put the whole into the flask; of course, a paper was used in running a blank. Sodium hydroxide, 0.020 *N* and sulfuric acid, 0.040 *N* were of suitable strength. This method does not require as much skill as Pregl's micro method, nor as large a sample as the usual procedure. Senior students used it with good results.

2,4-Dinitrophenylhydrazine did not give solid derivatives with methyl *n*-heptyl, *n*-octyl, and *n*-decyl ketones, di-*n*-butyl ketone, commercial ionone, pure α-ionone, fenchone or pulegone.

Summary

1. An inexpensive method is given for the preparation of 2,4-dinitrophenylhydrazine.
2. This substance has been shown to be a suitable reagent to use in preparing crystalline derivatives of a large number of aliphatic compounds containing a carbonyl group. It may also be used with certain cyclic compounds, but the production of solid derivatives is not as general.
3. It is not as useful with α-hydroxyketones, owing to the difficulty in separating the mixtures formed.
4. A semi-micro method for determining nitrogen by the Kjeldahl method is outlined.

MONTREAL, CANADA

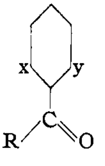
[CONTRIBUTION FROM THE CHEMICAL LABORATORY OF THE UNIVERSITY OF ILLINOIS]

STUDY OF THE POSSIBLE ISOMERISM OF CERTAIN ANALOGS OF RESOLVABLE DIPHENYL COMPOUNDS. VII[1]

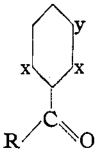
BY R. W. MAXWELL[2] AND ROGER ADAMS

RECEIVED MARCH 28, 1930 PUBLISHED JULY 3, 1930

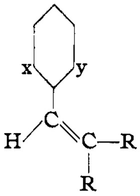
It was pointed out in a previous paper[1a] that certain substances somewhat similar to diphenyl compounds might show the phenomenon of optical isomerism which exists in the ortho tri, and tetra-substituted members of the former class of compounds. These general types are given in formulas I to VI.



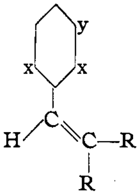
I



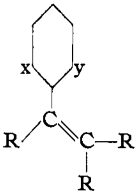
II



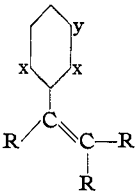
III



IV



V



VI

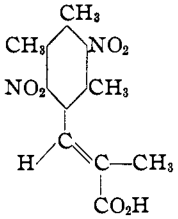
---

[1] For previous papers see (a) Hyde and Adams, THIS JOURNAL, **50**, 2499 (1923); (b) Moyer and Adams, *ibid.*, **51**, 630 (1929); (c) Stanley and Adams, *Rec. trav. chim.*, **48**, 1035 (1929); (d) Stanley and Adams, THIS JOURNAL, **52**, 1200 (1930); (e) Bock, Moyer and Adams, *ibid.*, **52**, 2054 (1930); (f) Stearns and Adams, *ibid.*, **52**, 2070 (1930).

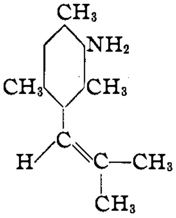
[2] This communication is a portion of an abstract of a thesis submitted by R. W. Maxwell in partial fulfilment of the requirements for the Degree of Doctor of Philosophy in Chemistry at the University of Illinois.

In the communication of Hyde and Adams,[1a] representatives of formulas I and II were prepared and shown not to be capable of resolution. In this paper compounds belonging to classes III and IV are described. Not one of them could be resolved. It is obvious then that there is in these compounds sufficient mobility of the groups around the carbon atom attached to the ring so that the ortho substituting groups have no blocking effect and free rotation between the ring and the carbon atom is not prevented. The side chain must either be flexible or extend in such a direction that interference does not take place. Several attempts to prepare compounds of types V and VI have so far met with failure. In these latter compounds, analogy to trisubstituted diphenyl compounds is most complete and there is most likelihood that optical isomerism might be possible. The group replacing the side-chain hydrogen of III and IV corresponds to the unsubstituted ortho position which may play a part in preventing free rotation.

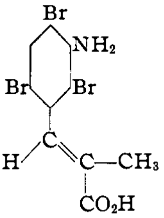
The particular compounds which were studied were α,3,4,6-tetramethyl-2,5-dinitrocinnamic acid (VII); amino-isobutenylmesitylene (VIII); and α-methyl-3-amino-2,4,6-tribromocinnamic acid (IX).



VII

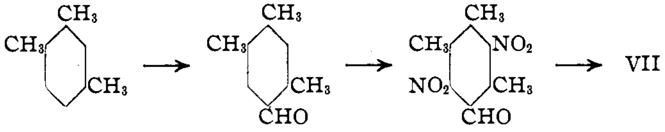


VIII

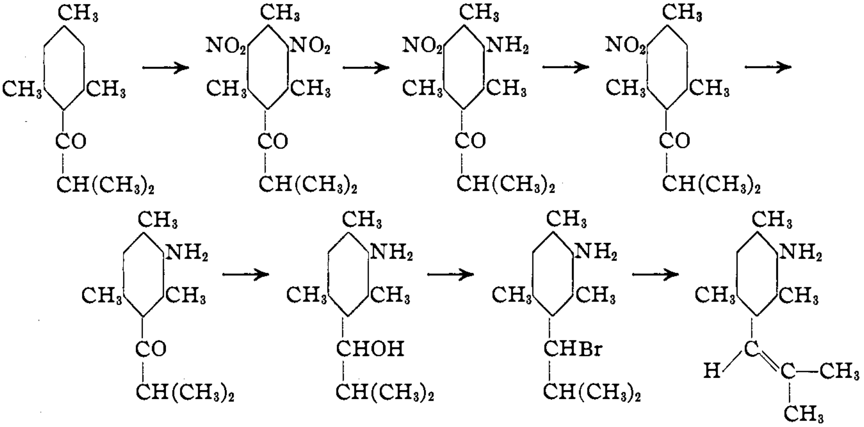


IX

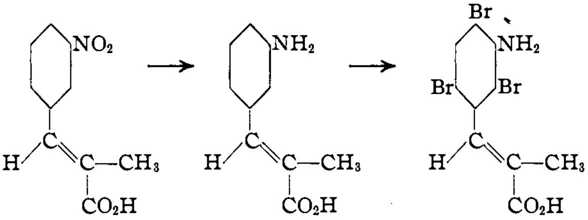
α,3,4,6-Tetramethyl-2,5-dinitrocinnamic acid was made by nitrating pseudocumenic aldehyde and then condensing with sodium propionate and propionic anhydride.



