by washing the chloroform solution twice with 3% hydrochloric acid, once with dilute sodium bicarbonate solution, and crystallization of the sirup, recovered from the dried extract; from ether–petroleum ether at 0°. After one recrystallization from 90% ethanol, the acetate rotated +13.4° in chloroform and melted at 98.5–99° (corr.) alone or mixed with pure β-tetraacetate prepared from β-triacetylrhamnose by the directions of Fischer, Bergmann and Rabe,[6] whose method gave a product rotating, after purification, +13.3° in chloroform (*c*, 3.87) and +14.2° in acetylene tetrachloride compared with their $[\alpha]^{16}_{D}$ +13.75° in the latter solvent.

The lower rotating form of anhydrous rhamnose was acetylated as described for the β-sugar. One gram of sugar with initial rotation +13.2° yielded 0.85 g. (43%) of β-tetraacetate, most of which melted at 97–98° (corr.) and rotated +12.5° in chloroform. The remainder of the product was a sirup.

Summary

Anhydrous rhamnose, hitherto obtainable only in small yield, has been prepared in 85–90% yield by two methods. The initial rotation of Fischer's β-rhamnose was found to be +38° in water; Minsaas recently reported about +44°. During the preparation of β-rhamnose a second form of the anhydrous sugar rotating about +14° in water frequently separated; this substance appears to be a molecular compound having the composition α,β-rhamnose if the rotation of β-rhamnose is +38° or 3-α,2-β-rhamnose if it is +44°. The presence of the β-isomer as one component of this molecular compound is confirmed by the preparation from it of crystalline β-tetraacetylrhamnose in 43% yield. Acetylation of β-rhamnose yields about 90% of the crystalline β-tetraacetate, which is now best obtained in this way.

WASHINGTON, D. C. RECEIVED APRIL 24, 1937

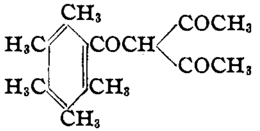
[CONTRIBUTION FROM THE SCHOOL OF CHEMISTRY OF THE UNIVERSITY OF MINNESOTA]

Acetopentamethylbenzene[1]

BY LEE IRVIN SMITH, ISABELLA M. WEBSTER AND CYRUS GUSS

In a recent paper, Henri Clément[2] has discussed the properties of pentamethylphenylmagnesium bromide, which was prepared by the entrainment method of Grignard[3] by allowing an equimolecular mixture of bromopentamethylbenzene and ethyl bromide in ether to react with magnesium. Among other reactions discussed by Clément was that between acetyl chloride and pentamethylphenylmagnesium bromide, which was claimed to give acetopentamethylbenzene in 34% yield. This substance was described as crystallizing in small rods which melted at 110°. In view of the work of Kohler and Baltzly[4] and of Smith and Guss[1] upon the behavior toward Grignard reagents of diortho substituted aromatic ketones of the type of acetomesitylene and acetopentamethylbenzene, it seemed very unlikely that any enolizable ketone of this type could be prepared by dropping acetyl chloride into a highly hindered Grignard reagent especially when ethylmagnesium bromide also was present. When Smith and Guss[1] prepared acetopentamethylbenzene from the hydrocarbon by the Friedel–Crafts synthesis and found the substance to melt at 84°, it was obvious that Clément's compound which melted at 110° could not be acetopentamethylbenzene.

At first it was supposed that Clément's compound was the triketone I, formed from pentamethylphenylmagnesium bromide and acetyl chloride by a sequence of reactions which included: (a) formation of acetopentamethylbenzene, a slow reaction; (b) enolization of the ketone by excess Grignard reagent, a more rapid reaction; and (c) reaction of the enolate with acetyl chloride to give the triketone, also a reaction faster than (a). Accordingly acetopentamethylbenzene was con-



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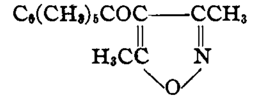

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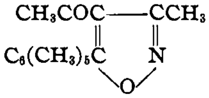

III

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[1] Polymethylbenzenes. XVII. Paper XVI. Smith and Guss, THIS JOURNAL, **59**, 804 (1937).

[2] Henri Clément. *Compt. rend.*, **202**, 425 (1936).

[3] (a) Grignard, *ibid.*, **198**, 625 (1934); (b) Clément and Grignard, *ibid.*, **198**, 665 (1934); (c) Grignard, *ibid.*, **198**, 2217 (1934); (d) see also Urion, *ibid.*, **198**, 1244 (1934).

