0.2% or 0.005° for deuterium; 0.3% or 0.007° for tritium. Other sources of error, namely, the radioactive heat (amounting to 8.63 × 10^{-5} watt/std. cc. of gas[19]) and possible rapid equilibration between ortho and para forms of tritium seem to be inapplicable in the present measurements.

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[19] G. H. Jenks, *J.* A. Ghormley and F. H. Sweeton, *Phys. Rev.*, **76**, 701 (1949).

Summary

1. The vapor pressures of hydrogen, deuterium and tritium have been measured up to three atmospheres.

2. Triple points and heats of vaporization and of sublimation have been derived from the vapor pressures.

RECEIVED JULY 31, 1950

NOTES

Simple Preparation of Optically Active Secondary Alcohols[1]

BY AKSEL A. BOTHNER-BY

It has been well established that reduction of some classes of organic compounds by lithium aluminum hydride is accomplished by transfer of a hydride ion to an electrophilic center of the molecule being reduced.[2] The nature of the ions or neutral molecules donating the hydride ion has not been determined, but a reasonable hypothesis is that in the reduction of a ketone, the forms $Al(OR)_mH_n$ are present, where –OR represents the alkoxyl group derived from the ketone, and *m* and *n* are small integers. If this is the case, partial reaction of lithium aluminum hydride with *d*-camphor would give a species capable of asymmetric reduction of ketones. Similar asymmetric reductions have been reported by Vavon and co-workers,[3] Mosher and LaCombe,[4] and Doering.[5] Reductions of methyl ethyl ketone and pinacolone with lithium aluminum hydride–*d*-camphor have been performed. Table I shows for three runs the ketone reduced, the number of moles of lithium aluminum hydride, *d*-camphor and ketone used, and the boiling point and optical activity of the alcohol obtained.

TABLE I

Ketone reduced	Moles $LiAlH_4$	Moles *d*-Camphor	Moles Ketone	Alcohol B.p., °C.	Alcohol $[\alpha]^{25}\text{D}$
Methyl ethyl	0.100	0.200	0.200	99.5–100	+2.50
Pinacolone	.118	.118	.354	118–120	+0.04
Pinacolone	.111	.222	.222	118–120	+0.82

Experimental

The reductions were in each case similar to the following:

Optically Active *s*-Butyl Alcohol.—To a stirred solution of 3.80 g. of lithium aluminum hydride in 300 ml. of ether under nitrogen, was added dropwise a solution of 30.0 g. of *d*-camphor in 50 ml. of ether. Addition required one-half hour. A mixture of 15.0 ml. of methyl ethyl ketone and 50 ml. of ether was then dropped in over one-half hour, followed immediately by 100 ml. of 17% HCl. Stirring was continued until two clear layers were present. The layers were separated, and the ether layer, after drying with calcium chloride pellets, was fractionated through a small Vigreux column. The *d*-isoborneol solidified in the pot. The distillate was refractionated twice to obtain 10.0 g. of *s*-butyl alcohol; $n^{25}\text{D}$ 1.3975, b.p. 97–100°, $d^{20}{}_4$ 0.8084.

A subsequent fractionation through a 40-plate column packed with glass helices gave alcohol having $n^{25}\text{D}$ 1.3974, b.p. 99.5–100.0°, $d^{20}{}_4$ 0.8081, $[\alpha]^{25}\text{D}$ +2.50°.

BROOKHAVEN NATIONAL LABORATORY
UPTON, LONG ISLAND, N. Y.

RECEIVED OCTOBER 9, 1950

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[1] Work done under the auspices of the Atomic Energy Commission.

[2] L. W. Trevoy and W. G. Brown, THIS JOURNAL, **71**, 1675 (1949).

[3] (a) Vavon and Angelo, *Compt. rend.*, **224**, 1435 (1947); (b) Vavon, Riviere and Angelo, *ibid.*, **222**, 959 (1946).

[4] Mosher and LaCombe, THIS JOURNAL, **72**, 3994 (1950).

[5] W. von E. Doering, *ibid.*, **72**, 631 (1950).

$\Delta^{5,7}$-Steroids. IV.[1] 7-Dehydrocholesteryl Methyl Ether

BY SEYMOUR BERNSTEIN AND KARL J. SAX

In this note we wish to record the preparation in a pure state of 7-dehydrocholesteryl methyl ether from cholesteryl methyl ether *via* the NBS[2] method.[1,3] This compound has been described previously only in the patent literature,[4] and was prepared by a modified Windaus method.[5]

Cholesteryl methyl ether in petroleum ether was brominated with NBS, and the intermediate bromo compound (not isolated) was dehydrobrominated with *s*-collidine in xylene in the usual manner[1] of this Laboratory. This gave a mixture of the desired $\Delta^{5,7}$-ether and the expected by-product, $\Delta^{4,6}$-cholestadienyl methyl ether. Recrystallization from acetone gave the pure $\Delta^{5,7}$-ether, m. p. 123–125°. This m. p. is in contrast to that given by Rosenberg and Turnbull, Jr.,[4] m. p. 109–111°. Our product was further characterized by optical rotatory power, ultraviolet and infrared absorption spectra (Fig. 1, cholesteryl methyl ether included for comparison purposes).

The material in the mother liquors was triangularly recrystallized from acetone and acetone–methanol. This gave an additional quantity of $\Delta^{5,7}$-ether, and a constant melting mixture of

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[1] Paper I, Bernstein, Sax and SubbaRow, *J. Org. Chem.*, **13**, 837 (1948); Paper II, Bernstein, Binovi, Dorfman, Sax and SubbaRow, *ibid.*, **14**, 433 (1949); Paper III, Bernstein, Oleson, Ritter and Sax, THIS JOURNAL, **71**, 2576 (1949).

[2] NBS = N-bromosuccinimide.

[3] Bide and Wilkinson, British Patent 614,194 (Dec. 10, 1948); *C. A.*, **43**, 5810 (1949), have claimed to have prepared several 7-dehydrocholesteryl ethers, *e.g.*, ethyl ether, by the NBS method, but this work is not definitive.

[4] Rosenberg and Turnbull, Jr., U. S. Patent 2,386,636 (Oct. 9, 1945).

[5] Windaus, Lettré and Schenck, *Ann.*, **520**, 98 (1935); Haslewood, *J. Chem. Soc.*, 224 (1938).

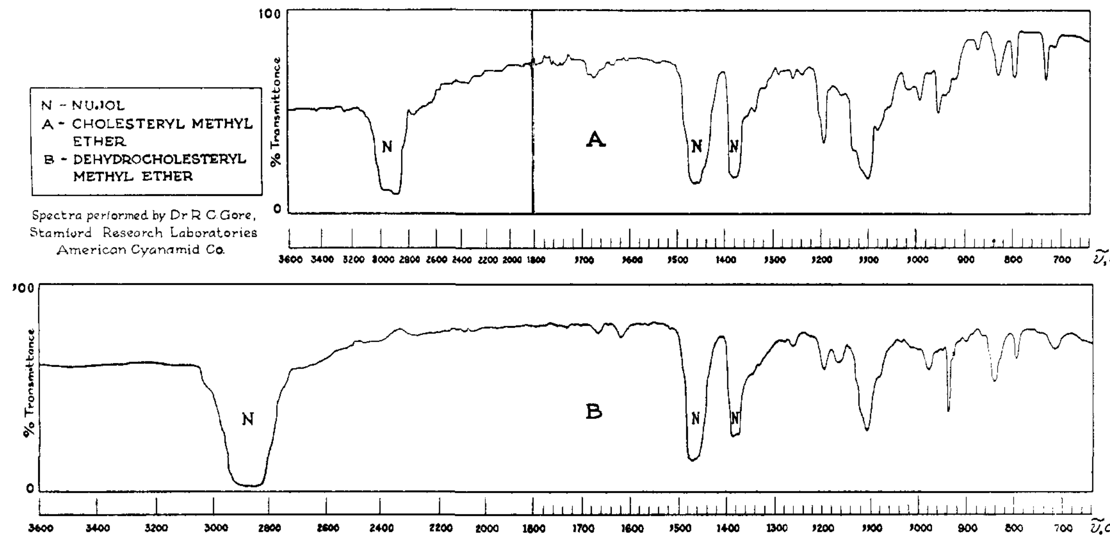

Fig. 1.—Infrared spectra (Nujol mull).

$\Delta^{5,7}$- and $\Delta^{4,6}$-ethers. No further experiment to isolate pure $\Delta^{4,6}$-ether was attempted.

Experimental

7-Dehydrocholesteryl Methyl Ether.—A mixture of 8.0 g. (0.02 *M*) of cholesteryl methyl ether and 4.28 g. (0.024 *M*) of NBS in 100 ml. of petroleum ether, b.p. 64–66° (purified with concd. sulfuric acid and potassium permanganate) was refluxed and irradiated for 3.5 minutes by the heat and light of 2 photospot lamps (type RSP-2, General Electric Co.). Eight ml. of *s*-collidine was then added to the refluxing mixture, which was cooled and filtered. The filtrate was evaporated *in vacuo* (nitrogen atmosphere); the distillation temperature was maintained at room temperature and below. Eighty ml. of xylene was added to the residue. The mixture was refluxed for 12 minutes (nitrogen atmosphere), cooled, and the solid was separated by filtration. The filtrate on evaporation *in vacuo* (nitrogen atmosphere) gave an oily residue which crystallized on treatment with acetone; wt. 5.06 g., m.p. 83–109°; $\lambda_{\text{max.}}^{1\%\ \text{CA}^{6}}$ 240, 272, 282 and 294 mμ; ϵ_{240} = 9050, ϵ_{282} = 6360. Six recrystallizations to constant melting point from acetone gave the pure $\Delta^{5,7}$-ether, wt. 0.76 g., m.p. 123–125°; $\lambda_{\text{max.}}^{1\%\ \text{CA}}$ 272, 282 and 294 mμ; ϵ_{272} = 9900, ϵ_{282} = 10600, ϵ_{294} = 5950; $[\alpha]^{27}\text{D}$ −104.3° (19.55 mg. in 2 ml. of chloroform, 1 dcm. semi-micro tube, gave $\alpha^{27}\text{D}$ −1.02°), $[\text{M}]\text{D}$ −415.

