

[CONTRIBUTION FROM THE CHEMICAL LABORATORY OF BROWN UNIVERSITY]

## The Stability of Pinacolates in Liquid Ammonia Solution

BY CHARLES BUSHNELL WOOSTER AND DONALD S. LATHAM

Although the formation of metal ketyl radicals has been reported in the case of benzaldehyde,<sup>1</sup> hexamethyl- and hexaethyl-acetone,<sup>2</sup> and a wide variety of carbonyl compounds of more or less complex structure,<sup>3</sup> the similar investigation of such well-known ketones as acetone and acetophenone has been hampered by the tendency of alkali metals to react with these substances in their enolic forms. However, information regarding the stability of the simpler ketyl radicals may be obtained by studying the behavior of the corresponding alkali metal pinacolates in liquid ammonia solution. Bachmann<sup>4</sup> has shown that the typical metal ketyls exist in dynamic equilibrium with the corresponding pinacolates and it has also been found<sup>5</sup> that liquid ammonia is a solvent especially favorable to dissociation of pinacolates into ketyl radicals.

Benzopinacol is only slightly soluble in liquid ammonia, yet it reacts rapidly with solutions of alkali metal amides yielding blue solutions of the metal ketyls. The presence of the ketyl radicals has been demonstrated by auto-oxidation to benzophenone and by measurement of the electrolytic conductance of the solutions.<sup>6</sup>

Ordinary anhydrous pinacol is very soluble in liquid ammonia and reacts smoothly with sodium amide, yielding solutions of disodium pinacolate. However, these solutions are quite colorless and acetone-free pinacol is regenerated on hydrolysis. It may be concluded, therefore, that disodium pinacolate does not dissociate appreciably into ketyl radicals in liquid ammonia and that if such radicals were formed as intermediates in a reaction they might in general be expected to undergo association with practically quantitative formation of disodium pinacolate.

The behavior of acetophenone pinacol is analogous to that of ordinary pinacol. It reacts readily with sodium amide forming the disodium

pinacolate which is also colorless and which yields on hydrolysis only acetophenone pinacol quite free from acetophenone.

However, the influence of the phenyl groups on the carbon to carbon bond is revealed by the ease with which acetophenone pinacol is cleaved by metallic sodium in liquid ammonia, whereas the reaction between ordinary pinacol and sodium is confined to the replacement of *one* of the hydroxyl hydrogen atoms.

Hydrobenzoin is too insoluble in liquid ammonia to react with solutions of alkali metal amides.

### Experimental Part

All reactions in liquid ammonia were carried out at the boiling point of the solvent under atmospheric pressure. The various types of apparatus employed have been described adequately in previous papers.<sup>7</sup>

**The Action of Alkali Metal Amides on Benzopinacol in Liquid Ammonia.**—Benzopinacol was added to solutions of potassium amide and sodium amide in liquid ammonia. It dissolved at once, yielding a deep blue opaque solution. A stream of dry air rapidly discharged the blue color leaving a pale yellow solution. Ammonium chloride was added, the ammonia allowed to evaporate and the residue extracted with water and ether. The residue on evaporation of the dried ethereal extract crystallized after seeding with benzophenone and was identified as this ketone by mixed melting point determinations and by the preparation of the oxime.

**The Preparation and Stability of Disodium Pinacolate.**—The reaction between anhydrous pinacol and sodium in liquid ammonia proceeds rather slowly and apparently ceases when one of the hydrogen atoms of pinacol has been replaced. Solutions of pinacol in liquid ammonia were treated with excess sodium and the evolved hydrogen collected and measured. Hydrogen equivalent to one atom per mole of pinacol was collected over a period of two hours. After twenty-eight hours the excess sodium was destroyed by adding ammonium chloride. From the hydrogen evolved in this reaction the amount of free sodium present at the end of the experiment was calculated. The amount of sodium consumed in the reaction with pinacol corresponded to 0.95 atom per mole.

Although other investigators<sup>8</sup> have prepared the dimethyl ether of pinacol from pinacol, sodium and methyl iodide, there is no evidence that they actually obtained

(1) Blicke, *THIS JOURNAL*, **46**, 2560 (1924).