[4] Kohler and Baltzly, THIS JOURNAL, **54**, 4015 (1932).

verted to the bromomagnesium enolate by methylmagnesium iodide and by ethylmagnesium bromide, and when the enolate was subjected to the action of acetyl chloride, there resulted a white crystalline substance having the composition $C_{17}H_{22}O_3$ (I), which melted at 110° and which formed a dusty blue, insoluble copper compound from which it could be regenerated by the action of acids. Clément[3b] stated that he had prepared the oxime (m. p. 190.6°) and the semicarbazone (m. p. 241.7°) of his acetopentamethylbenzene. That his "ketone" should form an oxime was in itself an indication that it was not acetopentamethylbenzene, for Baum[5] and also Meyer[6] found that acetomesitylene could not be converted into an oxime by any of the usual methods, although Feith and Davies[7] obtained acetylmesidine, the Beckmann rearrangement product of the oxime, by heating acetomesitylene with hydroxylamine hydrochloride at 160°. Although Clément stated that the analysis of his oxime was in accordance with the theory, he did not publish the figures nor the procedure used, and the logical supposition was that his oxime was the isoxazole II or III, derived from the triketone I. When the triketone I was subjected to the action of hydroxylamine, there resulted the isoxazole II which however, melted at 176° and not at 190.6° as recorded by Clément for his "oxime."

Because the triketone II melted at 110°, the melting point given by Clément for his "acetopentamethylbenzene," the work of Clément was repeated many times before the conviction gradually arose that the agreement between the two melting points was a coincidence and that Clément never had in hand either acetopentamethylbenzene or the triketone. Pentamethylphenylmagnesium bromide was prepared both by the full entrainment method of Grignard, and by the modified method of Kohler and Blanchard.[8] The yield, determined roughly by conversion of an aliquot portion into the acid, was 80 ± 10%. Yet when an ethereal solution of pure acetyl chloride was run into this same Grignard solution, although there was a vigorous reaction, not a trace of acetopentamethylbenzene or of the triketone could be obtained from the reaction product. The product consisted of pentamethylbenzene, bromopentamethylbenzene, and an oily material which, judging from its odor, was largely methyldiethylcarbinol although an appreciable amount of a very high boiling material (b. p. about 180° at 10^{-5} mm.) also was present. Experiments on a known mixture of bromopentamethylbenzene (0.5 g.), pentamethylbenzene (2.0 g.), acetopentamethylbenzene (0.5 g.), triketone (0.39 g.) and ether (25 cc.) showed that 0.12 g. of triketone could be recovered *via* the copper compound, and 0.45 g. of acetopentamethylbenzene could be recovered by treating the remainder of the material with ethylmagnesium bromide, decanting from the insoluble enolate of the ketone, washing the latter thoroughly with ether and then decomposing it with dilute acid.

No product was ever obtained from the reaction between pentamethylphenylmagnesium bromide and acetyl chloride which gave a precipitate when shaken with copper acetate solution; in most cases the yellow or brown ethereal solution merely turned green. And with one exception, no product was ever obtained which gave any enolate of acetopentamethylbenzene when treated with ethylmagnesium bromide. The one exception was the product which resulted when an aliquot portion of a Grignard solution was *added to* excess acetyl chloride. This product (2.5 g.) gave no copper compound, but it did give a crystalline enolate when treated with ethylmagnesium bromide. Decomposition of this enolate gave 0.15 g. (6%) of acetopentamethylbenzene.

Although acetyl chloride, when added to an ethereal solution of pentamethylphenylmagnesium bromide, did not produce either the monoketone or the triketone, nevertheless the Grignard reagent was destroyed by this procedure and the product of the reaction was pentamethylbenzene. This was shown by carbonation of an aliquot portion of the reagent before addition of acetyl chloride, when pentamethylbenzoic acid was obtained; after the reaction with acetyl chloride, carbonation produced no pentamethylbenzoic acid; the only alkali soluble material was a very small amount of a thick orange oil.

The failure to obtain acetopentamethylbenzene from acetyl chloride and the Grignard reagent was surprising in view of the fact that Kohler and Blanchard[8] (p. 370) obtained acetotriphenylbenzene from 2,4,6-triphenyl-phenylmagnesium bromide and acetyl chloride. However, this result was not due to any peculiarity of pentamethylphenylmagnesium bromide, for essentially the

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(5) Baum, *Ber.*, **28**, 3207 (1895).