Anal.[7] Calcd. for $C_{28}H_{46}O$ (398.65): C, 84.35; H, 11.63; OCH_3, 7.78. Found: C, 84.19; H, 11.80; OCH_3, 7.99.

The material in the mother liquors was triangularly recrystallized from acetone and acetone–methanol, and gave an additional 0.26 g. of the $\Delta^{5,7}$-ether, m.p. 122–124°, and two fractions consisting of a mixture of $\Delta^{4,6}$- and $\Delta^{5,7}$-ethers, m.p. 86.5–88.5° and 86–88°, $\lambda_{\text{max.}}^{1\%\ \text{CA}}$ 239, 271.5, 282 and 293–294 mμ.

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[6] Solvent was 1% chloroform-absolute alcohol; the substance was dissolved in 1 ml. of chloroform and rapidly diluted to 100 ml. with absolute alcohol.

[7] We are indebted to Messrs. Louis M. Brancone and Samuel M. Modes for the microanalytical data.

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RECEIVED SEPTEMBER 18, 1950

The Reduction of Estrone and Estrogen Esters

BY JOHN H. BIEL

Difficultly hydrolyzable esters of β-estradiol have been shown to possess a greater clinical usefulness than β-estradiol itself.[1] It was desirable therefore to develop a process for the reduction of highly branched esters of estrone to the corresponding β-estradiol 3-esters. Various hydrogenation procedures for estrone and its esters have been described in the chemical and patent literature. Thus Miescher and Scholz[2] were able to reduce aliphatic esters of estrone to estradiol 3-esters by catalytic hydrogenation in ethyl acetate. Marker and Rohrmann[3] converted the trimethylacetate and *t*-butylacetate of estrone to the corresponding β-estradiol derivatives with Adams catalyst in neutral medium at atmospheric pressure and room temperature. Estrone has also been reduced by means of lithium aluminum hydride[4] to β-estradiol and by aluminum isopropoxide[5] to a mixture of β-estradiol and α-estradiol.

While estrone esters could be reduced successfully by catalytic hydrogenation, the method was impracticable for our purpose. Both lithium aluminum hydride and calcium hydride cleaved the esters to β-estradiol and estrone, respectively, during hydrogenation even under mild conditions (see Experimental). Dirscherl[6] reported a similar cleavage of estrone esters during catalytic reduction.

The use of sodium borohydride for the reduction of aldehydes, ketones and acid chlorides was first reported by Chaikin and Brown.[7] We found that this reagent afforded a simple and convenient method for obtaining β-estradiol and two of its highly branched aliphatic esters in excellent yield and high purity from estrone and the corresponding estrone esters. Estrone esters where the acid moiety did not contain a highly branched side chain such as the acetate, propionate, butyrate and benzoate yielded either β-estradiol or a mixture of prod-

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[1] W. Brown and J. T. Bradbury, *J. Clin. Endocrinol.*, **8**, 612 (1948).

[2] K. Miescher and C. Scholz, U. S. Patent 2,156,599 (1939).

[3] R. E. Marker and E. Rohrmann, THIS JOURNAL, **61**, 1922 (1939).

[4] A. C. Ott and M. F. Murray, Abstracts of the 113th Meeting of the American Chemical Society, April, 1948.

[5] R. E. Marker and E. Rohrmann, THIS JOURNAL, **60**, 2927 (1938).

[6] W. Dirscherl, *Z. physiol. Chem.*, **239**, 53 (1936).

[7] S. W. Chaikin and W. G. Brown, THIS JOURNAL, **71**, 122 (1949).

ucts from which only β-estradiol could be isolated in pure form.

Experimental

The estrone esters were prepared in excellent yield by the method of Miescher and Scholz.[8]

β-Estradiol.—A mixture of 400 mg. of estrone, 0.2 cc. of 20% sodium hydroxide solution and 20 cc. of methanol was added to a solution of 150 mg. of sodium borohydride in 20 cc. of methanol. After the evolution of hydrogen had ceased, the reaction mixture was poured into 30 cc. of water and neutralized with dilute hydrochloric acid. The precipitate was filtered, washed with water and immediately recrystallized from aqueous methanol; yield 360 mg. (90%), m.p. 172–174°. A mixed m.p. with an authentic sample of β-estradiol showed no depression.

The Reduction of Estrone Trimethylacetate. A. By Lithium Aluminum Hydride.—To 900 mg. (0.0025 mole) of estrone trimethyl acetate dissolved in 100 cc. of anhydrous ether was added with stirring 200 mg. (0.0052 mole) of lithium aluminum hydride in 15 cc. of anhydrous ether. The mixture was stirred for another hour, cooled and 10 cc. of water added. A precipitate formed, which was dissolved by the addition of 10 cc. of ice-cold 10% sulfuric acid.[9] The aqueous layer was separated and the ether layer concentrated to dryness *in vacuo*. The white, crystalline residue was suspended in 50% aqueous methanol and filtered; yield 700 mg. (100%), m.p. 175–177°. A mixed m.p. with an authentic sample of β-estradiol showed no depression.

When stoichiometric amounts of lithium aluminum hydride were used 85% of the estrone trimethylacetate was recovered unchanged. The remainder could not be purified further, but gave a very strong positive test for free phenolic groups with diazotized sulfanilic acid.

B. **By Calcium Hydride.**—A mixture of 900 mg. (0.0025 mole) of estrone trimethylacetate, 210 mg. (0.0050 mole) of calcium hydride and 75 cc. of 97% aqueous methanol was allowed to stand until the evolution of hydrogen had ceased. The filtrate was added to an equal volume of water, the precipitate filtered and 250 mg. of material collected, m.p. 156–160°. After recrystallization from methanol 200 mg. of the product was recovered; m.p. 165.5–166.5°. A mixed m.p. with an authentic sample of estrone trimethylacetate showed no depression. The aqueous methanol filtrate was chilled and 250 mg. of a solid collected, m.p. 247–255°. After recrystallization from methanol the material melted at 254–256°. A mixed m.p. with an authentic sample of estrone showed no depression.

β-Estradiol 3-Trimethylacetate.—To 250 mg. (0.0062 mole) of sodium borohydride in 10 cc. of methanol was added 900 mg. of estrone trimethylacetate dissolved in 10 cc. of hot methanol. After hydrogen evolution had ceased (*ca.* 30 minutes), 20 cc. of water was added slowly with stirring, the precipitate collected by filtration, washed with 50% methanol and immediately recrystallized from aqueous methanol; yield 600 mg., m.p. 179–181°. To the boiling filtrate water was added to a point just short of turbidity. On cooling, 200 mg. of product was obtained after filtration, m.p. 178–180°. The two fractions were combined; yield 800 mg. (89%); a mixed m.p. with a sample of β-estradiol 3-trimethylacetate obtained from the catalytic hydrogenation of estrone trimethylacetate[9] gave no depression. A test with diazotized sulfanilic acid showed the absence of free phenolic groups.

β-Estradiol 3-*t*-Butylacetate.—The procedure was identical with the one described for the preparation of the trimethylacetate. From 500 mg. of estrone ester there was obtained 350 mg. (70%) of the β-estradiol 3-ester, m.p. 127–129°. A mixed m.p. with a sample obtained from the catalytic hydrogenation of estrone *t*-butylacetate[9] gave no depression.

The Reduction of Estrone Acetate with Sodium Borohydride.—A solution of 500 mg. of estrone acetate in 10 cc. of methanol was added to 150 mg. of sodium borohydride in 10 cc. of methanol and the reaction mixture allowed to stand for 1 hour at room temperature, at which time no more hydrogen was evolved. Thirty cc. of water was then added slowly to the cooled solution and the resulting precipitate filtered and washed with cold 50% methanol; yield 400 mg., m.p. 170–175°. After recrystallization from aqueous methanol 350 mg. of a crystalline precipitate was obtained, m.p. 174–175°. A mixed m.p. with an authentic sample of β-estradiol showed no depression. The product coupled readily with diazotized sulfanilic acid showing the presence of a free phenolic group.

Lakeside Laboratories, Inc.
Milwaukee 1, Wisconsin
Received October 26, 1950

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[8] K. Miescher and C. Scholz, *Helv. Chim. Acta*, **20**, 263 (1937).

[9] An aqueous alcoholic acid solution of β-estradiol trimethylacetate showed no signs of hydrolysis after standing at room temperature for several hours.

The Oxidation of Glucose and Related Compounds with Oxides of Nitrogen[1]

By Ed. F. Degering[2] and Robert A. Berntsen[3]

Saccharic acid has been prepared in moderate (40–46%)[4] yields by the oxidation of glucose with nitric acid.[4,5,6] The importance of saccharic acid[4] and the fact that acids have been obtained by the nitrogen tetroxide oxidation of certain compounds containing a primary hydroxyl group, such as cellulose,[7,8] starch[9] and galactose,[10] prompted this experimental work.