The amino-isobutenylmesitylene resulted from the following series of reactions: mesitylene, isobutyrylmesitylene, dinitro-isobutyrylmesitylene, nitro-amino-isobutyrylmesitylene, nitro-isobutyrylmesitylene, amino-isobutyrylmesitylene, isopropyl-(2,4,6-trimethyl-3-aminophenyl)-carbinol, isopropyl-(2,4,6-trimethyl-3-aminophenyl)-methyl bromide, amino-isobutenylmesitylene.



α-Methyl-3-amino-3,4,6-tribromocinnamic acid was obtained by condensation of *m*-nitrobenzaldehyde with propionic anhydride and sodium propionate, reduction of the nitro product to the corresponding amine and then bromination.



The unsuccessful attempts to prepare compounds of the types V and VI are described briefly below.

1. The condensation of 2,5-dinitro-3,4,6-trimethylacetophenone with malonic acid would not take place.

2. Ethyl α-phenyl-2,4,6-trimethylphenylacetate was readily prepared by esterification of the condensation product of α-bromophenylacetic acid with mesitylene. It was hoped to prepare a carbinol by means of excess of Grignard reagent and then dehydrate to the desired product. The Grignard condensation, however, would not take place.

3. Desyl mesitylene, (ω-phenyl-ω-(2,4,6-trimethylphenyl)-acetophenone) prepared by condensation of desyl chloride with mesitylene reacted with a large excess of phenylmagnesium bromide to give a small amount of tar but no carbinol.

4. Ethyl-α-methyl-3-nitrocinnamate readily formed a dibromide which by alcoholic potassium hydroxide gave α-methyl-β-bromo-3-nitrocinnamic acid. It was found that after reduction to the amino compound a product which was not very pure was obtained in which only two bromines entered the ring and probably only one in an ortho position.

5. Ethyl α-methyl-3-aminocinnamate was brominated in acetic acid to give ethyl α-methyl-2,4,6-tribromo-3-aminocinnamate but no further bromination occurred in the side chain.

6. 1 - (2,4,6 - trimethyl -3- *p* - nitrobenzoylaminophenyl) - 1 - bromo-2,2-dimethylethylene was produced from nitrobenzoylamino-isobutenylmesitylene by bromination and treatment of the product with pyridine. It was hoped that reduction of the nitro of the *p*-nitrobenzoyl residue might give a satisfactory resolving group but the salts formed were too readily hydrolyzed.

7. Isobutenylmesitylene gave upon bromination in carbon tetrachloride and subsequent treatment with alcoholic potassium hydroxide a dibromo compound with one bromine in the 3-position and the other in the beta position. It was found impossible, however, to introduce a salt-forming group.

8. Acetamino and carbo-ethoxyamino-isobutenylmesitylene could be converted to the β-bromo compound but it was found impossible to remove the acyl group without affecting the side chain.

Experimental

Bromo-*m*-xylene—A mixture of 106 g. of *m*-xylene, 100 g. of carbon tetrachloride and several iron nails was placed in a 500-cc. flask provided with a mercury-sealed stirrer, a dropping funnel and a condenser from which a tube led to the hood. The mixture was surrounded by an ice-bath, stirring commenced and 168 g. of bromine in 168 g. of carbon tetrachloride was added over a period of five hours. The flask was protected from the light by a towel. After standing for ten hours the red liquid was washed with water and 20% sodium hydroxide solution. The carbon tetrachloride was distilled off and the residue treated with 10 g. of sodium dissolved in 200 cc. of 95% ethyl alcohol to remove side-chain bromination products and hydrobromic acid. (The sodium ethylate was added cautiously to prevent a violent reaction.) This solution was heated to boiling for one hour and allowed to stand overnight. It was then diluted with much water and sufficient ether added to bring the oily layer to the top. The ethereal layer was washed thoroughly with water and dried with calcium chloride. The yield was 130 g. (70%) of material boiling at 200–205° (mostly 202–203°).

Pseudocumene.—This compound was prepared by a slight modification of the method of L. I. Smith[3] for the preparation of isodurene. A mixture of 20 g. of magnesium turnings, 37 g. of bromo-*m*-xylene, 1 g. of methyl iodide and 65 g. of dry ether was placed in a one-liter, three-necked flask provided with a mercury-sealed stirrer, dropping funnel and condenser. After the reaction had started 115 g. of bromo-*m*-xylene in 200 cc. of dry ether was run in at such a rate as to cause gentle refluxing. Stirring was continued for one hour after the magnesium had dissolved. Into the mixture was run 250 g. of freshly distilled dimethyl sulfate in 150 cc. of dry ether. Refluxing was continued with stirring for eight hours. The Grignard was then decomposed with dilute hydrochloric acid and water. The ether layer was washed three times with water to remove magnesium salts and then treated cautiously with sodium ethylate solution to remove any remaining dimethyl sulfate. When all danger of a vigorous reaction was over, the

---

[3] L. I. Smith, "Organic Syntheses," **1931**, John Wiley and Sons, Inc., New York, Vol. XI.

alkali and alcohol were washed out with water and the ether layer was dried over calcium chloride. The crude product was heated for three to four hours with 10 g. of sodium shavings to remove any remaining bromide, and then distilled with a free flame through a long column. The yield was 50–60 g. (50–60%), b. p. 165–170°.

2,5-Dinitro-3,4,6-trimethylcinnamic Acid.—A mixture of 4 g. of acetic anhydride, 1.2 g. of sodium acetate and 1.7 g. of 2,5-dinitro-3,4,6-trimethylbenzaldehyde (prepared from pseudocumene by the method of Gattermann[4]) was heated in a 50-cc. flask in an oil-bath at 140–150° for eight hours. The mixture was warmed with water and filtered. The residue was digested with 5% sodium carbonate solution and filtered. The two filtrates were poured into dilute hydrochloric acid solution. A slimy precipitate was formed which, after filtration and two crystallizations from dilute acetic acid, melted at 238–239° (corr.); yield, 1.2 g.

