# NOTES

## New Types of Racemization Reactions

By Ernst Bergmann and Alfred Bondi

To the number of racemization reactions which obviously are of fundamental importance for our knowledge of the stability of spacial configurations, three new types have recently been added: (a) the racemization of methylalkyliodomethanes by interaction with iodide ions,[1] (b) the racemization of 2-bromohexane during its conversion into the Grignard compound,[2] and (c) the racemization occurring during the interaction between active ethyl propylmethylacetate and phenylmagnesium bromide.[3] Only the first of these three types has so far a theoretical and experimental treatment.

For case (b) one would perhaps be inclined to assume that racemization is due to electrolytic dissociation of the Grignard compound. But this assumption seems inadmissible, since negative carbonium ions seem to be sufficiently stable,[4] while positive ions of carbon are unstable.[5] Therefore one has probably to conclude that the racemization belongs to type (a): the bromide is racemized by bromide ions, which are formed by the ordinary equilibrium reaction $2RMgBr \rightleftarrows R_2Mg + MgBr_2$. The case, therefore, is analogous to the racemization of phenylmethylchloromethane by interaction with magnesium or sodium metal.[1,6]

For case (c) the following suggestion has been advanced by Bergmann and Hartrott.[3] The ester does not undergo racemization—it is unstable only in alkaline solution[7]—but the carbinol is subjected to an equilibrium $(Me)(Pr\text{-}\alpha)CH\text{-}C(OH)Ph_2 \rightleftarrows H_2O + (Me)(Pr\text{-}\alpha)C{=}CPh_2$, whereby the asymmetry is destroyed. It is well known that diphenylalkylcarbinols are easily dehydrated. If this explanation is correct, ethyl propylmethylacetate should give optically active carbinols with simple aliphatic alkylmagnesium halides, since compounds like (2-pentyl)-diethylcarbinol, $(Me)(Pr\text{-}\alpha)CHC(OH)Et_2$, do not lose water so easily. The conclusion has been confirmed by experiment. Into a solution of ethylmagnesium bromide (from 2.5 g. of magnesium and 11 g. of ethyl bromide), active methyl propylmethylacetate (4 g., rotation in acetone, $l = 1$, $c = 2.70$, $\alpha_D$ $-0.19°$; hence $[\alpha]_D$ $-7.04°$) was introduced. The rather violent reaction was completed by boiling for thirty minutes, then the mixture was decomposed with ice and ammonium chloride and the ethereal layer dried with anhydrous sodium sulfate and evaporated. The (2-pentyl)-diethylcarbinol boiled at 92–93° (32 mm.); yield 2.9 g. Calcd. for $C_{10}H_{22}O$: C, 75.9; H, 14.0. Found: C, 75.8, 75.4; H, 14.4, 14.1. Rotation in acetone: $l = 1$, $c = 2.80$, $\alpha^{22}_D$ $-0.365°$; hence $[\alpha]^{22}_D$ $-13.04°$.

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[1] Bergmann, Polanyi and Szabo, *Z. physik. Chem.*, **20B**, 161 (1933); *Trans. Faraday Soc.*, **32**, 843 (1936).

[2] Porter, This Journal, **57**, 1436 (1935).

[3] Bergmann and Hartrott, *J. Chem. Soc.*, 1218 (1935).

[4] Wallis and Adams, This Journal, **54**, 4753 (1932); **55**, 3838 (1933).

[5] Bergmann and Polanyi, *Naturwissenschaften*, **21**, 378 (1933).

[6] Ott, *Ber.*, **61**, 2124 (1926).

[7] Menon and Peacock, *J. Ind. Chem. Soc.*, **12**, 268 (1935).

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## The Preparation of Pure Apocodeine and its Hydrochloride

By Karl Folkers

Early preparations of apocodeine were complex mixtures.[1] Knorr obtained "pseudoapocodeine"[2] by melting codeine with oxalic acid, and later he showed[3] that his apocodeine was identical with the monomethylation product of apomorphine; although this latter product had been reported earlier by Pschorr,[4] but with widely different physical properties. Later methods[5] of making apocodeine from codeine with zinc and sodium chlorides still introduced apomorphine impurities, which necessitated the use of a troublesome perchlorate, chromate or phosphate salt for purification.