(2) Favorski and Nazarov, *Bull. acad. sci. U. R. S. S.*, 1309-51 (1933); Nazarov, *Compt. rend. acad. sci. U. R. S. S.*, [N. S.] **1**, 123-5, 325-8 (1934); Favorski and Nazarov, *Compt. rend.*, **196**, 1229-31 (1934).

(3) Schlenk and Weickel, *Ber.*, **44**, 1182 (1911); Schlenk and Thal, *ibid.*, **46**, 2840 (1913).

(4) Bachmann, *THIS JOURNAL*, **55**, 1179 (1933).

(5) Wooster, *ibid.*, **56**, 2436 (1934).

(6) Kraus and Bien, *ibid.*, **55**, 3609 (1933).

(7) Wooster, *ibid.*, **51**, 1858 (1929); Wooster and Mitchell, *ibid.*, **52**, 691 (1930); Wooster and Smith, *ibid.*, **53**, 180 (1931); Wooster and Ryan, *ibid.*, **56**, 1134 (1934).

(8) Lindner, *Monatsh.*, **32**, 409 (1911).

disodium pinacolate because the methylation was carried out stepwise. On the other hand, both hydroxyl hydrogens of pinacol may be replaced with sodium through the action of sodium triphenylmethyl and of sodium amide in liquid ammonia.

Sodium triphenylmethyl prepared from 0.470 g. sodium and the corresponding quantity of triphenylchloromethane in liquid ammonia<sup>9</sup> was titrated with a solution of pinacol in absolute ether. The red color was just discharged by the addition of 10.5 cc. of solution containing 5.41 millimoles of pinacol; the molar ratio of sodium triphenylmethyl to pinacol was therefore 1.89.

Sodium amide in liquid ammonia readily converts triphenylmethane to the intensely red sodium triphenylmethyl.<sup>10</sup> It has also been shown above that a solution of sodium triphenylmethyl in liquid ammonia can be decolorized by reaction with pinacol. Accordingly, liquid ammonia solutions of sodium amide may be titrated with pinacol solutions using triphenylmethane as an indicator.

Sodium (0.4912 g.) was converted to the amide in liquid ammonia by the method of Vaughn, Vogt and Nieuwland,<sup>11</sup> and a very small amount of triphenylmethane (dissolved in toluene) was added, imparting a definite red color to the solution containing the sparingly soluble amide. A quantity of anhydrous pinacol (2.523 g.) was then dissolved in dry ether, diluted to 50 cc. with dry toluene, and added drop by drop with stirring to the contents of the reaction tube. Very little change was noted until 15 cc. of this solution had been run in, at which time the amount of precipitate (sodium amide) was decidedly smaller, the liquid appeared somewhat darker and a scum had begun to appear on the walls. With the addition of more toluene a better separation into layers was obtained and a sharp end-point was observed when 24.5 cc. of the pinacol solution had been used. Although these figures would indicate 2.04 atoms of sodium introduced per mole of pinacol, a correction for the possible loss of amide due to reaction with the water in the approximately 0.05 g. of  $\text{Fe}(\text{NO}_3)_3 \cdot 6\text{H}_2\text{O}$  used as catalyst, would lower this value to 1.95 atoms. A second similar experiment yielded the value 1.98. The method was also tested using benzyl alcohol in place of pinacol with satisfactory results.

A larger scale experiment was carried out to determine the amount of pinacol which could be recovered after the treatment with sodium amide. Sodium (3.5 g.) was converted to the amide with 0.1 g. of the catalyst using 500 cc. of liquid ammonia. A solution of 6.21 g. of anhydrous pinacol in 20 cc. of dry ether was added with vigorous stirring. After allowing the mixture to evaporate to about 150 cc., 11 g. of ammonium chloride was added and the mixture evaporated almost to dryness. The residue was extracted with 150 cc. of dry ether. This was concentrated to about 7 cc. and then 5.6 cc. of water was added. This amount corresponded to that necessary for the formation of the pinacol hexahydrate. On seeding, the pinacol hydrate crystallized out almost solid, the ether being driven off by the heat evolved. The yield of dry, solid hydrate was 10.8 g. corresponding to the recovery of 91% of the original anhydrous pinacol.