(6) Meyer, *ibid.*, **29**, 830 (1896).

(7) Feith and Davies, *ibid.*, **24**, 3546 (1891).

(8) Kohler and Blanchard, THIS JOURNAL, **57**, 367 (1935).

same results were obtained when mesitylmagnesium bromide was treated with acetyl chloride. Neither acetomesitylene nor the triketone[4] (p. 4017) derived from it was obtained; the chief product was mesitylene, but along with the hydrocarbon there resulted a small amount of an oily by-product. It appears, therefore, that two methyl groups ortho to the functional group in an aromatic Grignard reagent give rise to a greater hindrance to addition than do two phenyl groups in the same position.

We have not repeated all of Clément's work. He claimed to have obtained (42% yield) acetopentamethylbenzene, also melting at 110°, from the reaction between the Grignard reagent and ethyl acetate. Certainly this is in error. In addition, Clément prepared pentamethylbenzophenone from the Grignard reagent and either benzoyl chloride or ethyl benzoate, and this ketone also gave an "oxime" and a "semicarbazone," a statement which, if true, would indicate that the ketone was not pentamethylbenzophenone. With ethyl formate, Clément obtained *pentamethylbenzaldehyde* in 34% yield, and he reported that the substance melted at 130.5°. Some time ago, Mr. J. H. Paden of this Laboratory prepared this aldehyde from the hydrocarbon, zinc cyanide, hydrochloric acid and aluminum chloride. He found that the aldehyde melted at 142–147° and it was not possible to get a narrower range in the melting point by recrystallizing it, or by distilling it (b. p. 144° at 6 mm.) in an atmosphere of carbon dioxide, followed by crystallization. Nevertheless the aldehyde was analytically pure; it gave an oxime (m. p. 187–188°) and a semicarbazone (m. p. 270–275°), both of which gave excellent analytical values, and on oxidation the aldehyde readily gave the known pentamethylbenzoic acid (m. p. 209–210°).

Experimental Part[9]

Acetopentamethylbenzene was prepared in 80% yield by the method of Smith and Guss.[1] The ketone boiled at 144–145° under 8 mm. pressure, and after crystallization from methanol, the melting point was 84°.

Anal. Calcd. for $C_{13}H_{18}O$; C, 82.11; H, 9.47. Found: C, 82.09; H, 9.21.

When an ethereal solution of the substance was shaken with saturated aqueous copper acetate, no copper compound was formed, nor was there any color developed in the ethereal layer. When subjected for twenty-four hours to the action of hydroxylamine and alkali in aqueous-alcoholic solution according to the procedure of Kamm[10] the ketone (0.2 g.) was recovered quantitatively. No trace of an oxime could be found in the reaction mixture. As shown by Smith and Guss[1] the ketone was enolized completely by methylmagnesium iodide, one equivalent of methane being liberated.

Diacetylpentamethylbenzoylmethane (I).—Acetopentamethylbenzene (5 g.) in ether (50 cc.) was dropped slowly into a solution of ethylmagnesium bromide (25 cc.) prepared from 0.75 g. of magnesium and 2.5 g. of ethyl bromide. The solution developed a light tan color and the white crystalline enolate precipitated. Acetyl chloride (10 cc. freshly distilled from dimethylaniline) in ether (30 cc.) was added slowly. A copious tan precipitate formed, and the ether solution became yellow. The mixture was refluxed for two hours and then allowed to stand for two days, after which it was decomposed by addition of iced hydrochloric acid. The ether layer was separated, the aqueous layer was extracted thoroughly with ether and the combined ethereal solutions shaken with excess saturated aqueous copper acetate. The ethereal layer became blue, and in a short time a bluish-gray precipitate appeared, which was removed and washed with ether. The dull blue copper compound (2.01 g.) turned brown at 234°, sintered at 242° and melted at 244–247° to a deep reddish-brown liquid. The ethereal layer after removal of the copper compound, contained 3.43 g. of acetopentamethylbenzene (m. p. 76–81°) which was contaminated by a small amount of yellow oil.

The copper compound was suspended in ether and decomposed by shaking it with hydrochloric acid (1:1). There resulted 1.67 g. of the triketone (I) which melted at 95–108°. After repeated recrystallization from methanol (6 cc.) the substance melted at 110–111°.