Nevertheless, a certain confusion exists in the

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[1] Small, "Chemistry of the Opium Alkaloids," Supp. No. 103, Public Health Reports, 1932, pp. 183, 362.

[2] Knorr and Roth, *Ber.*, **40**, 3355 (1907). The name pseudoapocodeine was introduced by Knorr as he believed pseudocodeine to be an intermediate in the transformation of the morphine nucleus to the aporphine nucleus. Apocodeine is the generally accepted name, and it suggests the same relationship to codeine that apomorphine has to morphine.

[3] Knorr and Raabe, *ibid.*, **41**, 3050 (1908).

[4] Pschorr, Jaeckel and Fecht, *ibid.*, **35**, 4377 (1902).

[5] German Patent 489,185, *Frdl.*, 16, 2485.

literature[6] concerning the chemical properties of pure apocodeine.

The herein described method is an improvement of the Knorr reaction, and a confirmation of Knorr's properties of apocodeine with ethanol of crystallization. The pure anhydrous base and hydrochloride have not been described previously.

**Apocodeine.**—Twenty grams of anhydrous codeine and 60 g. of anhydrous oxalic acid,[7] were heated for one and one-half hours at 150–155° bath temperature with very slow stirring. The melt was cooled and diluted with 250 ml. of water. After complete solution, it was further diluted to 600 ml. in a separatory funnel, shaken with 300 ml. of ether, and the bases precipitated with addition of concentrated ammonia solution. Too slow operation caused troublesome crystallization of ammonium oxalate. The ether layer was separated, filtered and distilled *in vacuo*. A residue of 5.8 g. remained, which was dissolved in 15 ml. of absolute ethanol. Nearly pure apocodeine with a molecule of ethanol crystallized on standing at 10°; yield 2.7–2.8 g. (12.8%). One crystallization gave pure white products of m. p. 104.5–106.5° with gas evolution $[\alpha]^{23}D$ $-90.0$, *C*, 0.533, abs. ethanol, $l = 1$. Further crystallization did not change the melting point or optical rotation.

*Anal.* Calcd. for $C_{18}H_{19}O_2N \cdot C_2H_5OH$: C, 73.35; H, 7.70; $C_2H_5OH$, 14.06. Found: C, 72.99, 73.01; H, 7.57, 7.76; $C_2H_5OH$, 13.76.

The base was best purified by recrystallization from absolute ethanol. The use of the hydriodide as Knorr suggested resulted in partial oxidation. The crystals showed no ready tendency to oxidize, unless they were finely pulverized. The ethanol was lost very slowly at 25° (2 mm.), but readily at 78° (2 mm.). The anhydrous base showed m. p. 122.5–124.5°.

*Anal.* Calcd. for $C_{18}H_{19}O_2N$: C, 76.82; H, 6.81. Found: C, 76.63, 76.80; H, 7.02, 7.06.

As Knorr described, there were ether and water insoluble bases present. It was found, however, that nearly all the apocodeine was extracted by the ether. In one experiment very little more was obtained by redissolving the insoluble bases with acid, reprecipitating, extracting etc. A third repetition of this process yielded no more apocodeine. Thus it was not necessary to bring all the precipitated bases into ether solution as Knorr described. In fact, the moderate insolubility of pseudocodeine[8] and the amorphous products in ether make the first extraction one of considerable purification.

**Apocodeine Hydrochloride.**—To a solution of the base in absolute ethanol was added the calculated amount of dry hydrogen chloride in absolute ethanol and, while hot, absolute ether was added until crystallization started. The yield of pure white salt was quantitative; m. p. softening started at 140°, dec. at 260–263°; $[\alpha]^{22}D$ $-41.3$ to 43.3°; *c*, 0.508; $H_2O$, $l = 1$. Recrystallization from 95% ethanol and ether did not alter the physical constants. The salt was practically anhydrous.

