshly prepared and thoroughly washed silver carbonate followed by removal of silver chloride and precipitation of dissolved silver with hydrogen sulfide. Evaporation to dryness *in vacuo* gave *α*-pyridylacetic acid, m. p. 98°.

Methylethyl-*α*-pyridylacetic Acid (I). (a) **From *α*-*s*-Butylpyridine.**—After an attempt to prepare I by carbonation of the reaction mixture obtained by treating ethereal phenyllithium with II had given only recovered II, optically active II (14.3°) was treated with one equivalent of phenyllithium in ether for seventy-five minutes and then with ethylchloroformate. On distillation of the basic product, II was recovered (75%) with undiminished rotation (14.3°). When the reaction was forced by heating a hexane solution of II with phenyllithium at 48–58° for two and a half hours and then treated with ethylchloroformate, distillation of the basic product gave material of b. p. 50–55° (0.5 mm.).

Anal. Calcd. for $C_{15}H_{17}N$: C, 85.25; H, 8.11; N, 6.62. Found: C, 83.13; H, 7.67; N. 6.39.

The picrate of this product melted at 144.5°.

Anal. Calcd. for $C_{21}H_{20}N_4O_7$: C, 57.26; H, 4.58. Found: C, 56.69; H, 4.85.

Neither at room temperature for forty-five hours nor on refluxing in benzene did triphenylmethylsodium react with II (persistence of red color). After treatment with ethyl chloroformate. the reaction mixture afforded only recovered II.

(b) **From *α*-Bromopyridine.**—The following model experiment is reported: fifteen minutes after mixing 7 cc. of ethyl isobutyrate with 0.06 mole of triphenylmethylsodium in ether. there was added 6.55 g. of *α*-bromopyridine. prepared from 2-aminopyridine according to Craig.[22] After replacement of the ether by decalin, the reaction mixture was heated for nineteen hours under nitrogen at 183°. The dilute hydrochloric acid extract of the reaction mixture was neutralized with sodium bicarbonate and extracted with ether. Distillation gave a small amount of *α*-bromopyridine, b. p. 84–90° (26 mm.), and **ethyl dimethyl-*α*-pyridylacetate**, b. p. 70–78° (0.6 mm.).

Anal. Calcd. for $C_{11}H_{15}NO_2$: C, 68.36; H, 7.82; N, 7.25. Found: C, 67.84; H, 8.09; N, 7.38.

Ethyl methylethylacetate, prepared from 380 cc. of ethyl chloroformate and 3.2 moles of *s*-butylmagnesium bromide and fractionally distilled in a 15-plate column before use (350 cc., b. p. 131.5–132°), was added (0.325 mole) to a solution of triphenylmethylsodium (0.352 mole) in ether. After the addition of 57 cc. of *α*-bromopyridine and replacement of the ether by decalin. the reaction mixture was heated at 180° for sixty-eight hours. Proceeding as above, we obtained 32.0 cc. of recovered *α*-bromopyridine and 24 g. of **ethyl methylethyl-*α*-pyridylacetate** (VIII), b. p. 99–105° (2–3 mm.).

Anal. Calcd. for $C_{12}H_{17}NO_2$: C, 69.53; H, 8.27; N, 6.76. Found: C, 69.52; H, 8.38; N, 7.23.

(c) **Resolution of I.**—The resolution was effected by fractional crystallization from absolute ethanol of the crystalline hydrogen dibenzoyl-*d*-tartrate of ethyl methylethyl-*α*-pyridylacetate, initial m. p. 121°.

Anal. Calcd. for $C_{30}H_{31}NO_{10}$: C, 63.70; H, 5.52. Found: C, 62.95; H, 5.87.

Regeneration of a sample of salt, m. p. 123–124° (9.7 g.). obtained after four crystallizations, gave 2.75 g. of distilled VIII, $[\alpha]^{25}\mathrm{D}$ −0.50° (neat). From the mother liquors, distilled ester of $[\alpha]^{27}\mathrm{D}$ + 0.25 to +0.28° was obtained.

(d) **Hydrolysis of VIII.**—A solution of 8.0 g. of VIII. $[\alpha]^{27}\mathrm{D}$ +0.27°, in concentrated hydrochloric acid was refluxed for eight hours. Removal of the solvent *in vacuo* gave crystalline material which was washed with acetone and dried; 4.80 g., m. p. 98–100°, $[\alpha]^{26}\mathrm{D}$ +0.32 (c = 46.7, hydrochloric acid).

Anal. Calcd. for $C_{10}H_{14}NO_4Cl$: C, 55.69: H, 6.54; N, 6.49. Found: C, 55.81: H, 6.68; N, 5.90.

Recrystallization from acetone containing 10% alcohol raised the m. p. to 103–104° and the $[\alpha]^{25}\mathrm{D}$ to +0.40° (c = 25.0, dil. hydrochloric acid).

(e) **Decarboxylation.**—A solution of I-hydrochloride prepared as above from 6.0 g. of VIII, $[\alpha]^{27}\mathrm{D}$ +0.28, was treated with excess potassium hydroxide and refluxed for three hours without the appearance of any II. After neutralization, the solution immediately became turbid and on warming gave a second phase. Distillation of the ether-extractable material gave II showing no optical activity; picrate, m. p. 89°. A similar experiment in which the boiling in alkali was omitted and in which 7.0 g. of VIII, $[\alpha]^{25}\mathrm{D}$ −0.50°, was used gave 4.2 g. of completely racemic II.