The accompanying experimental work shows that glucose when oxidized by nitrogen tetroxide at 35° in the presence of potassium carbonate gives potassium acid saccharate in 50% yield. Gluconic acid can be oxidized in a nitrogen tetroxide medium to give the same substance in 42% yield. Oxalic acid was not attacked. Potassium acid saccharate could be recovered in 85% yield after treatment with nitrogen tetroxide, but since the salt is relatively soluble in water the loss appears to be mechanical in nature.

Experimental

Materials.—Anhydrous dextrose (C.P., Mallinckrodt) dried in a vacuum desiccator over phosphorus pentoxide or glucose (American Maize Products Co.) dried in a vacuum desiccator at 70° and 10 mm. pressure was used. Nitrogen tetroxide (Solvay Process Company) was dried over phosphorus pentoxide before use.

Oxidation of Glucose in an Inert Medium.—Glucose (0.1 mole) was added to 100 ml. of the inert medium (carbon tetrachloride, petroleum ether or toluene) in a 500-ml., round-bottom three-neck flask which contained a Dry Ice finger-type condenser and an efficient stirrer. The nitrogen tetroxide (0.09 or 0.17 mole) was added through a graduated ice water-cooled West condenser with attached stopcock and ground-glass joint. The experiments were carried out in a constant temperature water-bath at 25 ± 1° for a period of time from 1 to 96 hours. After the period of oxidation, the excess nitrogen tetroxide was blown out and the inert medium decanted off. The oxidation product was washed once with ether and then dissolved in water and the *p*H of the solution was adjusted to 9 using potassium carbonate, potassium hydroxide or both. After hydrolysis of the lactone ring, enough acetic acid was added to adjust the *p*H to 4. The resulting potassium acid saccharate was filtered off, air-dried, and weighed. The yield varied from 10 to 44%.

In a similar manner except for the presence of 0.1 g. of aluminum chloride, cobalt oxide, copper acetate, copper

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[1] From the Ph.D. Thesis of Robert A. Berntsen, Purdue University.

[2] Miner Laboratories, 9 South Clinton, Chicago 6, Ill.

[3] Augustana College, Rock Island, Ill.

[4] C. L. Mehltretter, U. S. Patent 2,436,659 (Feb. 24, 1948).

[5] A. A. Dietz, Ph.D. Thesis, Purdue University, 1941.

[6] J. W. Mench, Ph.D. Thesis, Purdue University, 1944.

[7] C. Unruh and W. O. Kenyon, This Journal, **64**, 127 (1942).

[8] E. C. Yackel and W. O. Kenyon, *ibid.*, **64**, 121 (1942).

[9] J. W. Mench with Ed. F. Degering, *Proc. Ind. Acad. Sci.*, **55**, 69 (1946).

[10] K. Maurer and G. Drefahl, *Ber.*, **75**, 1489 (1942).

powder, fused vanadium pentoxide, iron filings, manganese dioxide, potassium nitrite or sodium fluoride in the carbon tetrachloride medium, the yields of potassium acid saccharate varied from 12 to 44%.

Oxidation of Glucose in Nitrogen Tetroxide Medium.—In a similar manner except for a 100-ml. round-bottom flask and 60 ml. of nitrogen tetroxide as solvent, a 25 to 44% yield of potassium acid saccharate was obtained by the oxidation of glucose (0.1 mole). A solution of urea was used to remove the last traces of the oxides of nitrogen. When 5 g. of potassium carbonate was added to the reaction mixture the yield of potassium acid saccharate, neut. equiv. 247.6, increased to 45%. When 5 g. of potassium carbonate was added to the reaction mixture at 35 ± 0.2°, the yield of potassium acid saccharate, neut. equiv. 247.4, was 50%.

Treatment of Gluconic Acid and Its Lactone with Nitrogen Tetroxide.—D-Gluconolactone (0.05 mole) was dried over phosphorus pentoxide under a vacuum and then treated with nitrogen tetroxide (0.17 mole) in 150 ml. of carbon tetrachloride for 24 hours at 25 ± 1°. The product was treated as was the glucose oxidation run to obtain 4.6 g. (37%) of potassium acid saccharate, neut. equiv. 246.5. Gluconic acid (0.1 mole) was dried in a vacuum over phosphorus pentoxide and treated with nitrogen tetroxide (0.35 mole) in 150 ml. of carbon tetrachloride for 9 hours at 25 ± 1°. The product was treated as was the glucose oxidation run to obtain 8.39 g. (34%) of potassium acid saccharate, neut. equiv. 252.5. Gluconic acid (0.1 mole) was also treated with nitrogen tetroxide in a nitrogen tetroxide medium for 3 hours at 25 ± 1°. The product was treated as was the glucose oxidation run to obtain 10.4 g. (42%) of potassium acid saccharate, neut. equiv. 248.2.

Treatment of Oxalic Acid with Nitrogen Tetroxide.—Anhydrous oxalic acid (0.05 mole) was treated with nitrogen tetroxide (0.17 mole) in carbon tetrachloride at a temperature of 25 ± 1° for 24 hours. After the period of oxidation, the excess nitrogen tetroxide was blown out and the water soluble component was extracted and transferred to a 250-ml. volumetric flask. To aliquots was added ammonium hydroxide to a *p*H of approximately 4. The calcium salt was precipitated out using calcium acetate. Following isolation and the dissolution of the calcium oxalate in sulfuric acid, the solution was titrated with standard potassium permanganate. The amount of oxalic acid found agreed within experimental error with that initially treated with nitrogen tetroxide.

Treatment of Potassium Acid Saccharate with Nitrogen Tetroxide.—Potassium acid saccharate (0.1 mole) and 6 ml. of glacial acetic acid were treated with nitrogen tetroxide (0.35 mole) in 150 ml. of carbon tetrachloride at 25 ± 1° for 8 hours. The product was treated to obtain 22.3 g. (90%) unreacted potassium acid saccharate, neut. equiv. 251.4. Potassium acid saccharate (0.1 mole) was also treated with nitrogen tetroxide in a nitrogen tetroxide medium for 3 hours at 25 ± 1°. The product was treated to obtain 20.9 g. (84%) of potassium acid saccharate, neut. equiv. 249.3.

CHICAGO, ILLINOIS RECEIVED AUGUST 14, 1950

L-Rhamno-2,4-dinitrophenylhydrazone

BY JORGE ALEJANDRO DOMÍNGUEZ

In 1927 Glaser and Zuckermann[1] reported the preparation of glucose and galactose 2,4-dinitrophenylhydrazones. Subsequently, Allen[2] and Brady,[3] unaware of this work, claimed that 2,4-dinitrophenylhydrazine did not give precipitates with the sugars.

L-Rhamno-2,4-dinitrophenylhydrazone.—Five ml. of glacial acetic acid and 0.8 g. of 2,4-dinitrophenylhydrazine were added to a solution of 1 g. of rhamnose in 5 ml. of water. This mixture was heated at 50° during 20 minutes, and allowed to stand at room temperature for 12 hours. The precipitated orange mass was collected, washed with water and a little cold alcohol, and recrystallized from hot alcohol. The yield of the dry yellow crystals was 1.0 g. (71%) m. p. 164–165° (uncor.). The melting point did not change after three recrystallizations.

Anal. Calcd. for $C_{12}H_{16}O_8N_4$: N, 16.27. Found: N, 16.18.

LABORATORIO DE QUÍMICA ORGÁNICA
INSTITUTO TECNOLÓGICO Y DE ESTUDIOS SUPERIORES
DE MONTERREY
MONTERREY N. L., MEXICO RECEIVED SEPTEMBER 14, 1950

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[1] E. Glaser and N. Zuckermann, *Z. physiol. Chem.*, **167**, 37 (1927).

[2] C. F. H. Allen, THIS JOURNAL, **52**, 2955 (1930).

[3] O. L. Brady, *J. Chem. Soc.*, **133**, 756 (1931).

The "Exponential" Adsorption Isotherms of Fatty Acids on Activated Charcoal

BY E. GLUECKAUF

F. H. M. Nestler and H. G. Cassidy[1] have investigated the simultaneous adsorption of acetic, propionic and butyric acids on active charcoal from aqueous solution. They have tried to interpret these data by utilizing the binary exponential isotherm by Glueckauf[2] which should apply when the exponential form is caused by a statistical distribution of adsorbing centers of different affinity.[2,3] However, they were able to obtain agreement with the observations only, by introducing an extra constant not provided by the theory. This note is intended to show that the exponential single-solute isotherms in this case need not be due to non-uniformity of the adsorbent, but can be caused by the strong affinity of activated charcoal for hydrogen ions, and that Nestler and Cassidy's binary adsorption data can be explained as an anion exchange process.

It has been shown by Steenberg[4] that charcoal in a mixture of strong acids displays all the characteristics of an anion-exchanger, the primarily adsorbed group being the H_3O^+ ion. The chromatographically obtained data of Nestler and Cassidy fully support this view also for the weaker fatty acids, as the values obtained for the exchange factor k_3 are independent of the concentrations both for the pairs of acetic + propionic and propionic + butyric acids (see Table I). This feature is characteristic of exchange and of Langmuir isotherms, but is quite improbable for exponential ones.