Anal. Calcd. for $C_{17}H_{22}O_3$: C, 74.45; H, 8.03. Found: C, 74.66; H, 7.71.

When examined quantitatively in the Grignard machine, the triketone in contrast to the analogous compound of Kohler and Baltzly[4] (p. 4021) liberated 1.9 moles of gas and consumed 1.26 moles of reagent by addition (average of two closely agreeing determinations).[11] A few milligrams of the triketone in ether was shaken with copper acetate. After removal of the copper compound, the colorless ether layer was evaporated. Only a trace of material remained.

Isoxazole, II or III.—Two formulas are possible for this substance. It could be 3,5-dimethyl-4-pentamethylbenzoylisoxazole (II) or 3-methyl-4-acetyl-5-pentamethylphenylisoxazole (III), depending upon which carbonyl group enolized after addition of hydroxylamine. The exact structure was not determined. The triketone (0.2 g.) was added to a mixture of hydroxylamine hydrochloride (0.5 g.) in water (2 cc.) and sodium hydroxide (2 cc., 10%). A little alcohol was added to dissolve the triketone, and the mixture was heated on the steam-bath for forty-five minutes. Dilution with water precipitated the isoxazole, which was removed and crystallized from methanol. The melting point was 176°.

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[9] Micro analyses by J. W. Opie.

[10] Kamm, "Qualitative Organic Analysis," John Wiley & Sons, Inc., New York, 1932, p. 172.

[11] The authors are indebted to Mr. Wm. Prichard for the Grignard analyses.

Anal. Calcd. for $C_{17}H_{21}O_2N$: C, 75.28; H, 7.75. Found: C, 75.62; H, 7.85.

Before starting the work on the reactions of pentamethylphenylmagnesium bromide, a control experiment was carried out in order to test the efficiency of the method of analysis which it was proposed to use in handling the products. A mixture (total weight 3.09 g.) of triketone (0.39 g., 0.00146 mole), acetopentamethylbenzene (0.50 g., 0.00338 mole), bromopentamethylbenzene (0.50 g., 0.00186 mole) and pentamethylbenzene (2.00 g., 0.0135 mole) was dissolved in ether (25 cc.) and shaken with copper acetate. There resulted 0.18 g. of copper compound from which 0.12 g. of triketone was obtained. The remaining ethereal solution was shaken with hydrochloric acid, washed with water, and dried. Evaporation of the ether left 2.23 g. of solid material. This was taken up in dry ether (50 cc.) and the solution was added to excess ethereal ethylmagnesium bromide. A white precipitate slowly formed. Stirring and refluxing were continued for six hours and then the mixture was allowed to stand for thirty-six hours at room temperature. The ethereal solution was removed by decantation, the precipitate was washed with a little ether and decomposed in the usual way. There resulted 0.45 g. of crude acetopentamethylbenzene which melted at 64–78°; when mixed with acetopentamethylbenzene, the melting point was 68–78°. The combined ethereal solutions were evaporated; the residue weighed 1.23 g.

The Grignard Reactions.—To a mixture of bromopentamethylbenzene (20 g., 0.088 mole), ether (70 cc.) and magnesium (5.26 g., 0.22 mole) was added dropwise a solution of ethyl bromide (9.62 g., 0.088 mole) in ether (30 cc.). The reaction started at once and the bromopentamethylbenzene began to dissolve. When about half of the ethyl bromide had been added, the Grignard reagent began to precipitate as a white crystalline solid. After all the ethyl bromide was added, the mixture was stirred and refluxed for about an hour. The volume was then made up to 150 cc. by addition of ether and while stirring vigorously 25 cc. was drawn out with a pipet and immediately run onto crushed dry ice in an open beaker. After all the dry ice had disappeared, the mixture was worked up in the usual way. The portion soluble in alkali yielded 1.49 g. (53%) of pentamethylbenzoic acid melting at 202–206°, which when mixed with an authentic specimen (m. p. 209–210°) melted at 205–209°. The alkali insoluble material weighed 0.83 g. and was largely pentamethylbenzene. It melted at 50–58° and the melting point was not changed by addition of pure pentamethylbenzene. Based upon the weights of pentamethylbenzoic acid and pentamethylbenzene (80% pure) obtained, and assuming that both these substances were derived from the Grignard reagent, then the yield of the latter was 80%.