Anal. Calcd. for $C_{12}H_{12}N_2O_6$: C, 51.43; H, 4.29. Found: C, 51.10; H, 4.31.

α,3,4,6-Tetramethyl-2,5-dinitrocinnamic Acid.—A mixture of 12 g. of propionic anhydride, 3.5 g. of sodium propionate and 4.4 g. of 2,5-dinitro-3,4,6-trimethylbenzaldehyde was heated in an oil-bath at 160° for ten hours. The mixture was warmed with water until all propionic anhydride was destroyed and then made alkaline with 5% sodium carbonate. The solution was heated to boiling with decolorizing charcoal and filtered. On cooling, the sodium salt of the acid separated in golden plates. The suspension of the sodium salt was poured into dilute hydrochloric acid. A granular precipitate resulted which was crystallized first from 95% alcohol and then from glacial acetic acid. The product formed plates melting at 277–278° (corr.) and amounted to 2.75 g.

Anal. Calcd. for $C_{13}H_{14}N_2O_6$: C, 53.06; H, 4.76. Found: C, 52.70; H, 4.71.

The acid does not add bromine on long standing in carbon tetrachloride solution in the dark.

Attempt to Resolve α,3,4,6-Tetramethyl-2,5-dinitrocinnamic Acid with Strychnine.—The salt was prepared by mixing an ethyl alcohol solution of 3.550 g. of strychnine with an ethyl alcohol solution of 3.128 g. of the acid. After standing for a short time no crystals appeared, so the solution was evaporated to a small volume. Vigorous agitation with a stirring rod caused crystals to form. The salt was redissolved in 200 cc. of hot ethyl alcohol, filtered and allowed to stand. Needle-shaped crystals soon appeared. These were filtered; weight, 1 g.

Rotation. 0.4070 g. made up to 20 cc. in chloroform gave $\alpha_D = -0.728°$; $l = 1$; $[\alpha]_D^{25}$ −17.9.

The filtrate was heated to dissolve a small amount of precipitated salt, filtered and allowed to stand until another crop of crystals separated; weight, 1.7 g., $[\alpha]_D^{25}$ −16.4. Successive crops of the salt from the filtrate gave the same rotation within experimental error. The amount of salt recovered was 97% of the theoretical. The first fraction melted at 145–149° (corr.).

Anal. Calcd. for $C_{34}H_{36}O_8N_4$: C, 65.0; H, 5.8. Found: C, 64.2; H, 6.1.

A chloroform solution of the salt was extracted with ammonium hydroxide. The ammonium salt solution so obtained was washed twice with chloroform and the rotation determined. The value obtained was zero.

Attempt to Resolve α,3,4,6-Tetramethyl-2,5-dinitrocinnamic Acid with Morphine.—The salt was prepared by mixing a methyl alcohol solution of 1.41 g. of morphine with a methyl alcohol solution of 1.37 g. of the acid. The solvent was evaporated from a steam-bath, the gummy residue dissolved in 35 cc. of a mixture of 70 parts of ethyl acetate and 30 parts of 95% ethyl alcohol and allowed to stand. The salt crystallized out in

---

[4] Gattermann, *Ann.*, **347**, 375 (1906).

very stout needles. It was separated into fractions by filtering off and washing the crystals and allowing the filtrate and washings to stand until crystals formed again. The results of the fractionation are given below.

I. Weight 1.3 g., 0.097 g. made up to 20 cc. in 95% ethyl alcohol gave $\alpha_D = -0.590°$; $l = 1$; $[\alpha]^{25}_D$ −60.8; M. p., 178–184° (corr.).

The successive fractions all gave the same rotation within experimental error. The first crystals obtained weighed 0.65 g. and gave $[\alpha]^{25}_D$ −61.8. The amount of salt recovered was 93.5% of the theoretical.

Anal. Calcd. for $C_{30}H_{33}O_9N_3$: C, 62.1; H, 5.70. Found: C, 61.6; H, 5.74.

Decomposition of the salt was effected by dissolving 0.3 g. in 10 cc. of hot 95% ethyl alcohol and pouring this solution into dilute hydrochloric acid. The acid separated as a fine powder. It was filtered by suction, washed with dilute hydrochloric acid and dissolved in 20 cc. of dilute ammonium hydroxide. The solution was optically inactive.

Attempt to Resolve α,3,4,6-Tetramethyl-2,5-dinitrocinnamic Acid with Brucine.—The salt was prepared by mixing an ethyl alcohol solution of 1.176 g. of the acid with an ethyl alcohol solution of 1.858 g. of crystallized brucine. The solution was evaporated to 100 cc. and allowed to stand. The salt crystallized as stout needles. These were filtered, washed with 95% ethyl alcohol and the filtrate allowed to stand until a new crop of crystals had formed. This was repeated until all of the compound had been deposited.

I. Weight, 1.8 g. This fraction was separated into an insoluble fraction, (a), weight, 0.75 g. 0.2215 g. made up to 15 cc. in ethyl acetate gave $\alpha_D = -0.347°$; $l = 1$; $[\alpha]^{25}_D$ −23.5, and a soluble fraction (b), $[\alpha]^{25}_D$ −18.4.

II. Weight, 0.5 g. $[\alpha]^{25}_D$ −22.7.

III. 0.5 g. (mother liquor), $[\alpha]^{25}_D$ −31.2.

The amount of recovered salt was 92.4% of the theoretical. Fraction (a) melted at 129–132° (corr.).

Anal. Calcd. for $C_{36}H_{40}O_{10}N_4 \cdot 2H_2O$: C, 59.64; H, 6.12. Found: C, 59.47; H, 6.07.

Anal. Subs., 0.6025: loss on heating at 110° for three hours, 0.0342. Calcd. for $C_{36}H_{40}O_{10}N_4 \cdot 2H_2O$: H_2O, 5.2. Found: H_2O, 5.8.

The salt was decomposed by dissolving it in 10 cc. of warm ethyl alcohol and pouring this solution into dilute hydrochloric acid. The acid separated as a fine, white precipitate. It was washed with dilute hydrochloric acid, dissolved in dilute ammonium hydroxide and the rotation determined. The value obtained was zero.