TABLE I

ACETIC (1) AND PROPIONIC (2) ACID

$$k_3 = \frac{q_1 c_2}{c_1 q_2} = 1 - \frac{c_{1,1}(w_2 - w_1^0)}{c_1^0 w_2} \qquad (1)$$

$c_{1,1}$ and w_1^0 = concentration and breakthrough volume of solute 1 (concentrations in wt. %). c_1^0 = concentration of solute 1 at breakthrough of solute 2. w_2 = breakthrough volume of solute 2 (see ref. 1)

c_1^0	$c_{1,1}$	w_2	w_1^0	k_3
0.982	1.521	18.35	9.47	0.25
.759	1.145	22.35	11.05	(.24)
.752	1.153	22.75	11.79	.26
.503	0.751	27.70	14.24	.28
.379	.566	32.96	16.83	.27
.251	.376	41.35	20.75	.26
.152	.210	55.60	27.0	.29

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[1] F. H. M. Nestler and H. G. Cassidy, THIS JOURNAL, **72**, 680 (1950).

[2] E. Glueckauf, *J. Chem. Soc.*, 1322 (1947).

[3] G. D. Halsey and H. S. Taylor, *J. Phys. Chem.*, **15**, 624 (1947).

[4] B. Steenberg, Thesis, Uppsala University, Sweden, 1944.

The following mechanism is suggested:

(1) H_3O^+ is adsorbed according to a Langmuir adsorption. The H_3O^+ concentration of the dilute solutions of the weak acids is proportional to $\sqrt{c}$ (c = total acid concentration), the coefficient of adsorption being somewhat dependent on the nature of the anion which, for reason of electroneutrality, must remain close to the adsorbed H_3O^+, presumably forming an ion-pair. As long as only one species of acid is present, this mechanism is indistinguishable from molecular adsorption following an "exponential" isotherm.

(2) When two or more acids are present, the adsorbed H_3O^+ acts as an anion-exchanger with respect to the acids in solution according to the mechanism

$$[H_3O^+_{ads} + A_1^-] + HA_2 \overset{k_3}{\rightleftarrows} [H_3O^+_{ads} + A_2^-] + HA_1$$

(3) In mixtures of two acids, the coefficient $k_{1,2}$ of adsorption of H_3O^+ is taken as the appropriate mean of the single solute coefficients k_1 and k_2, *i.e.*

$$k_{1,2} = (c_1k_1 + c_2k_2)/(c_1 + c_2) \qquad (2)$$

which covers at the same time differences in the dissociation constants of the two acids. Equation 2 is an approximation only, but exact treatment would be unjustifiably laborious; it implies that total adsorption of acids (q) can be calculated from the single-solute data without the introduction of the new constant k_3 (see Fig. 1 line C.).

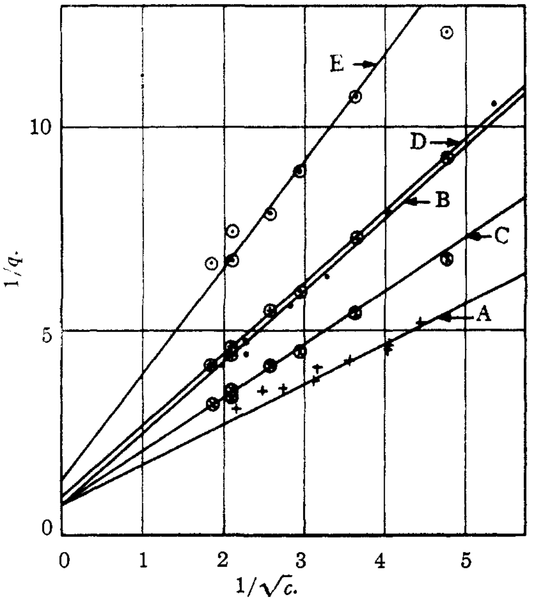

Fig. 1.—Adsorption from mixture of acetic and propionic acids calculated from adsorption data of the pure acids (c = total acid concentration in moles/liter, q in millimoles/g.): A, + + +, propionic acid (single solute) (eqn. 3); B, . . ., acetic acid (single solute) (eqn. 3); C, ⊗⊗⊗, total adsorption from mixture (eqn. 3); D, ⊕⊕⊕, propionic acid (from mixture) (eqn. 5a); E, ⊙⊙⊙, acetic acid (from mixture) (eqn. 4a); (curve E shows $1/q$-values halved).

The assumption of a Langmuir adsorption for H_3O^+ means then that the total adsorption of acids is in all cases represented by the equation

$$q = \frac{Qk\sqrt{c}}{1 + k\sqrt{c}} \qquad (3)$$

where k is k_1, k_2 or $k_{1,2}$ according to whether one deals with single or multiple solutes. In the example of the acetic and propionic acids, the constants $Q = 1.43$, $k_1 = 0.399$ and $k_2 = 0.690$ are obtained from Nestler and Cassidy's single solute experiments, *i.e.*, from the slopes and intercepts of line A and B of the figure. For the 5:4 molar mixture of acids used, the value $k_{1,2} = 0.528$ follows from eqn. 2 as the mean of k_1 and k_2. The only new constant to be obtained from the binary adsorption data is thus the ion-exchange constant $k_3 = 0.27$ (from Table I). These constants are to be applied to concentrations in mole/liter and to specific adsorptions (q) in millimole/g.

The final equations for q_1 and for q_2 in mixed adsorption taking account of the anion-exchange, then follow from eqn. (1) and (3) combined with the fact that $q_1 + q_2 = q$

$$q_1 = \frac{Qk_{1,2}\sqrt{c}}{(1 + k_{1,2}\sqrt{c})}\frac{k_3c_1}{(c_2 + k_3c_1)} \qquad (4)$$

$$q_2 = \frac{Qk_{1,2}\sqrt{c}}{(1 + k_{1,2}\sqrt{c})}\frac{c_2}{(c_2 + k_3c_1)} \qquad (5)$$

and for the fixed molar ratio of 5:4 we obtain for acetic (subscript 1) and propionic (subscript 2) acids the equations

$$q_1 = 0.191\sqrt{c}/(1 + 0.528\sqrt{c}) \qquad (4a)$$

$$q_2 = 0.565\sqrt{c}/(1 + 0.528\sqrt{c}) \qquad (5a)$$

For a check of the experimental data it is convenient to plot $1/q$ against $1/\sqrt{c}$, whence the equations 3, 4a and 5a result in straight lines. The experimental data of Nestler and Cassidy are shown as points in the figure and they agree well, within the limits of their accuracy, with the calculated lines.

This calculation does not exclude the possibility that some acid is adsorbed in undissociated form as well, but such an assumption alone does not explain the data satisfactorily, while the ion-exchange model alone does. This discussion is intended to emphasize the need to differentiate between exponential isotherms due to dissociation phenomena and those due to a statistical distribution of adsorbing sites of different affinity. This difference, though not apparent in single solute isotherms, becomes important for the adsorption of mixtures.

ATOMIC ENERGY RESEARCH ESTABLISHMENT
HARWELL, BERKSHIRE, ENGLAND
RECEIVED JUNE 6, 1950

Dicyclic Hydrocarbons. II. 2-Alkylbicyclohexyls

BY I. A. GOODMAN AND P. H. WISE

The syntheses and physical properties of a series of 2-substituted alkylbiphenyls have recently been reported from this Laboratory.[1] The alkyl substituents included methyl, ethyl, propyl, isopropyl and butyl. In this communication we wish to present the results of the catalytic hydrogenation of these hydrocarbons, including data on the separation of the geometrical isomers, and the analyses and physical properties of the five pairs of isomers which were obtained. The

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(1) I. A. Goodman and P. H. Wise, THIS JOURNAL, 72, 3076 (1950).

TABLE I

PHYSICAL PROPERTIES, YIELDS AND ANALYSES OF 2-ALKYLBICYCLOHEXYLS

Bicyclohexyl hydrocarbon	M.p., °C.	B.p., °C. at 760 mm.	n^{20}D	d^{20}, g./ml.	ΔH_f, kcal./mole	Est. purity, mole %	Heat of comb.,[c] kcal./mole	Relative yield, %	Carbon, %		Hydrogen, %		Viscosity, centistokes[d]			
									Calcd.	Found	Calcd.	Found	32° F.	100° F.	140° F.	210° F.
2-Methyl[a]	−26.43	249.87	1.4791	0.88447	4.4	98.9	1855	41	86.58	86.65	13.42	13.35	8.84	3.11	2.08	1.22
2-Methyl[b]	−10.27	255.00	1.4836	.89450	4.6	99.2	1870	59	86.58	86.58	13.42	13.41	12.85	4.20	2.69	1.51
2-Ethyl[a]	Glass	266.23	1.4827	.89065	...	..	1995	34	86.51	86.60	13.49	13.48	16.33	4.20	2.58	1.40
2-Ethyl[b]	−0.35	269.54	1.4851	.89624	5.4	99.9	2015	66	86.51	86.46	13.49	13.47	18.53	4.75	2.89	1.54
2-Propyl[a]	Glass	279.40	1.4807	.88527	...	..	2145	35	86.46	86.44	13.54	13.56	28.32	5.38	3.05	1.56
2-Propyl[b]	0.25	282.22	1.4838	.89205	5.7	99.8	2160	65	86.46	86.47	13.54	13.56	34.08	6.20	3.46	1.71
2-Isopropyl[a]	Glass	277.18	1.4843	.89305	...	..	2140	49	86.46	86.45	13.54	13.54	46.82	6.94	3.75	1.80
2-Isopropyl[b]	−9.13	283.06	1.4901	.90365	5.7	99.9	2165	51	86.46	86.50	13.54	13.53	29.12	6.54	3.78	1.91
2-Butyl[a]	Glass	294.15	1.4799	.88227	...	..	2300	40	86.40	86.42	13.60	13.48	42.37	6.74	3.64	1.76
2-Butyl[b]	−6.51	296.56	1.4827	.88819	6.5	..	2300	60	86.40	86.44	13.60	13.48	51.18	7.65	4.05	1.91

[a] Low-boiling isomer. [b] High-boiling isomer. [c] ASTM procedure: D240-39. [d] ASTM procedure: D445-46T.

synthesis of 2-methylbicyclohexyl and 2-ethylbicyclohexyl from cyclohexylidenecyclohexanone has been reported,[2] but no reference is made to the existence of geometrical isomerism in these hydrocarbons.