A second 25 cc. of the Grignard solution was pipetted out and dropped slowly into a well-stirred solution of acetyl chloride (10 cc.) in ether (25 cc.). There was a vigorous reaction, a yellow color developed and a precipitate formed. After addition of the Grignard solution the mixture was refluxed for one and one-half hours and then set aside at room temperature for two days. The product was decomposed in the usual way and the combined ethereal solution and extracts when evaporated, gave 2.5 g. of a granular solid which melted at 55–77°. The solid was dissolved in ether and shaken with copper acetate; no copper compound precipitated. The ethereal solution (30 cc.) was dried thoroughly and added slowly to an excess of ethylmagnesium bromide in ether (50 cc.). The mixture was stirred and refluxed for several hours and then set aside overnight. The ether was decanted from the small amount of crystalline precipitate (needles), the latter was washed with ether and then decomposed with acid. There resulted 0.15 g. (6%) of acetopentamethylbenzene which melted at 78–81° and which did not depress the melting point of a known specimen. The ethereal solution and washings, when evaporated, gave 1.19 g. of impure pentamethylbenzene which melted at 50–67°.

Several experiments were carried out in which acetyl chloride in ether was added to the mixed Grignard reagents prepared by the entrainment method. The reaction mixtures were decomposed in the usual way, and the products were worked up as follows.

I. (From 13.3 g. of bromo compound.) The ethereal solution gave no precipitate when it was shaken with copper acetate. The ether was then evaporated and the residue was vacuum distilled. The products were: (a) a colorless oil (1.5 g.) with a sharp odor, which boiled at 33–34.5 under 23 mm., and was probably the chloride of diethylmethylcarbinol; (b) a white solid (6.0 g.) which boiled at 107–114° under 14 mm., and melted at 47.5–51.5° (pentamethylbenzene); (c) a residue of dark viscous liquid in the distilling flask. This was distilled in a high vacuum apparatus. The first material to collect in the receiver was a white solid (0.23 g.) which melted at 95–110° and which gave no copper compound. It was impure bromopentamethylbenzene. When the residue remaining in the distilling flask was heated to 180° under 10^{-5} mm. it gave a distillate (1.39 g.) of light orange oil which darkened immediately on exposure to the air. The non-volatile residue weighed 1.16 g.

II. (From 20 g. of bromo compound.) Before decomposition 50 cc. of the material (total volume 186 cc.) was pipetted out and run into a sufficient excess of ethylmagnesium bromide to destroy the acetyl chloride and enolize any acetopentamethylbenzene that might have been present. Acetyl chloride was then added and the mixture was allowed to stand overnight. Decomposition in the usual way resulted in a dark brown liquid which gave no copper compound. The substance was then steam distilled. The distillate contained pentamethylbenzene (2.97 g.) which melted at 52–55°. The residue remaining in the distilling flask was 1.8 g. of dark oil.

The remainder of the material (136 cc.) after decomposition was first tested with copper acetate (negative) and then steam distilled. From the distillate there was isolated 8.92 g. of pentamethylbenzene which melted at 53–55.5°. The residue consisted of a thick brown oil (3.57 g.).

The total recovery of pentamethylbenzene (11.89 g.) was 91% based on 20 g. of bromo compound used.

III. A Grignard reagent was prepared by refluxing together a dilute ethereal solution of ethylmagnesium bromide (5 cc.), magnesium (2.1 g.), bromopentamethylbenzene (10 g.) and xylene (30 cc.). After refluxing for five hours, excess acetyl chloride was added and refluxing was continued for another hour. The reaction mixture, decomposed in the usual way, gave a negative test with copper acetate, and after drying, gave only a trace of precipitate with excess ethylmagnesium bromide. Acid was added and the mixture was steam distilled. The distillate contained 4.38 g. (68%) of pentamethylbenzene which melted at 54–55° and in the distilling flask there remained 1.79 g. of a thick yellow oil.