Isobutyrylmesitylene.—Essentially the method of Klages[5] was used. A mixture of 107 g. of isobutyryl chloride, 120 g. of mesitylene and 500 cc. of dry carbon disulfide was placed in a one-liter, three-necked flask equipped with a mercury-sealed stirrer and a tube to carry off hydrogen chloride fumes. The flask was surrounded by an ice–salt mixture. To this was added 135 g. of anhydrous aluminum chloride in 10-g. portions over a period of one hour and fifteen minutes. After another hour and fifteen minutes the solvent was distilled off and the residue poured onto a mixture of ice and hydrochloric acid. The product was a brown oil. It was taken up in ether, washed with water and dilute sodium hydroxide, and dried with anhydrous magnesium sulfate. The product boiled at 122–126° at 7 mm. and amounted to 140 g. (75%).

Dinitro-isobutyrylmesitylene.—Twenty-eight grams of isobutyrylmesitylene was allowed to flow slowly into 200 g. of nitric acid (sp. gr. 1.52) cooled to −10°. The time of addition was ten minutes and the acid temperature was not allowed to pass 15°.

---

[5] Klages, *Ber.*, 37, 928 (1904).

Stirring was continued for five minutes more, after which the reaction mixture was poured into ice water. A longer time of contact with the acid was undesirable because of danger of side-chain nitration. The product precipitated as heavy crystals. It was filtered by suction, dried and recrystallized from 95% ethyl alcohol to a constant melting point 137.5–138.5°. The yield was 28 g.

Anal. Calcd. for $C_{13}H_{16}N_2O_5$: C, 55.7; H, 5.76. Found: C, 55.8; H, 5.86.

Nitro-amino-isobutyrylmesitylene.—To 250 g. of dinitro-isobutyrylmesitylene dissolved in 900 cc. of 95% ethyl alcohol was added a solution of 275 g. of crystallized sodium sulfide and 37 g. of sulfur in 750 cc. of water. The mixture was refluxed with stirring for six hours. It was then poured into four liters of water. The product separated as an oil which crystallized as the solution cooled. It was filtered and washed with water. The crude product was dissolved in hot 3 *N* hydrochloric acid and the solution filtered. On cooling, the hydrochloride separated as yellow plates. The free base was obtained by neutralization with ammonium hydroxide either from the solution of the hydrochloride or from the solid. It separated as an oil which soon crystallized in bright yellow needles. After purification from 95% ethyl alcohol it melted at 98–99° (corr.). The yield was 185 g.

Anal. Calcd. for $C_{13}H_{18}N_2O_3$: C, 62.4; H, 7.26. Found: C, 62.5; H, 7.26.

Nitro-isobutyrylmesitylene.—A solution was made of 100 g. of crude nitro-amino-isobutyrylmesitylene in a warm mixture of 90 cc. of concentrated sulfuric acid and 460 cc. of 95% ethyl alcohol. A 3-liter, three-necked flask equipped with a mercury-sealed stirrer, reflux condenser and dropping funnel was used. The solution was cooled to below 10° and 40 g. of sodium nitrite in 70 cc. of water allowed to run in slowly, care being taken that the temperature did not pass above 10°. Stirring was continued for twenty minutes after addition of the sodium nitrite in order to complete the diazotization. Ten grams of copper bronze freshly washed with ether was then stirred into the mixture. An evolution of gas commenced which proceeded for about thirty minutes. The flask was then placed upon a steam cone, warmed cautiously at first and then refluxed for half an hour. The boiling point was very low because of the acetaldehyde formed.

The contents of the flask were poured into two volumes of water, whereupon the product separated as a heavy brown oil. It was extracted with ether. The product boiled at 157–158° at 7 mm. and amounted to 31 g. A considerable quantity of tar always remained behind.

Anal. Calcd. for $C_{13}H_{17}NO_3$: C, 66.4; H, 7.28. Found: C, 65.9; H, 7.25.

Amino-isobutyrylmesitylene.—A mixture of 50 g. of mossy tin, 60 cc. of 95% ethyl alcohol and 32 g. of nitro-isobutyrylmesitylene was placed in a 500-cc. round-bottomed flask equipped with a reflux condenser. One hundred and twenty cc. of concentrated hydrochloric acid was added at such a rate that the temperature of the flask was kept just below the boiling point. After the reaction had apparently ceased, the contents of the flask were refluxed for fifteen minutes. There was no sign of hydrogen evolution during the reaction. The alcoholic solution was diluted with 300 cc. of water made alkaline with ammonia and filtered by suction. The filter cake of tin oxides was placed in a beaker, warmed with 250 cc. of 95% ethyl alcohol and filtered. This process was repeated and the filter cake washed thoroughly with warm alcohol. The alcoholic filtrate was added to one and one-half volumes of water and the precipitated oil separated from the water by extraction with ether. The product amounted to 24 g. and boiled at 167° at 7 mm.

Anal. Calcd. for $C_{13}H_{19}NO$: C, 76.10; H, 9.27. Found: C, 75.69; H, 9.24.

Isopropyl (2,4,6-Trimethyl-3-aminophenyl) Carbinol.—To 41 g. of amino-isobutyrylmesitylene in 300 cc. of absolute ethyl alcohol in a 500-cc. round-bottomed flask equipped with a reflux condenser was added through the condenser 18.5 g. of sodium metal cut in small strips at such a rate that the alcohol refluxed gently. Toward the end of the reaction and for one hour after the last addition of the sodium the mixture was heated on a steam-bath. The solution was poured into two volumes of water. The product separated as a white, crystalline solid. It was extracted from the water with ether. The crystalline product was washed thoroughly with low-boiling petroleum ether. After recrystallizations from ligroin (b. p. 60–115°), the melting point was 118.5–119.5° (corr.). The yield was 22 g.

Anal. Calcd. for $C_{13}H_{21}NO$: C, 75.4; H, 10.2. Found: C, 75.1; H, 10.2.