The general application of von Auwers' rule[3] has been shown to be susceptible to error[4,5] as indicated by the recent change in the name of the *cis* and *trans* isomers of 1,3-dimethylcyclohexane. Consequently, since the pertinent thermodynamic properties have not been investigated, no specific assignment of *cis* and *trans* configurations can be made, and the products isolated are referred to simply as the low- and high-boiling isomers.

The high-boiling isomer of each isomeric pair and the low-boiling isomer of 2-methylbicyclohexyl could be successfully crystallized. An estimation of their purities on the basis of their time–temperature melting curves and heats of fusion is shown in Table I. Because of the short length of the equilibrium portion of the melting curve for the high-boiling isomer of 2-butylbicyclohexyl, the estimation of purity of this compound was not deemed valid and is not recorded.

For the low-boiling isomers which could not be crystallized, fractions were combined on the basis of constant refractive index and density values. A systematic evaluation of purity could not be made for these isomers, but the distinct plateaus of refractive index and density values indicated purities of the same order of magnitude as those recorded for the compounds obtained in the crystalline state.

All of the physical properties were determined by methods previously described,[1] and the estimated mole % purities were determined according to the method of Glasgow, Streiff and Rossini.[6]

Experimental[7]

Materials and Procedure.—The 2-alkylbiphenyls used in this investigation had physical properties similar to those previously reported.[1] The quantity of each hydrocarbon hydrogenated varied according to the amount available for such use. Hydrogenations were carried out in a 3-liter bomb at 1500–2000 p.s.i. and 190–210°. A volume of methylcyclohexane equal to that of the hydrocarbon was used as solvent, and 10–12% by weight of UOP nickel was used as catalyst except for the hydrogenation of 2-butylbiphenyl. Small amounts of halogen-containing olefin were present in this material; consequently 18–20% by weight of UOP nickel was used in this case.

The quantities of material hydrogenated were as follows: 2590 g. (15.4 moles) of 2-methylbiphenyl; 1925 g. (10.6 moles) of 2-ethylbiphenyl; 1100 g. (5.6 moles) of 2-propylbiphenyl; 950 g. (4.8 moles) of 2-isopropylbiphenyl; and 1015 g. (4.8 moles) of 2-butylbiphenyl. Yields of completely hydrogenated product were essentially quantitative, although the rate of hydrogenation was much lower for the 2-butylbiphenyl than for any of the other hydrocarbons (23 hours compared to an average of 5 hours for each of the others), because of the presence of halogen impurity.

Purification.—Separation and purification of the five isomeric mixtures was effected by passage of the hydrogenation products through silica gel columns followed by careful fractionation at reduced pressure through six-foot Podbielniak distillation columns.

NATIONAL ADVISORY COMMITTEE FOR AERONAUTICS
LEWIS FLIGHT PROPULSION LABORATORY
CLEVELAND, OHIO
RECEIVED SEPTEMBER 29, 1950

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[2] C. E. Garland and E. E. Reid, THIS JOURNAL, **47**, 2333 (1925).

[3] K. von Auwers, *Ann.*, **420**, 92 (1920).

[4] K. S. Pitzer and C. W. Beckett, THIS JOURNAL, **69**, 978 (1947).

[5] F. D. Rossini and K. S. Pitzer, *Science*, **105**, 647 (1947).

[6] A. R. Glasgow, Jr., A. J. Streiff and F. D. Rossini, *J. Research Natl. Bur. Standards*, **35**, 355 (1945).

[7] Macroanalyses by Mr. A. B. McKeown, heats of combustion by Mr. A. M. Busch, viscosities by Mr. W. J. Yankauskas, and other physical properties by Mr. J. F. Thompson of this Laboratory.

Paper Chromatography in the Separation of Estradiol-17α from Estradiol-17β and of Equilin from Equilenin

BY ERICH HEFTMANN

It has recently been shown that paper chromatography may be used for the identification of mixtures of estrone, estradiol-17β ("α"-estradiol) and estriol.[1] The same method is applicable to the binary mixtures of estradiol-17α and estradiol-17β and of equilin and equilenin with only a minor change in the developing solvent. The separation of the 17-epimers of estradiol and of dihydroequilenin by partition chromatography on Celite has also been accomplished by Haenni.[2]

Experimental

Conditions for the preparation of the *p*-nitrobenzeneazodimethoxyaniline derivatives of the estrogens and for the development of the chromatogram are exactly as previously described,[1] except that equilin and equilenin couple more readily without heating than the other estrogens studied and that the development with the modified solvent mixture takes only 1.25 hours. The new solvent mixture is prepared by equilibration of 200 cc. of petroleum ether (boiling range 35–60°), 100 cc. of toluene, 10 cc. of ethanol and 90 cc. of distilled water. The R_f values of estrogen derivatives in the new solvent mixture and in the solvent mixture previously described are given in Table I.

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[1] E. Heftmann, *Science*, **111**, 571 (1950).

[2] Unpublished work, mentioned in J. Carol, E. O. Haenni and D. Bates, *J. Biol. Chem.*, **185**, 267 (1950).

TABLE I

COLOR AND LOCATION OF SPOTS IN THE PAPER CHROMATOGRAM OF ESTROGENS

Compounds	Color of spots	*Rf* values in New solvent	*Rf* values in Old solvent[1]
Estradiol-17α[3]	Purple	0.32	0.96
Estradiol-17β	Purple	.09	.82
Estradiol-17α + estradiol-17β	Purple	.35 + 0.08	.96 + 0.83
Equilin	Purple	.49	.96
Equilenin[3]	Blue	.05	.80
Equilin + equilenin	Purple + blue	.45 + 0.05	.97 + 0.81
Estrone	Purple	.29	.96
Estriol	Purple	.00	.10

Discussion.—Paper partition chromatography is capable of resolving such closely related pairs as the epimeric estradiols and the equine estrogens equilin and equilenin, which differ only in the degree of saturation in ring B. The new solvent improves the separation of estradiol-17β from estrone and removes the latter farther from the yellow solvent front, but the estriol spot is not moved. This makes the identification of estriol difficult if other immobile pigments are present, as in urine. By using both the new and the old solvent mixtures in a two-dimensional chromatogram this difficulty can be avoided and the resolution further increased.

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[3] Provided by Ayerst, McKenna and Harrison, Ltd., through the courtesy of Dr. Gordon Grant.

NATIONAL CANCER INSTITUTE
BETHESDA 14, MARYLAND RECEIVED SEPTEMBER 20, 1950

Specific Gravities of Ferrous Sulfate Solutions

BY HARRIS HOLTZMAN AND LEONARD MAY

In view of the variable degree of hydration of commercial grade ferrous sulfate heptahydrate crystals known as copperas, it is necessary that each individual lot be tested before use. The compositions of different lots of copperas may run as low as $FeSO_4 \cdot 3\text{–}4H_2O$ instead of $FeSO_4 \cdot 7H_2O$.

Routine evaluations of commercial salts such as copperas are most readily performed by use of specific gravity or Baumé tables for aqueous solutions. However, when the currently accepted tables for aqueous ferrous sulfate solutions are used,[1] we have found that the values for composition of the salt are approximately 9% in error over values as determined by oxidimetric titrations of the same solutions, lower values being obtained by the chemical analysis.

An investigation of the literature indicated that the values given in the "International Critical Tables"[1] were based almost entirely on work performed prior to 1900.[2,3,4] Except for some work at very low concentrations,[5,6] it would appear that chemical analytical procedures were not used. It is also possible that, in the very earliest work, the monohydrate ($FeSO\cdot_4H_2O$), which breaks down only at high temperatures,[7] was mistaken for the anhydrous salt. Such a discrepancy would result in an error of 6.5% (based on $FeSO_4 \cdot 7H_2O$), or 11.8% (based on $FeSO_4$).

In view of the discrepancies encountered in our laboratory, we decided to set up a specific gravity *vs.* concentration curve based on new analytical data.

Experimental Work.—Baker C.P. ferrous sulfate heptahydrate was used for this work. Analyses were run, using 0.100 *N* $KMnO_4$ and $K_2Cr_2O_7$ solutions for oxidation of ferrous iron. Titanous chloride titrations indicated less than 0.01% ferric iron, so that direct titrations with $KMnO_4$ or $K_2Cr_2O_7$ gave the total amount of iron without significant error. The differences between permanganate and dichromate titrations were less than 1 part in 400. Specific gravity determinations using pycnometer and hydrometer were made on solutions of several concentrations, temperature being maintained at 18°.

Results.—Titrations indicated that the C.P. ferrous sulfate was 99.0% pure, as $FeSO_4 \cdot 7H_2O$.

Table I, column A gives the concentration of $FeSO_4 \cdot 7H_2O$, in g. per liter at 18°, by actual analysis. Column D gives the concentration of $FeSO_4 \cdot 7H_2O$, in g. per liter at 18°, on the basis of "I.C.T." values,[1] and column E indicates the percentage error in composition introduced by use of "I.C.T." or chemical handbook tables.