IV. A Grignard reagent was prepared by refluxing together the bromo compound (10 g.), magnesium (1.46 g.), ether (100 cc.) and ethyl bromide (1 cc.). The reaction was very slow, but a considerable amount of the Grignard reagent had precipitated after three hours. One-fourth (25 cc.) of the solution was removed and this, dropped onto crushed dry ice and worked up in the usual way yielded 0.65 g. (34.5%) of pentamethylbenzoic acid and 1.12 g. of a mixture of bromo compound and pentamethylbenzene which melted at 77–123°. To the remainder of the Grignard reagent was added acetyl chloride (10 cc.). The mixture was refluxed for two hours and then excess crushed dry ice was added. After carbonation there was obtained as alkali soluble material only 0.3 g. of a yellow malodorous oil which, however, gave a deep green color when it was dissolved in ether and shaken with copper acetate. The alkali insoluble material (5.81 g.) was steam distilled. The distillate contained 3.17 g. of pentamethylbenzene which melted at 51–55° and the residue contained 1.59 g. of yellowish impure bromopentamethylbenzene which melted at 130–140°. Thus, although the Grignard reagent was not converted into acetopentamethylbenzene or the triketone by acetyl chloride, nevertheless it was destroyed by this reagent and in the process it was converted into pentamethylbenzene.

V. An experiment similar to IV was carried out starting with bromomesitylene (10 g.), magnesium (1.3 g.), ether (30 cc.) and ethyl bromide (8 drops). Carbonation of an aliquot portion gave the known carboxymesitylene which melted at 146–150° and which showed no depression in melting point when mixed with an authentic specimen. The remainder of the Grignard solution was refluxed for three hours with acetyl chloride (6 cc.). After decomposition in the usual way, a distillate of 2.98 g. of mesitylene (b. p. 53° under 23 mm.) was removed. The residue (3.59 g.) was taken up in ether and added slowly to excess ethylmagnesium bromide.[4] No precipitate of the enolate of acetomesitylene was obtained after the mixture had stood overnight, nor was any obtained when half the ether was evaporated. The mixture was decomposed and steam distilled, giving a distillate containing 1.2 g. of bromomesitylene and a residue of dark, thick oil (0.89 g.). Hence the Grignard reagent from bromomesitylene behaved toward acetyl chloride in the same manner as the reagent from bromopentamethylbenzene.

Summary

1. Contrary to the report of Clément, pentamethylphenylmagnesium bromide does not give acetopentamethylbenzene when it reacts with acetyl chloride. The products of the reaction are pentamethylbenzene and condensation products of the acid chloride.

2. Mesitylmagnesium bromide behaves toward acetyl chloride in the same manner as does the reagent from bromopentamethylbenzene, no acetomesitylene resulting. The behavior of the two methylated Grignard reagents differs from that of 2,4,6-triphenyl-phenylmagnesium bromide, which Kohler and Baltzly found gave the aceto compound with acetyl chloride, and these results indicate that two methyl groups in the ortho position to the functional group of a Grignard reagent offer more hindrance to addition than do two phenyl groups similarly placed.

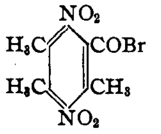
MINNEAPOLIS, MINN. RECEIVED MARCH 15, 1937

[CONTRIBUTION FROM THE SCHOOL OF CHEMISTRY OF THE UNIVERSITY OF MINNESOTA]

Polymethylbenzenes. XVIII. The Action of Nitric Acid upon Bromodurene[1]

BY LEE IRVIN SMITH, F. LOWELL TAYLOR AND ISABELLA M. WEBSTER

In a recent paper, Smith and Tenenbaum[2] have shown that the product obtained by Willstätter and Kubli[3] by action of fuming nitric acid upon bromodurene, and regarded by them as dinitrodurylic acid bromide (I), could not possibly be an acid bromide. Moreover, the analyses of Smith and Tenenbaum, as well as those of Willstätter and Kubli, agreed much better with the formula $C_{10}H_{11}O_5N_2Br$ than with the formula $C_{10}H_9O_5N_2Br$ (I). The chief reactions of the substance which was discovered by Smith and Tenenbaum were the ready conversion to 3-bromo-5,6-dinitropseu-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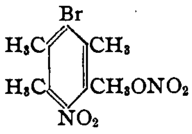
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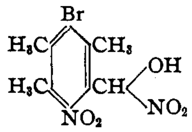
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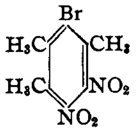
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(1) Paper XVII. THIS JOURNAL, 59, 1078 (1937).

(2) Smith and Tenenbaum, *ibid.*, 57, 1293 (1935).

(3) Willstätter and Kubli, *Ber.*, 42, 4151 (1909).