Iodoform tests for the presence of acetone according to Gunning's method<sup>12</sup> were made on the recovered hydrate. A modification of this test similar to Fuson's modification of the usual iodoform test<sup>13</sup> was also applied to the ether distillate. In both cases no evidence of acetone was found, although control tests showed that even small amounts of acetone could be detected without interference by the pinacol.

**The Preparation and Stability of Disodium Acetophenone Pinacolate.**—Solutions of sodium amide in liquid ammonia were titrated with solutions of acetophenone pinacol in ether and toluene using triphenylmethane as an indicator. Two experiments yielded the values 1.83 and 1.97 moles of sodium amide per mole of the pinacol for the reaction ratio. This indicates that acetophenone pinacol like pinacol reacts with two moles of sodium amide to form the disodium pinacolate.

In a larger scale experiment 5 g. of sodium was converted to the amide, and 20 g. of the acetophenone pinacol was added with stirring. About 150 cc. of dry ether was added to aid in solution. When most of the pinacol had been added the appearance of the mixture changed quickly, the solution lost the opaque gray color and became clear but slightly yellow. After standing for three hours, 15 g. of ammonium chloride was added, the ammonia allowed to evaporate and the residue steam distilled for two hours. No water-insoluble material (except a small amount of ether) distilled over. The solid left in the flask was filtered off, taken up in ether, the ether evaporated and the residue recrystallized from petroleum ether. Of the 20 g. of starting material 15 g. was recovered in fine crystalline form.

A method was sought for detecting acetophenone in the presence of acetophenone pinacol. Iodoform tests, both according to Fuson and Tullock and following Gunning's use of ammoniacal ammonium iodide solution, proved of no use as the original pinacol also gave a positive test. It was found, however, that the sodium nitroprusside color test<sup>14</sup> could be used to detect even small amounts of the ketone in the presence of a large excess of the pinacol. This test failed to show the presence of any acetophenone in the products of hydrolysis of disodium acetophenone pinacolate.

**The Action of Sodium on Acetophenone Pinacol.**—Acetophenone pinacol (24.2 g., 0.1 mole) was mixed with one liter of liquid ammonia and while the mixture was stirred vigorously, 12.5 g. of metallic sodium (0.54 atom) cut into twenty pieces of approximately equal size, was added slowly. The reaction was very rapid at first, slowing up noticeably, however, when one atomic equivalent of sodium had been added. By this time all of the sparingly soluble pinacol had disappeared, leaving a clear solution with only a trace of sediment. The addition of more sodium resulted in an increase in the rate of reaction, and the appearance of increasing amounts of voluminous, sticky precipitate. After about two atomic equivalents of sodium had been added the reaction rate again began to decrease and the precipitate also appeared to dissolve until, when the blue color was no longer removed (even

(9) Kraus and Kawamura, *THIS JOURNAL*, **45**, 2756 (1923).

(10) Kraus and Rosen, *ibid.*, **47**, 2739 (1925).

(11) Vaughn, Vogt and Nieuwland, *ibid.*, **56**, 2120 (1934).

(12) Hofmeister, *Z. anal. Chem.*, **24**, 147 (1885).

(13) Fuson and Tullock, *THIS JOURNAL*, **56**, 1633 (1934).

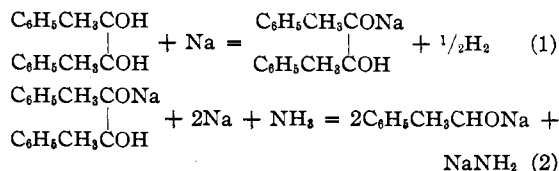
(14) Mulliken, "Identification of Pure Organic Compounds," John Wiley & Sons, New York City, 1904, Vol. I, p. 146.

on waiting twenty-five minutes) no precipitate was evident. When the solution became permanently blue, 2 g. of the sodium (0.22 atom) still remained unadded. The reaction ratio then is probably close to three atoms of sodium per mole of pinacol.