*Anal.* Calcd. for $C_{18}H_{19}O_2N \cdot HCl$: C, 68.00; H, 6.35. Found: C, 68.26, 67.92; H, 6.35, 6.22.

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(6) For example, see Krayer, *Arch. exptl. Path. Pharm.*, **111**, 60 (1920). Schwartze, *Arch. intern. pharmacodynamie*, **41**, 461 (1931).

(7) "Organic Syntheses," Coll. Vol. I, John Wiley and Sons, Inc., New York, 1932, p. 415.

(8) Lutz and Small, THIS JOURNAL, **54**, 4723 (1932).

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## The Thermal Decomposition of Acetone

BY JOHN R. HUFFMAN[1]

The present experiments were undertaken to discover whether the unimolecular rate constant for the thermal decomposition of acetone fell off at low pressures and in such a case to apply the theories of Rice and Ramsperger and of Kassel.[2] Recently Winkler and Hinshelwood[3] working at 875°K. and pressures down to 2.5 mm. reported that this decrease of rate constant started at 100 mm.

Acetone was decomposed in a 200-cc. silica bulb in a furnace automatically controlled to

TABLE I

| Run | $P_0$, mm. | $k \times 10^4$ | Run | $P_0$, mm. | $k \times 10^4$ |
|---|---|---|---|---|---|
| 59 | 128.6 | 10.86 | 46 | 56.2 | 9.70 |
| 65 | 127.2 | 11.39 | 63 | 55.9 | 9.85 |
| 64 | 124.3 | 11.17 | 42 | 53.5 | 9.41 |
| 69 | 120.4 | 10.72 | 22 | 47.8 | 9.38 |
| 71 | 115.5 | 11.42 | 37 | 45.9 | 8.80 |
| 58 | 112.6 | 11.33 | 35 | 41.6 | 8.68 |
| 73 | 107.0 | 10.96 | 24 | 34.9 | 9.05 |
| 72 | 101.2 | 10.32 | 75 | 35.2 | 8.50 |
| 57 | 100.2 | 10.69 | 76 | 35.1 | 8.66 |
| 61 | 100.2 | 11.31 | 36 | 27.8 | 8.12 |
| 66 | 99.0 | 11.27 | 32 | 27.8 | 7.98 |
| 70 | 98.6 | 11.35 | 45 | 25.6 | 8.18 |
| 60 | 86.7 | 10.78 | 31 | 22.9 | 7.65 |
| 68 | 83.4 | 10.42 | 23 | 21.5 | 8.07 |
| 74 | 80.4 | 10.60 | 52 | 21.85 | 8.36 |
| 50 | 78.8 | 10.93 | 34 | 18.54 | 7.43 |
| 40 | 78.3 | 10.75 | 29 | 17.86 | 7.68 |
| 51 | 78.2 | 10.48 | 27 | 17.08 | 7.43 |
| 55 | 74.3 | 10.79 | 44 | 16.60 | 7.48 |
| 62 | 79.1 | 10.32 | 43 | 16.53 | 7.37 |
| 56 | 76.3 | 10.13 | 25 | 15.53 | 6.83 |
| 49 | 72.5 | 10.53 | 33 | 12.80 | 6.86 |
| 39 | 72.9 | 10.60 | 30 | 9.71 | 5.92 |
| 41 | 66.0 | 9.79 | 28 | 7.51 | 5.51 |
| 48 | 62.1 | 10.08 | 26 | 7.49 | 5.40 |
| 38 | 60.7 | 9.54 | 54 | 5.65 | 5.06 |
| 47 | 57.7 | 9.90 | 53 | 4.68 | 4.50 |
| 67 | 58.5 | 9.88 | | | |

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(1) Sterling Research Fellow in Chemistry, Yale University, 1933–1934.

(2) For a detailed discussion and references see Kassel, "Kinetics of Homogeneous Gas Reactions," A. C. S. Monograph No. 57, Chemical Catalog Company, New York, 1932.

(3) Winkler and Hinshelwood, *Proc. Roy. Soc.* (London), **A149**, 340 (1935).