TABLE I

A $FeSO_4 \cdot 7H_2O$ g. per l. by analysis	B Specific gravity 18°/18°	C Baumé = 145 − 145/B	D $FeSO_4 \cdot 7H_2O$ g. per l. ("I.C.T." values)	E % error in "I.C.T." tables
180.5	1.099	13.0	198.0	+ 9.9
198.2	1.107	14.0	215.2	+ 8.6
215.4	1.115	15.0	232.6	+ 8.0
230.5	1.124	16.0	250.2	+ 7.8
244.2	1.133	17.0	268.9	+10.1
			Av. deviation	+ 8.9

From these results, it is evident that the values given in the literature for specific gravities of ferrous sulfate solutions are in error, particularly for ranges around 10 to 20% or higher.

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[1] "International Critical Tables," Vol. III, 1929. These values have been repeated and recalculated in terms of Baumé readings in several handbooks.

[2] Klein, *Ann. Physik*, **27**, 151 (1886).

[3] Gerlach, *Dinglers Polytechnisches Journal*, **181**, 129 (1866).

[4] Gerlach, *Z. Anal. Chem.*, **8**, 245 (1869).

[5] Trotsch, *Ann. Physik*, **41**, 259 (1890).

[6] Pasea, *Proc. Roy. Soc. Can.*, **6-III**, 27 (1900); MacGregor, *Chem. News* (Nov. 7, 1890).

[7] Mellor, "Treatise on Inorganic Chemistry," Vol. 14, p. 248.

RESEARCH LABORATORY
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RECEIVED SEPTEMBER 5, 1950

Paper Partition Chromatography of Simple Phenols[1]

BY RALPH L. HOSSFELD

The application of paper partition chromatography to the qualitative separation of phenolic compounds has been reported.[2–5] However, the results indicated that the method did not effectively separate mixtures of simple phenols of closely

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[1] University of Minnesota Agricultural Experiment Station Scientific Journal Series Paper No. 2584.

[2] R. A. Evans, W. H. Paar and W. C. Evans, *Nature*, **164**, No. 4172, 675 (1949).

[3] E. C. Bate-Smith and R. G. Westall, *Biochim. Biophys. Acta*, **4**, 427 (1950).

[4] A. E. Bradfield and E. C. Bate-Smith, *ibid.*, **4**, 441 (1950).

[5] G. Lindstedt, *Acta Chem. Scand.*, **4**, 448 (1950).

related structure. The adsorption chromatography of the azo dyes derived by coupling simple phenols with diazotized p-nitroaniline was reported by Bielenberg[6] who also found that practical separations were limited to relatively few simple mixtures.

In the course of studying the phenolic degradation products of lignin[7] an urgent need was felt for a supplementary technique to fractional distillation which would increase the ease and thoroughness of identification of the constituents of the complex mixtures. It has been found that satisfactory qualitative separation of many simple phenols can be accomplished by the application of paper partition chromatography to a mixture of the sodium salts of phenyl azo dyes derived by coupling the phenols, pure or in mixture, with diazotized sulfanilic acid.

In preliminary experiments, dyes were prepared by coupling o-cresol with diazotized sulfanilic acid, anthranilic acid, p-nitroaniline and β-naphthylamine-6-sulfonic acid. The dyes were then chromatographed both as the free acids and as the sodium salts. In the first instance, untreated Whatman No. 1 filter paper was used, and in the second the paper was first sprayed to fiber saturation with 4% sodium carbonate and dried before spotting. n-Butanol–water, methyl ethyl ketone–water and n-butanol (5 vol.)–water (5 vol.)–ethanol (1.5 vol.) were studied as irrigating solvents.

Of these various combinations of experimental conditions the development of the sodium salt of o-cresyl-azo-benzenesulfonic acid on the carbonate treated paper using methyl ethyl ketone–water proved most effective. Spots developed with methyl ethyl ketone–water showed less tendency to trail than when developed with other solvents, and development of the dyes as the sodium salts both reduced the tendency to trail and resulted in a more favorable spread of R_f values.

The separation of dye mixtures was observed both by superimposed spotting of the individual dyes at a single location on the paper, and by spotting the mixed dye resulting from the coupling of a mixture of phenols with the diazotized sulfanilic acid. In the latter case, it was not always possible to isolate the mixed dyes from the aqueous reaction mixture. In these instances the reaction mixture, after acidification, was extracted with a suitable solvent such as benzene or chloroform to remove the unreacted phenol; then a small portion of the aqueous solution was diluted with alcohol and used in spotting the paper strip.

The results of this technique as it was applied to a mixture of phenol, guaiacol and o-cresol are illustrated in Fig. 1. Figure 2 illustrates the degree of differentiation which is possible with guaiacol, phenol, o-cresol, p-cresol and 2-hydroxy-1,4-dimethylbenzene. It is apparent, however, that mixtures of 4-hydroxy-1,2-dimethylbenzene with p-cresol,

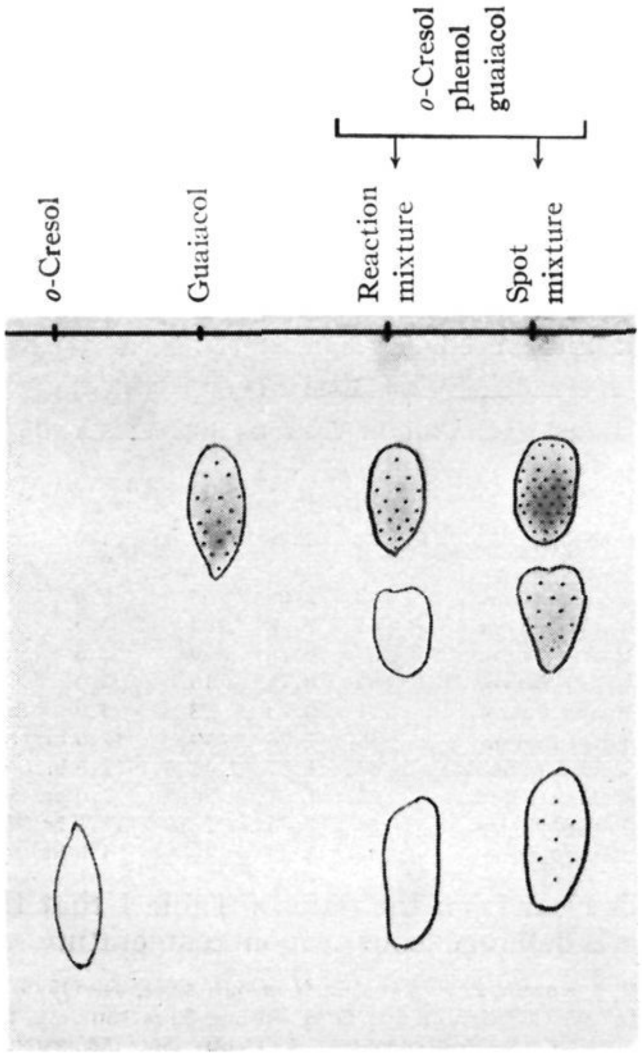

Fig. 1.—n-Butanol–H_2O.

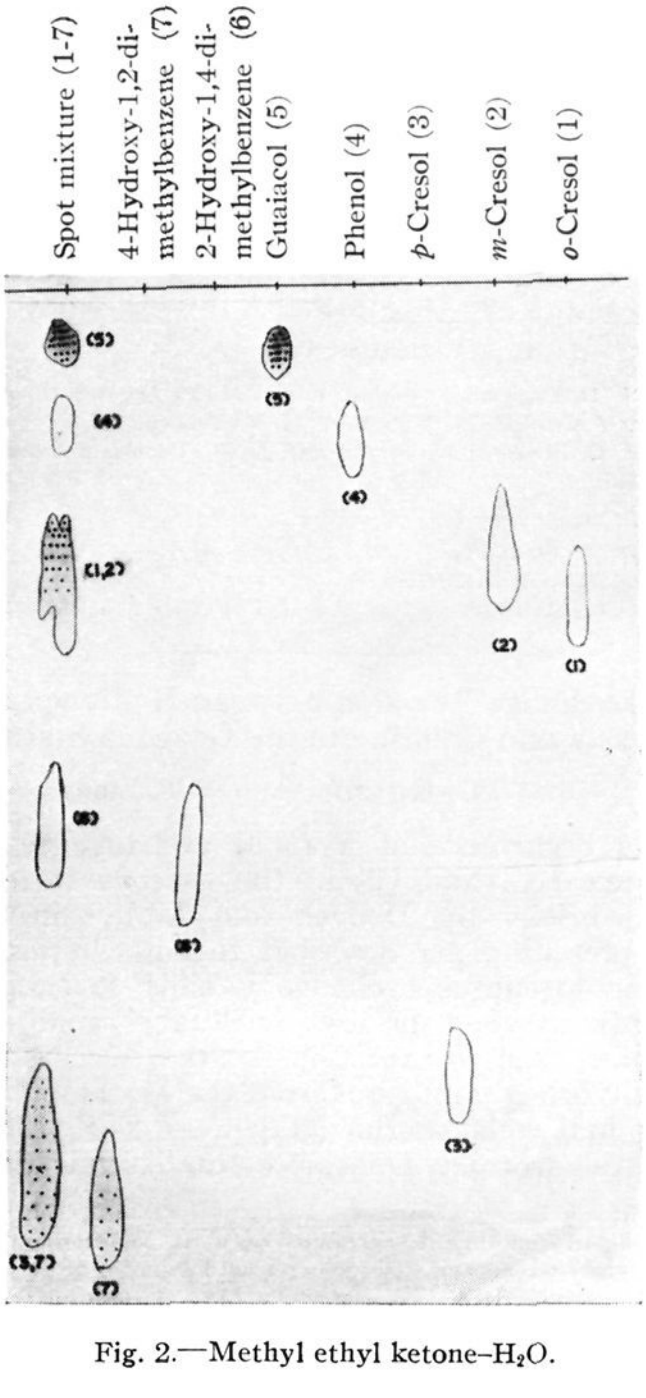

Fig. 2.—Methyl ethyl ketone–H_2O.