Amino-isobutenylmesitylene.—A mixture of 48 g. of isopropyl-2,4,6-trimethyl-3-aminophenyl carbinol in 450 cc. of 40% hydrobromic acid was heated to boiling for several hours. The crystals which formed shortly after the reaction started melted, floated to the surface and resolidified in needles. Refluxing was continued for two hours, after which the contents of the flask were cooled and the product filtered. Without further purification the solid hydrobromide was mixed with a solution of 90 g. of potassium hydroxide in 500 cc. of 95% ethyl alcohol. An immediate precipitation of potassium bromide took place. The mixture was refluxed for half an hour and then poured into two volumes of water. A light oil separated. It was extracted from the water with ether. The product boiled at 127–128° at 6 mm. and amounted to 35 g.

Anal. Calcd. for $C_{13}H_{19}N$: C, 82.5; H, 10.1. Found: C, 82.2; H, 10.1.

Attempt to Resolve Amino-isobutenylmesitylene with *d*-Camphorsulfonic Acid.—The salt was formed by mixing 3.8 g. of the amine in 50 cc. of chloroform with 4.64 g. of *d*-camphorsulfonic acid. The acid dissolved slowly as the liquid was boiled. The solution was evaporated to about 10 cc. and 150 cc. of ligroin (b. p. 65–115°) added. This solution was allowed to stand where it could evaporate very slowly. After twenty-four hours silky needles were deposited but the solution was becoming very dark. The crystals were filtered and washed with a solution of 10 cc. of chloroform in 90 cc. of ligroin.

I. Weight, 1.0 g. 0.0985 g. made up to 15 cc. in chloroform gave $\alpha_D = +0.208°$; $l = 1$; $[\alpha]^{25}_D + 32.0$.

The filtrate was allowed to stand as before. The solution became even more tarry. A second crop of crystals soon deposited.

II. Weight, 1.2 g. $[\alpha]^{25}_D$ +32.3.

The same procedure was carried out as before.

III. Weight, 1.3 g. $[\alpha]^{25}_D$ +27.3. The filtrate was now so dark and tar-like that no more crystals could be obtained. A portion of salt which had not been subjected to fractionation, however, gave $[\alpha]^{25}_D$ +34.2. The melting point of fraction I was 93–102° (corr.).

Anal. (Parr Bomb). Calcd. for $C_{23}H_{35}O_4SN$: S, 7.6. Found: S, 7.3.

The salt was decomposed by dissolving 0.25 g. in chloroform and extracting the solution with dilute ammonia. The resulting chloroform solution was optically inactive.

Attempt to Resolve Amino-isobutenylmesitylene with *d*-Oxymethylenecamphor.—A mixture of 1.36 g. of amino-isobutenylmesitylene and 1.5 g. of *d*-oxymethylenecamphor in 10 cc. of 95% ethyl alcohol was heated on a steam-bath for half an hour. To this was added 50 cc. of water containing 10 cc. of dilute sodium hydroxide to precipitate the condensation product and to dissolve excess *d*-oxymethylenecamphor. The product separated as a gum. On warming the alkaline mixture on a steam cone, the gum floated to the surface of the liquid and crystallized. The crystals were filtered off, washed and recrystallized from methyl alcohol. The following fractions were obtained.

I. Weight, 1.12 g., m. p. 176–180°. 0.1284 g. made up to 15 cc. in chloroform gave $\alpha_D = +4.7°$; $l = 1$; $[\alpha]^{25}_D +190.4$.

II. Weight, 0.92 g. $[\alpha]^{25}_D +184.1$.

III. Weight, 0.25 g. $[\alpha]^{25}_D +200.0$.

Anal. Calcd. for $C_{24}H_{33}ON$: C, 82.0; H, 9.47. Found: C, 82.3; H, 9.46.

As the compound changed in rotation on standing, all readings were taken as nearly as possible at exactly ten minutes after the solution was made. The high rotation of fraction III is probably due to this. The amount of product recovered was 90.6% of the theoretical.

Attempts to decompose the condensation product with bromine in carbon tetrachloride followed by hydrolysis gave tarry products.

Acetamino-isobutyrylmesitylene.—A mixture of 8 g. of amino-isobutenylmesitylene and 30 cc. of acetic anhydride was allowed to stand for half an hour, after which the acetic anhydride was decomposed with cold water. After recrystallization from dilute alcohol the compound melts at 114–115°, resolidifies and remelts at 129–30° (corr.).

Anal. Calcd. for $C_{15}H_{21}NO$: C, 77.5; H, 9.16. Found: C, 77.3; H, 9.04.

α-Methyl-3-nitrocinnamic Acid.—The acid was prepared by a modification of the method of v. Miller and Rohde.[6] A mixture of 75 g. of *m*-nitrobenzaldehyde, 98 g. of propionic anhydride and 48 g. of sodium propionate was heated at 170° in an oil-bath for five hours. The reaction mixture was poured into water and saturated sodium carbonate solution added to strong alkalinity. The tarry liquid was boiled with decolorizing charcoal for ten minutes and then filtered. The alkaline liquid was poured into dilute hydrochloric acid. A white, curdy precipitate resulted. This was filtered by suction and allowed to dry overnight. The crude acid was crystallized once from 85% ethyl alcohol. The product consisted of white needles melting at 199.5–200.5° (corr.) and was used without further purification; yield, 70 g.

Ethyl α-Methyl-3-nitrocinnamate.—A mixture of 20 g. of α methyl-3-nitrocinnamic acid, 200 cc. of absolute alcohol and 6 g. of concentrated sulfuric acid was refluxed overnight. The solution was poured into two volumes of water. A heavy oil separated which did not crystallize on standing. It was extracted with ether. The product boiled at 197° at 11 mm. and amounted to 18 g.

Anal. Calcd. for $C_{12}H_{13}NO_4$: C, 61.3; H, 5.58. Found: C, 61.4; H, 5.59.

α-Methyl-3-amino-2,4,6-tribromocinnamic Acid.—A mixture of 20 g. of α methyl-3-nitrocinnamic acid, 25 cc. of water, 100 g. of iron powder and 1 cc. of concentrated hydrochloric acid was placed in a 500-cc. flask and warmed upon a steam-bath for four hours. The contents of the flask were then made alkaline with ammonia, water was added and the mixture filtered. The residue on the filter was very thoroughly washed with water. The clear filtrates were poured into dilute hydrochloric acid, whereupon a slight precipitate separated. This was removed by filtration. To the acid solution was added 10% bromine in concentrated hydrochloric acid until a yellow color persisted. A curdy, white precipitate settled out. The precipitate of bromo acid was filtered by suction, dried in the air and recrystallized three times from 90% ethyl alcohol. Twenty grams of product melting at 208–209° (corr.) was obtained.