Summary

The fact that optically active methylethyl-*α*-pyridylacetic acid (I), stable to decarboxylation in acid or alkali, decarboxylates in neutral solution to racemic *α*-*s*-butylpyridine (II) is consistent with a mechanism in which the inner salt of I decarboxylates to the symmetrical enamine tautomer of II. Racemization experiments on resolved II indicate a stability which is surprising in view of the many condensations of the *α*-picoline

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(22) Craig, This Journal, **56**, 231 (1934).

type and permit the conclusion that the tautomerization between α-*s*-butylpyridine and its isomeric enamine does not involve solvolytic ionization.

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[CONTRIBUTION FROM CHANDLER LABORATORY, COLUMBIA UNIVERSITY]

The Resolution of 2,4-Dimethylhexan-4-ol[1]

BY W. VON E. DOERING* AND HAROLD H. ZEISS[1a]

Despite the successful resolution of many secondary alcohols[2] an unequivocal resolution of a tertiary, aliphatic alcohol of the type RR'R"COH has not been reported.[3] The resolution of α-terpineol[4] involves a tertiary alcohol in which the carbinol group is not the center of asymmetry, while the resolution of phenyldiphenyl-α-naphthylcarbinol[5] is probably complicated by a molecular asymmetry due to hindered rotation. The resolution of linalool[6] suffers not only from incompleteness but, more seriously, from the absence of an experimental demonstration that the small observed activity is due to resolved linalool rather than to a resolved impurity. In this paper the resolution of 2,4-dimethylhexan-4-ol (I, methylethylisobutylcarbinol) is described.

The choice of I for resolution attempts has been dictated by the high molecular rotations of methylisobutylcarbinol (±20.4°) and ethylisobutylcarbinol (±24.6°) in contrast to the rotations of methyl- and ethyl-, *n*-propyl, isopropyl- and *n*-butylcarbinols (±2.0 – ±15.4°), and by the desire to minimize olefin formation by avoiding juxtaposition of a tertiary hydrogen with the tertiary carbinol.

The preparation of I by the method of Clarke[7] from methyl isobutyl ketone and ethylmagnesium bromide is more satisfactory than by the converse method of the reaction of methyl ethyl ketone with isobutylmagnesium bromide. Attempts to prepare hydrogen 2,4-dimethylhexyl-4-phthalate (II) by the reaction *in situ* of the bromomagnesium salt of I with phthalic anhydride are unsuccessful.[8] However, when a benzene solution of the potassium salt of I is added to a benzene solution of phthalic anhydride according to the general method of Fuller and Kenyon,[4] II is obtained in excellent yield. While II is not crystalline and decomposes slowly on standing, its barium salt can be crystallized from ether–pentane and is indefinitely stable.

The resolution of I, pursued through the fractional crystallization of brucine 2,4-dimethylhexyl-4-phthalate (III), proceeds slowly until the head fraction changes from heavy needles to a mixture of these and tight hemispherical pellets between the fourth and sixth crystallization. By the twelfth crystallization, the hemispherical form predominates and the resolution proceeds more rapidly. Toward the end the heavy needles no longer appear in the head fraction and the optical activity becomes constant. These relations are reflected in the variation of the m. p. of III and the rotation of corresponding II shown in Fig. 1.

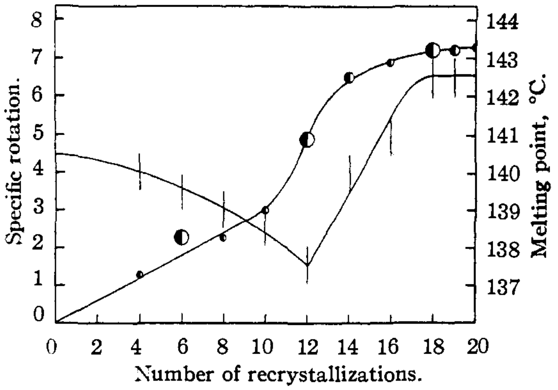

Fig. 1.—The vertical segments represent the m. p. of the head fractions in the fractional crystallization of III. The half-shaded circles represent the specific rotations of II derived from corresponding III.

Pure brucine (+)-2,4-dimethylhexyl-4-phthalate (+III), m. p. 142.5°, gives hydrogen (+)-2,4-dimethylhexyl-4-phthalate (+II), $[\alpha]^{25}\mathrm{D}$ + 7.3°. This dextrorotatory isomer is considered to be optically pure on the grounds that no significant improvement can be made by further crystallization of the brucine salt. However, in having failed to find a base capable of effecting complete resolution of (–)-II, we have left unsatisfied the more valid criterion of optical purity.

The melting point diagram of mixtures of *r*-III (m. p. 140.5°) and (+)-III (m. p. 142.5°) shows a slight but definite minimum (m. p. 138°) which permits the conclusion that the brucine salt of *r*-II

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[2] Ingersoll, "Organic Reactions," John Wiley and Sons, New York, N. Y., 1944, Vol. 2, p. 376.

[3] Of several explanations for the failure, that communicated between Wilson and Kenyon, *Trans. Faraday Soc.*, **37**, 706 (1941), is of interest.

[4] Fuller and Kenyon, *J. Chem. Soc.*, **125**, 2304 (1924).

[5] Wallis, THIS JOURNAL, **54**, 1695 (1932).

[6] Paolini and Diviza, *Atti accad. Lincei*, [5] **23**, 171 (1914).

[7] Clarke, THIS JOURNAL, **30**, 1144 (1908).

[8] Compare Fessler and Shriner, *ibid.*, **58**, 1384 (1936).