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(6) W. Bielenberg and L. Fischer, *Brennstoff-Chem.*, **23**, 283 (1942).

(7) D. L. Brink, R. L. Hossfeld and W. M. Sandstrom, THIS JOURNAL, **71**, 2275 (1949).

and of *o*-cresol with *m*-cresol were not separated under the conditions of these experiments.

Experimental

Preparation of Azo Dyes.—The method of Cheronis[8] was followed using 0.01 molar quantities of reactants. In many cases it was found that the dyes could be recovered in almost pure state by acidifying the final reaction mixture and filtering the product. The dyes so recovered were recrystallized from alcohol–benzene or alcohol alone as required. In other cases the dyes could not be isolated in crystalline form either as the free acid or by salting out of the sodium salts. The reaction mixtures containing these dyes were treated in the same manner as the mixtures described below.

The preparation of dyes from phenol mixtures was accomplished by the same method except that no attempt was made to isolate the crystalline products. The resulting reaction mixture was acidified with an excess of hydrochloric acid and extracted with benzene or chloroform to remove unreacted phenol. A small portion (1–3 drops) of the aqueous solution was then diluted with 2 ml. of ethanol and spotted, by means of a small platinum wire loop, at the appropriate position on the paper strip.

Development of the chromatograms was accomplished by the usual methods with an apparatus similar to that of Steward,[9] consisting of a stainless steel trough (2.25 × 1.5 × 6.5 in.) suspended by brackets from the lugs in the top of a conventional museum specimen jar (20 × 60 cm.). The irrigating solvents (*vidi supra*) were prepared by thoroughly shaking the mixture in a separatory funnel and allowing to stand until completely separated. The organic phase was used for irrigation. The paper strips (14 × 56 cm. Whatman No. 1 filter paper) were first sprayed to the point of fiber saturation with aqueous 4% sodium carbonate, dried, spotted with the dye and suspended from the trough in the jar. They were allowed to remain undisturbed for one hour before adding the irrigating solvent in order to allow them to attain equilibrium with the aqueous phase of the solvent mixture which had previously been placed in the bottom of the jar.

Acknowledgment.—The author wishes to express appreciation of a Grant-in-Aid of Research by the Graduate School of the University of Minnesota. Thanks are also due Mr. Wayne L. Meek for preparation of the dyes.

[8] N. D. Cheronis, "Semimicro and Macro Organic Chemistry," Thomas Y. Crowell Co., New York, N. Y., 1942, p. 285.

[9] F. C. Steward, W. Stepka and J. F. Thompson, *Science*, **107**, 451 (1948).

WOOD CHEMISTRY LABORATORY
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ST. PAUL, MINN.
RECEIVED AUGUST 21, 1950

The Exchange Reaction between Hydrogen Chloride and Chlorine in the Gaseous State

BY W. H. JOHNSTON[1] AND W. F. LIBBY

The occurrence of a rapid exchange reaction between HCl and Cl_2 in the gaseous state was noted briefly by Dodgen and Libby[2] in 1949. The present paper describes the discoveries that the homogeneous exchange is slow, is catalyzed by ordinary glass surfaces, and that a rapid photochemical exchange reaction occurs.

Anhydrous tank gases from the Matheson Company and radiochlorine-36 ($t_{1/2} = 2 \times 10^6$ yr.) from the Isotopes Division of the Atomic Energy Commission were used. The gases were measured with a Bourdon gage in a known volume of Pyrex vacuum line. The reactions were carried out generally in 500-cc. Pyrex flasks some of which were coated with a mixture of saturated long-chain fluorocarbons (du Pont perfluorolube oil, FCD 335). Following the reaction the mixed gases were expanded into a trap at liquid nitrogen temperature and separated by distillation under vacuum with a bath of ethanol and water at −130°. The HCl^{36} and $ClCl^{36}$ were counted in a cylindrical annular volume surrounding a Geiger counter. The specific activities of the initial gases were measured in units of counts per minute per millimole of "Cl." Pure chlorine free of HCl was obtained by the distillation following the reaction and its specific activity was measured in the same manner. The over-all pressure balance and activity balance were measured and were found to be between 90 and 100%. The extrapolation of the data to zero exchange at zero time was a further check on the separation.

In the photochemical studies nearly monochromatic light of 3650 Å. wave length was obtained with a medium pressure mercury arc (G. E. lamp, AH-4) and appropriate filters. Relative intensities were obtained with a Bowen type Photometer[3] and 931-A photomultiplier tube. Absolute intensities were measured with the uranyl oxalate actinometer[4] and, independently, with a thermopile and moving coil galvanometer.[5] All readings were referred to a reference light source which was known to be stable. All photochemical studies were done in a fluorocarbon coated vessel where the rate of the dark reaction was negligible by comparison.

Most of the experimental data on the dark exchange reaction are shown in Table I. The sparsely covered surface was a Pyrex glass bulb which was uniformly spotted with very small droplets of the fluorocarbon. The largely covered surface had a maximum of four per cent. of the Pyrex uncovered.

TABLE I

DARK EXCHANGE IN VARIOUS SURFACES AT 25°

Run	Surface	HCl m./l. $\times 10^3$	Cl_2 m./l. $\times 10^3$	Exchange, %	Time, min.	Half-time, min.
6	Pyrex	0.52	1.48	64	4.0	3
7	Pyrex	.46	1.54	90	7.5	3
8	Packed pyrex	.43	2.26	100	9.0	2
9	Packed pyrex	.45	2.29	103	5.0	2
10	Sparse fluoro.	.83	0.78	9	2.5	19
11	Sparse fluoro.	.85	0.74	16	5.0	20
12	Sparse fluoro.	.81	0.73	28	9.0	21
5	Large fluoro.	.88	1.66	49	11.0 hr.	11 hr.
1	Complete fluoro.	.85	1.52	42.5	12.5 hr.	16 hr.
2	Complete fluoro.	.87	1.64	26.5	7.0 hr.	16 hr.
3	Packed fluoro.	.88	1.35	78.5	11.1 hr.	5 hr.
4	Packed fluoro.	.87	1.36	43	4.0 hr.	5 hr.

It is clear from the data of Table I that the reaction is heterogeneous at room temperature.

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[1] Atomic Energy Commission Predoctoral Fellow. This paper is taken in part from the thesis presented by W. H. Johnston to the Faculty of the University of Chicago in partial fulfillment of the requirements for the degree of Doctor of Philosophy. Present address: Department of Chemistry, Purdue University, Lafayette, Indiana.

[2] H. Dodgen and W. F. Libby, *J. Chem. Phys.*, **17**, 951 (1949).

[3] E. J. Bowen, *Proc. Roy. Soc.* (*London*), **A154**, 349 (1936).

[4] (a) W. G. Leighton and G. S. Forbes, THIS JOURNAL, **52**, 3139 (1930); (b) G. S. Forbes and L. J. Heidt, *ibid.*, **56**, 2363 (1934); (c) L. J. Heidt and F. Daniels, *ibid.*, **54**, 2384 (1932).

[5] (a) A. Farkas and H. W. Melville, "Experimental Methods in Gas Reactions," Macmillan, Ltd., London, 1939, pp. 250-254. (b) J. D. Strong, "Procedures in Experimental Physics," Prentice-Hall, Inc., New York, N. Y., 1938, pp. 305-341.

The measurements of the absolute light intensities for the photo-chemical study by both the uranyl oxalate actinometer and a thermopile gave concordant values at 4.4 × 10^{16} quanta per minute for the beam passing through the reaction vessel.

The data on the quantum yield for the photo-exchange are shown in Table II. The quanta absorbed per minute were calculated from the known incident beam and the measured fractional absorption by the reaction mixture. The initial exchange rate is given in the last column as the exchange at one minute. The quantum yield is given by the product of the total number of molecules of HCl times the initial exchange rate divided by the quanta absorbed per minute. As shown in Table II the quantum yield is 110.

TABLE II

PHOTO-EXCHANGE AND QUANTUM YIELD

Run	HCl,[a] milli-mole	Cl_2, milli-moles	Quanta[b] absorbed per min. × 10^{16}	Exchange, %	Time, min.	Half-time, min.	Initial exchange rate, %/min.
1	0.27	1.49	2.6	9	5	37	1.9
2	.27	1.59	2.6	49	41	42	1.6
3	.22	1.11	2.3	30.5	20	38	1.8
4	.19	1.99	2.2	79.5	90	39	1.8
Mean	0.24	1.25	2.4	..	..	39	1.8

Molec. HCl exchanged at 1 min. = 2.6 × 10^{18}
Quanta absorbed per min. = 2.4 × 10^{16}
Quantum yield = 110^b

[a] Vol. = 0.510 liter. [b] Light of 3650 Å. wave length.

It appears likely that the photo-exchange occurs through Cl atoms exchanging rapidly with both HCl and Cl_2 molecules. Further work of a more quantitative character should reveal important data on the kinetics of this simple system.