Anal. Calcd. for $C_{13}H_8NO_2Br_3$: Br, 58.0. Found: Br, 57.7.

Attempt to Resolve α-Methyl-3-amino-2,4,6-tribromocinnamic Acid with Strychnine.—To a solution of 4.14 g. of the acid in 25 cc. of warm methyl alcohol was added a solution of 1.67 g. of strychnine dissolved in 250 cc. of hot methyl alcohol. The solution was evaporated to 125 cc., filtered and allowed to stand until crystals were deposited. These were filtered by suction and washed well with methyl alcohol.

---

[6] Miller and Rohde, *Ber.*, **23**, 1900 (1890).

I. Weight, 1.8 g. 0.2817 g. made up to 15 cc. in chloroform gave $\alpha_D = -0.451°$; $l = 1$; $[\alpha]_D^{25}$ −24.0.

To the filtrate was added 1.67 g. of strychnine dissolved in 250 cc. of methyl alcohol. The solution was again evaporated to 125 cc., filtered to remove a very fine precipitate which had formed and allowed to stand until another crop of crystals had appeared. The crystals were removed by filtration and the filtrate was allowed to stand until another crop was obtained.

II. Weight, 2.2 g. $[\alpha]_D^{25}$ −22.6.

III. Weight, 2.0 g. $[\alpha]_D^{25}$ −19.2.

IV. (Mother liquor), weight 1.3 g. $[\alpha]_D^{20}$ −20.6.

The amount of salt recovered was 98% of the theoretical. The melting point of fraction I was 123–127° (corr.).

Anal. Calcd. for $C_{31}H_{30}O_4N_3Br_3$: Br, 32.1. Found: Br, 31.7.

The salt was decomposed by dissolving a weighed portion in chloroform and extracting the chloroform with ammonium hydroxide. The solution of the ammonium salt was washed once with chloroform, and the rotation determined. The value obtained was zero.

Attempt to Resolve α-Methyl-3-amino-2,4,6-tribromocinnamic Acid with Brucine.—A mixture of 3.51 g. of crystallized brucine and 3.12 g. of α-methyl-3-amino-2,4,6-tribromocinnamic acid in 50 cc. of hot ethyl alcohol was evaporated to dryness on a steam cone, 300 cc. of water added and the mixture heated to boiling. The salt became crystalline under this treatment. The hot solution was filtered. Upon cooling 0.6 g. of white plates was deposited.

0.2953 g. made up to 15 cc. in ethyl acetate gave $\alpha_D = -0.55$; $l = 1$; $[\alpha]_D^{25}$ −28.2.

The residue from the water extraction was dissolved in 50 cc. of hot 95% ethyl alcohol and allowed to stand until crystals had appeared.

II. Weight, 4.0 g. $[\alpha]_D^{25}$ −30.4. This fraction was separated into three smaller fractions having specific rotations of −27.7, −31.2 and −31.2. A second crop of crystals was obtained from the filtrate from II.

III. Weight, 0.5 g. $[\alpha]_D^{25}$ −27.8. The mother liquor was evaporated to dryness.

IV. Weight, 1.5 g. $[\alpha]_D^{25}$ −39.4. The amount of salt recovered was 99.5% of the theoretical. The melting point of fraction I was 143–148° (corr.).

Anal. Calcd. for $C_{33}H_{34}O_6N_3Br_3$: Br, 29.7. Found: Br, 29.7.

The salt was decomposed by dissolving 0.25 g. in 10 cc. of 95% ethyl alcohol and pouring the solution into dilute hydrochloric acid. The precipitated acid was filtered washed with dilute hydrochloric acid, redissolved in dilute ammonium hydroxide, made up to 20 cc. and the rotation determined. The value found was zero.

Attempt to Resolve α-Methyl-3-amino-2,4,6-tribromocinnamic Acid with Quinine.—The quinine salt was prepared by dissolving 4.14 g. of the acid and 3.24 g. of quinine in 50 cc. of hot ethyl acetate and filtering. The filtrate was evaporated to 25 cc. and allowed to stand. Fine needles separated.

I. Weight, 0.7 g. 0.1750 g. made up to 15 cc. in ethyl acetate gave $\alpha_D = -0.69°$; $l = 1$; $[\alpha]_D^{25}$ −59.4.

The filtrate was set aside to crystallize again. This procedure was repeated until the salt had all separated. The six successive fractions obtained all gave rotations within experimental error of the first fraction. The amount of recovered salt was 93% of the theoretical. Fraction I melted at 208–209° (corr.).

Anal. Calcd. for $C_{30}H_{32}O_4N_3Br_3$: Br, 32.5. Found: Br, 32.0.

Decomposition of the salt was effected by shaking 0.25 g. of it in chloroform solution with dilute ammonium hydroxide and washing the ammoniacal solution twice with chloroform. The rotation of the salt so obtained was zero.

2,4,5-Trimethylacetophenone.—A mixture of 36 g. of pseudo-cumene, 90 g. of anhydrous aluminum chloride and 120 cc. of dry carbon disulfide was placed in a 1-liter, three-necked flask equipped with a reflux condenser, dropping funnel and mercury-sealed stirrer. The mixture was heated on a steam cone until gentle refluxing began and then 25 g. of acetic anhydride was allowed to flow in slowly from the dropping funnel. The time of addition was one hour. Refluxing was continued for another hour, after which the solvent was distilled from a steam-bath. The residue was poured into a mixture of ice and hydrochloric acid and the product extracted with ether. The product boiled at 121–124° at 5 mm.; yield, 36 g. (75%).

2,5-Dinitro-3,4,6-trimethylacetophenone.—Fifty grams of fuming nitric acid (sp. gr. 1.51) was cooled to $-15°$ and 5 g. of 3,4,6-trimethylacetophenone added slowly with rapid stirring. Stirring was continued for ten minutes and then the mixture was poured into ice water. The product separated as a heavy oil. The oil was separated from the water by decantation and crystallized on standing. After several recrystallizations from 95% ethyl alcohol, it melted at 120–21° (corr.); yield, 1.4 g.