The remainder of the sodium was added, the mixture allowed to stand one and one-half hours with intermittent stirring and then decolorized by the addition of ammonium chloride. No precipitate, outside of a thin scum on the walls of the flask, was present; 20 cc. of water was added, and the ammonia allowed to evaporate. The ether extract of the residue, dried with anhydrous sodium sulfate and evaporated, yielded about 20 cc. of yellowish oil with an odor like methylphenylcarbinol. This oil was distilled through an Eastman column and the fraction boiling at 195–210° was identified as methylphenylcarbinol by its refractive index, specific gravity and by the preparation of its phenyl urethan (mixed melting point).

In two quantitative experiments 2.3387 and 2.5123 g. of acetophenone pinacol was placed in a reaction tube, ammonia condensed upon it and sodium (0.9493 and 0.9338 g.) in small pellets added slowly with agitation. At first the sodium was used up quickly and some hydrogen was evolved. After all the sodium had been added and the reaction was complete, ammonium chloride was added and the evolved hydrogen was collected separately. The results were as follows: hydrogen collected during addition of sodium to the pinacol (corrected to N. T. P.) 29.4 and 29.8 cc.; hydrogen collected during addition of ammonium chloride, 149 and 149 cc. From the latter figures it may be calculated that the amounts of sodium reacting with the pinacol were in the ratios of 2.90 and 2.64 atoms per mole.

Although the reaction between sodium and acetophenone pinacol is obviously complex, the principal results may be summarized by the equations



That is, substitution of one of the hydroxyl hydrogens with sodium is followed by cleavage of the carbon-carbon bond and ammonolysis of the resulting organo-sodium compounds. The very noticeable decrease in the speed of reaction when one atomic equivalent of sodium had been added was probably due to completion of Reaction 1 followed by slow cleavage of the monosodium pinacolate. The subsequent increase in reaction rate may well be ascribed to the more rapid cleavage of the disodium pinacolate which would be formed from the monosodium compound as soon as appreciable quantities of sodium amide had been produced by Reaction 2. The cause of the discrepancy between the amounts of hydrogen collected and those calculated on the basis of Equation 1 is not known.

### Summary

1. The disodium derivatives of pinacol and acetophenone pinacol may be prepared by the action of sodium amide on these glycols in liquid ammonia. These pinacolates give no evidence of dissociation into metal ketyls.

2. Sodium in liquid ammonia replaces only one of the hydrogen atoms of pinacol; it reacts extensively with acetophenone pinacol, not only replacing hydrogen, but also cleaving the carbon-carbon bond.

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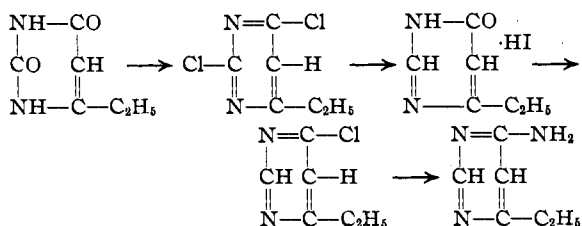
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## A Synthesis of 4-Ethyl-6-aminopyrimidine

BY WILLIAM T. CALDWELL AND WILLIAM M. ZIEGLER

Recently, R. R. Williams<sup>1</sup> suggested, as a probable structure of vitamin B<sub>1</sub>, a formula derived from 4-ethyl-6-aminopyrimidine. For this reason, and since we found no record of this compound in the literature, we thought its synthesis of interest and accordingly have carried it out by a series of reactions summarized thus



(1) Williams, THIS JOURNAL, 57, 229 (1935).

Our method makes use of procedures, previously described, for the synthesis of analogously constituted compounds. However, noting that ethyl pseudo thiourea is probably more stable in alcohol than in water,<sup>2</sup> we condensed propionylacetic ester with ethyl pseudo thiourea in absolute methanol solution of potassium hydroxide, at 0°, with a yield of pure product greater than that obtained when the condensation was carried out in the usual way in aqueous medium.

### Experimental Part

**4-Ethyluracil.**—This compound was prepared in 86.5% yield by hydrolyzing 2-ethylmercapto-4-ethyl-6-oxypyrimidine; the latter compound, melting at 89°, was obtained

(2) Arndt, Ber., 54, 2241 (1921).