Anal. Calcd. for $C_{11}H_{12}O_5N_2$: C, 52.38; H, 4.77. Found: C, 52.25, 52.19; H, 4.40, 4.94.

Attempts to condense 2,5-dinitro-3,4,6-trimethylacetophenone with malonic acid by Knoevenagel's[7] method for acetophenone were unsuccessful.

α-Bromophenylacetic acid.—A mixture of 152 g. of mandelic acid, 60 g. of concentrated sulfuric acid and 350 g. of 48% hydrobromic acid was refluxed for four hours. The mixture first formed a liquid which floated on the surface of the acid but which soon became heavier and sank to the bottom. The product was extracted from the reaction mixture with 400 cc. of dry ether. The crude product after removal of solvent was a viscous, dark, clear oil. It was used directly for the next reaction.

α-(2,4,6-Trimethyl)-phenylacetic Acid.—The α-bromophenylacetic acid from 1 mole of mandelic acid was placed in a 1-liter, three-necked flask equipped with a dropping funnel, mercury-sealed stirrer and reflux condenser. With it was mixed 400 cc. of dry carbon disulfide and 120 g. of mesitylene. Stirring was commenced and 135 g. of anhydrous aluminum chloride added in 10-g. portions in one hour. During this part of the reaction the flask was cooled by an ice-bath. Stirring was continued for another hour. The solvent was distilled from a steam-bath and the residue poured into a mixture of crushed ice and hydrochloric acid. The product separated as a viscous red-brown oil which soon crystallized. The crystals were filtered off, dissolved in benzene and the benzene extracted with dilute sodium hydroxide. The alkaline extract was allowed to run into dilute hydrochloric acid. The acid separated as a crystalline mass. It was filtered off, dissolved in hot 60% ethyl alcohol, decolorized with norite and set aside to crystallize. After several recrystallizations from 60% ethyl alcohol the melting point was 172–172.5° (corr.). The yield was 68 g. (27%) of white needles.

Anal. Calcd. for $C_{17}H_{18}O_2$: C, 80.31; H, 7.14. Found: C, 80.51; H, 7.12.

Ethyl α-(2,4,6-Trimethylphenyl)-phenylacetate.—Forty-three grams of α-(2,4,6-trimethylphenyl)-phenylacetic acid was dissolved in 250 cc. of absolute ethyl alcohol to which 2 cc. of concentrated sulfuric acid had been added. The mixture was refluxed for ten hours. The alcohol was then distilled off, the residue dissolved in low-boiling petroleum ether and the solution washed twice with water to remove sulfuric acid. After drying with anhydrous magnesium sulfate, the solvent was distilled from a steam-bath and the residue vacuum distilled. The ester boiled at 180–183° at 4 mm.; yield, 38 g. (81%).

Anal. Calcd. for $C_{19}H_{22}O_2$: C, 80.85; H, 7.79. Found: C, 80.45; H, 7.69.

---

[7] Knoevenagel, German Patent 162,281.

Ethyl α-(2,4,6-trimethylphenyl)-phenylacetate when treated with a large excess of phenylmagnesium bromide in the usual way gave a small quantity of an uncrystallizable tar but mostly unchanged material.

Desyl Chloride (Phenylbenzoylchloromethane.)—A mixture of 106 g. of benzoin and 72 g. of thionyl chloride was placed in a 500-cc. flask equipped with a reflux condenser. A reaction soon commenced. The mixture was allowed to stand without heating for two hours, at which time the reaction had almost stopped. The flask was then warmed on a steam cone for half an hour. The light brown liquid when cool was poured into water to decompose excess thionyl chloride. The product was extracted with ether. After washing and drying, the solvent was removed and the crude material used in the next reaction.

Desylmesitylene.—A mixture of 75 g. of mesitylene, 300 cc. of carbon disulfide and the crude desyl chloride from 0.5 mole of benzoin was placed in a 1-liter, three-necked flask equipped with a reflux condenser and mercury-sealed stirrer. The mixture was cooled by an ice-bath. Seventy-five grams of anhydrous aluminum chloride was added in 10-g. portions over a period of one hour. The solvent was distilled from a steam-bath and after cooling the residue was poured into a mixture of ice and hydrochloric acid. After standing for twelve to fifteen hours, the oily upper layer solidified. It was filtered off, dissolved in glacial acetic acid, boiled for fifteen minutes with norite, filtered and set aside to crystallize. After recrystallization to constant melting point from glacial acetic acid, the product melted at 111–112° (yield 63 g.).

Anal. Calcd. for $C_{23}H_{22}O$: C, 87.90; H, 7.01. Found: C, 87.53; H, 7.04.

Ethyl α-Methyl-3-nitrocinnamate Dibromide.—A mixture of 30 g. of ethyl α-methyl-3-nitrocinnamate and 125 cc. of glacial acetic acid was mixed with 125 cc. of glacial acetic acid containing 20 g. of bromine. After standing in the dark at room temperature for seventy-two hours, almost all of the bromine color had disappeared. The solution was poured into 1500 cc. of water and allowed to stand. Fine crystals separated slowly. After thirty-six hours these were filtered by suction. The product melted at 68–69° (corr.) after several recrystallizations from ligroin.

Anal. (Parr Bomb). Calcd. for $C_{12}H_{13}NO_4Br_2$: Br, 43.6. Found: Br, 43.4.

α-Methyl-β-bromo-3-nitrocinnamic Acid.—Sixteen grams of ethyl α-methyl-3-nitrocinnamate dibromide was dissolved in 100 cc. of 95% ethyl alcohol and added to a solution of 8 g. of potassium hydroxide in 60 cc. of 95% ethyl alcohol. A precipitation of potassium bromide took place at once. The mixture was refluxed until completely water soluble (two to five minutes). The solution was poured into dilute hydrochloric acid. The acid separated in long silky needles, which after crystallization from benzene melted at 131.5–132.5° (yield, 10 g.).

Anal. (Parr Bomb). Calcd. for $C_{10}H_8O_4NBr$: Br, 28.0. Found: Br, 28.2.

Reduction with iron and water and bromination of the product gave an impure mixture.

Ethyl α-Methyl-2,4,6-tribromo-3-aminocinnamate.—A mixture of 12 g. of ethyl α-methyl-3-nitrocinnamate and 75 g. of iron powder was treated with sufficient water to form a thin paste. To this was added 0.5 cc. of concentrated hydrochloric acid and the mixture warmed on a steam cone under a reflux condenser for three hours. The reduction proceeded very rapidly at first, enough heat being generated to cause refluxing. The iron suspension was made faintly alkaline with ammonia, extracted thoroughly with warm alcohol and the extract filtered. The filtrate was poured into cold water. A heavy oil separated. It was removed from the water by ether extraction. The ether was washed, dried and distilled from a steam-bath and the residue used in the next reaction without further purification; yield, 10 g.

The crude ester was dissolved in 75 g. of glacial acetic acid and mixed with 32 g. of bromine in 75 g. of glacial acetic acid. It was necessary to cool the solution as the bromine was added. The mixture was allowed to stand in the dark for three days. A mass of white crystals separated in the meantime. These were filtered and the filtrate poured into cold water. A gum separated which crystallized slowly. The white residue on the filter was recrystallized several times from 95% ethyl alcohol. The same product was obtained upon crystallizing the gummy precipitate. The compound, when pure, melted at 107.5–108° (corr.).

Anal. (Parr Bomb). Calcd. for $C_{10}H_8O_2NBr_3$: Br, 54.3. Found: Br, 54.7.

1-(2, 4, 6-Trimethyl-3-*p*-nitrobenzoylaminophenyl)-1-bromo-2, 2-dimethylethylene.—A mixture of 3.5 g. of amino-isobutenylmesitylene and a solution of 5 g. of *p*-nitrobenzoyl chloride in 25 cc. of benzene was allowed to stand for two hours. Dilute sodium hydroxide was then added and the benzene boiled off from a hot-plate. The product was left as a gum which soon crystallized. After one crystallization from alcohol it melted at 154–155° (uncorr.).

The product from the above reaction was dissolved in 100 cc. of glacial acetic acid and 32 g. of a 10% solution of bromine in glacial acetic acid allowed to flow in over a period of fifteen minutes with rapid stirring. A faint trace of hydrogen bromide was evolved. The solution was allowed to stand for ten minutes and was then poured into two volumes of water and allowed to stand overnight. The precipitate coagulated completely by that time. The product was filtered by suction, dried in the air, dissolved in 75 cc. of pyridine and refluxed for three hours. (The pyridine might be replaced by alcoholic alkali if the theoretical quantity were used. In one experiment an excess of alcoholic alkali caused tar formation.) The solution was poured into 500 cc. of water. A white cloudiness appeared and the solution began to deposit droplets which crystallized slowly. The mixture was stirred for four hours to aid crystallization and then the crystals were filtered by suction, washed well with water and dried. The crude product weighed 4 g. It was recrystallized from 95% ethyl alcohol and gave needles melting at 203.5–204.5° (corr.).

Anal. (Parr Bomb). Calcd. for $C_{20}H_{21}N_2O_3Br$: Br, 19.2. Found: Br, 18.9.

2,4,6-Trimethylphenylisopropyl Carbinol.—This compound was prepared by the reduction of the ketone by means of sodium and absolute alcohol. It boiled at 126° at 5 mm. (yield, 53 g., from 70 g. of ketone).

Isobutenylmesitylene.—This compound has been prepared by Klages[5] by decomposing 2,4,6-trimethylphenylisopropylmethyl chloride with pyridine. A mixture of 94 g. of 2,4,6-trimethylphenylisopropyl carbinol and 20 cc. of toluene was placed in a 200-cc., round-bottomed flask equipped with a reflux condenser. The flask was placed in an ice-bath and 55 g. of phosphorus tribromide allowed to run in slowly. After standing for one hour with occasional shaking and then heating for one hour on the steam cone, it was cooled and poured into cold water to decompose any phosphorus tribromide. The product was extracted with ether. After removing the solvent, 80 g. of potassium hydroxide in 450 cc. of 95% ethyl alcohol was added and the mixture refluxed for one hour. The solution became red and much potassium bromide separated. The alcohol suspension was poured into water and the product extracted with ether. The solvent was distilled from a steam cone and the olefin vacuum distilled. It boiled at 103–106° at 5 mm. (yield, 75 g.).

1-(2,4,6-Trimethyl-3-bromophenyl)-1-bromo-2,2-dimethylethylene.—A solution of 45 g. of carbon tetrachloride was allowed to flow into 29 g. of isobutenylmesitylene (thirty minutes) dissolved in 29 g. of carbon tetrachloride and cooled by an ice-bath. The mixture was stirred vigorously. After two and one-half hours a small amount of bromine had not reacted. The liquid was washed with water, dilute sodium hydroxide and then twice more with water. The bulk of the solvent was distilled from a steam-bath and the last traces from an oil-bath. At about 160° bath temperature, hydrogen bromide fumes were evolved copiously. The residue in the flask was added to a solution of 30 g. of potassium hydroxide dissolved in 175 cc. of 95% ethyl alcohol and refluxed for one hour. The reaction mixture was poured into cold water and the product extracted with ether. After purification by distillation, 27 g. of bromo compound boiling at 140–145° at 4 mm. was obtained.

Anal. (Parr Bomb). Calcd. for $C_{13}H_{16}Br_2$: Br, 48.2. Found: Br, 47.8.

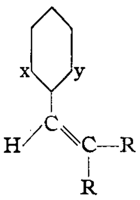
The mono Grignard reagent formed from the above compound, when treated with carbon dioxide, gave an acid which did not crystallize.

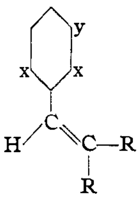
Amino-isobutenylmesitylene when brominated in either glacial acetic acid or carbon tetrachloride gave mostly tarry products. The acetylamino and carbo-ethoxyamino derivatives brominated in a satisfactory manner and gave a good-looking product upon removal of hydrogen bromide by alcoholic potassium hydroxide. It was found impossible, however, to remove the protecting group without affecting the unsaturated side chain.

Summary

1. α,3,4,6-Tetramethyl-2,5-dinitrocinnamic acid, amino-isobutenyl mesitylene and α-methyl-3-amino-2,4,6-tribromocinnamic acid have been prepared. They could not be resolved.

2. These substances are representative of the following two types:





It may be concluded that these compounds stereochemically do not resemble diphenyl compounds.

URBANA, ILLINOIS