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Addition Reactions in Phospho-organic Syntheses. II. The Addition of Phosphorus Pentachloride to Normal Olefins

BY GENNADY M. KOSOLAPOFF AND JOHN F. MCCULLOUGH

The investigations of the addition of phosphorus pentachloride to a variety of olefins that have been made by Thiele,[1] by Bergmann and Bondi[2] have shown that the reaction proceeds in accord with the Markovnikov rule and yields adducts of type $RCHCl—CH_2PCl_4$, which, on treatment with water, readily yield unsaturated phosphonic acids $RCH{=}CHPO(OH)_2$. Bergmann and Bondi[2] and one of us[3] noted that aliphatic olefins tend to retain the elements of hydrogen chloride in the hydrolytic step and treatment with alkali may be necessary to form the unsaturated acids.

Recent patents[4] indicate that aliphatic terminal olefins of the general type $RCH{=}CH_2$ may undergo the addition reaction in the reverse sense, *i.e.*, contrary to Markovnikov rule. To clarify this point, a typical olefin of this category, 1-butene, was subjected to the reaction of addition. The product was converted to the phosphonyl dichloride, which was esterified with ethanol. The resulting diethyl chlorobutanephosphonate was dehydrohalogenated with alcoholic potassium hydroxide and the unsaturated ester, thus formed, was ozonized. Formaldehyde could not be detected in the product, although it would have been the expected ozonolysis product from the anti-Markovnikov adduct. Hydrogenation of the unsaturated ester and hydrolysis of the ester linkage of the product yielded *n*-butanephosphonic acid, identical with an authentic sample.[5]

These results showed that the orientation of the addition reaction is in accord with the Markovnikov rule, and that the substances described in the aforementioned patents[4] are products of normal addition.

Experimental.—The nomenclature used in this section follows from the results obtained in the investigation. The locations of phosphorus and chlorine are reversed in respect to their assignment in the patent literature.[4]

2-Chlorobutylphosphorus Tetrachloride.—A stream of *n*-butene (C.P. grade, supplied by the Mathieson Chemical Corporation) was passed into a suspension of 154 g. of phosphorus pentachloride in 500 ml. of benzene, with good stirring and ice-cooling. The addition was continued until 70 g. of the olefin was absorbed by the mixture in the course of 2 hours. After continued stirring for 8 hours, the mixture was allowed to stand overnight in an ice-bath. The resulting adduct formed the usual "creamy" suspension in benzene, which was then used for subsequent reactions.

2-Chlorobutanephosphonyl Dichloride.—Preliminary experiments indicated that a direct hydrolysis or alcoholysis of the adduct yields intractable products: an acid which is extremely resistant to crystallization and a diethyl ester which tends to decompose on distillation. Hence, the reaction product described above was treated *in situ* with 38.5 g. of phosphorus pentoxide and the mixture was stirred for 2 hours at room temperature, for 2 hours at 35° and for 2 hours at 50°. This temperature regime has been specified[4] and was followed as closely as possible. Repetition of several such runs failed to show any necessity for the low temperature operation, as no apparent action took place until the temperature had been raised to 50°. The unreacted phosphorus pentachloride was removed by rapid decantation and filtration through glass wool. Distillation of the filtrate yielded the phosphonyl dichloride in the form of colorless oily liquid which distilled sharply at 127° at 24 mm. and which was obtained in 40–41% yield (average of several runs). The yield reported in the literature[4] was 48%.

Diethyl 2-Chlorobutanephosphonate.—The esterification was again carried out in a manner indicated by the literature.[4] The dichloride (51 g.) was added dropwise to 100 ml. of absolute ethanol with ice cooling and stirring under reduced pressure maintained by a water-pump. After evacuation for 12 hours, the mixture was distilled, yielding 48 g. of the ester (88%). The latter boiled at 120–124° at 4 mm. or 78–80° at 0.3 mm. Its physical constants were found to be $n^{30}{}_D$ 1.4389–1.4394, and $d^{30}{}_4$ 1.0939. This gave *MR* calcd. for $ClC_4H_8PO(OEt)_2$ 54.64, and *MR* found 54.98. It may be noted that the phosphonyl dichlorides and phosphonates cited as patent examples[4] have considerably wider boiling point ranges than the above.

Diethyl 1-Butenephosphonate.—The above ester (21.5 g.) was added dropwise to an ice-cooled and vigorously stirred solution of 5.5 g. of potassium hydroxide in 65 ml. of absolute ethanol. After 15 minutes the mixture was filtered and distilled. There was obtained a total of 16 g. of crude product (the reaction was not forced to completion

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[1] J. Thiele, *Chem. Ztg.*, **36**, 657 (1912).

[2] E. Bergmann and A. Bondi, *Ber.*, **63**, 1158 (1930); **64**, 1455 (1931); **66**, 278 (1933).

[3] G. M. Kosolapoff and W. F. Huber, THIS JOURNAL, **68**, 2540 (1946); (the material referred to was contained in the original manuscript of that paper).

[4] W. H. Woodstock, U. S. Patent 2,495,799 to Victor Chemical Works; January 31, 1950; *C. A.*, **44**, 3517 (1950); 2,471,472 to Victor Chemical Works; May 31, 1949; *C. A.*, **43**, 7499 (1949).

[5] G. M. Kosolapoff, THIS JOURNAL, **67**, 1180 (1945).

in order to avoid partial saponification). As a result of combined distillation of products of two such runs there was obtained a 46.3% yield of the unsaturated ester, which boiled at 99–100° at 1 mm.; $n^{29.6}_{D}$ 1.4376, $d^{29.6}_{4}$ 1.0112; *MR* found: 50.3; *MR* calcd., 49.53. The discrepancy of 0.8 unit is undoubtedly the conjugation exaltation effect.

***n*-Butanephosphonic Acid.**—The above ester (0.5 g.) in 25 ml. of ethanol was added to 0.3 g. of 5% palladium-on-charcoal catalyst and the mixture was subjected to the flow of hydrogen through a gas disperser placed at the bottom of the vessel. The reaction was complete within 30 minutes at room temperature. After filtration, the solution was treated with 100 ml. of concentrated hydrochloric acid and the whole was refluxed overnight. The alcohol was then largely distilled from the mixture and the residual liquid was refluxed for an additional 6 hours with a further addition of hydrochloric acid (50 ml.). Evaporation of the solution by means of an infrared lamp to near dryness, final drying by a similar evaporation with two small portions of benzene, and crystallization from benzene with a little charcoal, readily yielded substantially the theoretical yield of *n*-butanephosphonic acid, which melted at 105.5–106.0° whether alone or when mixed with an authentic specimen.

2-Chlorobutanephosphonic Acid.—The phosphonyl dichloride (17.8 g.) was added to 50 ml. of water and was permitted to hydrolyze with stirring and gentle warming. Removal of volatiles under reduced pressure yielded 14.7 g. of crude solid acid. Recrystallization from benzene gave the pure compound in the form of colorless plates which melted at 88–90° with slight decomposition. Titration of the substance with a *p*H meter was impossible as each addition of the standard alkali gave unstable voltage, indicating a rapid cleavage of hydrogen halide. A rapid addition of 0.1 *N* sodium hydroxide to methyl orange end-point, followed by acidification with nitric acid and addition of silver nitrate gave 18.6% chlorine content, against the theoretical value of 20.5%. The compound was not investigated further, but it was evident that its link to the chlorine atom was decidedly weak.

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The Dielectric Constant of Formamide[1]

BY GORDON R. LEADER

Formamide has long been known to have a high dielectric constant, but until recently, there have been no accurate values available for this property, the only reported determination being that of Walden[2] who gave its dielectric constant as >84. In 1947, Burdun and Kantor[3] reported measurements made by the Drude–Coolidge method with wave lengths in the range 1–5 meters. They found $\epsilon = 109 \pm 1.5$ at $20 \pm 1°$ and conclude from the absence of dispersion in this region that this is equivalent to the static value. An earlier reference to values for the dielectric constant of formamide determined by Burdun was made by Vasenko[4] who reported that $\epsilon = 126.07 - 0.7206\,t$ between 18 and 25°. Recently measurements of greater precision have been made in this Laboratory in the temperature range 15 to 35° which confirm in a general way the results of Burdun and Kantor, but indicate a smaller variation of dielectric constant with temperature than has previously been reported.

Capacitance measurements were made using a General Radio Type 821-A Twin-T Impedance Measuring Circuit.[5] Radio frequency current was supplied to the Bridge from a General Radio Type 1001-A Standard Signal Generator. A Hallicrafters Model S-40A multi-band receiver was used as null detector. Because of the relatively high conductivity of even carefully purified formamide, capacitance measurements were made at a frequency of 10 mc. The cell used was very similar in design to that described by Connor, Clarke and Smyth,[6] and was plugged directly into the unknown terminals of the bridge in order to minimize the effect of lead inductance. The cell construction was modified from the design of Connor, Clarke and Smyth chiefly in that the insulating plug was made of Teflon, and the lower portion of the central electrode which passed through the plastic was made of smaller diameter than the body of the electrode in order to reduce the invariant capacity of the cell and to permit a more rigid fit of this tapered stem in the similarly tapered hole in the plastic. The plug was held securely in place with the aid of small washers placed under the General Radio plugs and overlapping slightly on the plastic. The cell was made of brass, and all parts coming into contact with the liquids measured were first silver plated and then gold plated.

Temperature control was secured by circulating water through the cell jacket from a thermostat whose temperature was regulated to ±0.05°. Temperatures were measured using a 0.1° thermometer calibrated by the National Bureau of Standards. It was established by measurements on water and methanol whose dielectric constants are accurately known at these temperatures that within the temperature range 15 to 35° the cell contents were held at the indicated bath temperatures.

The procedure in making measurements was essentially that described by Connor, Clarke and Smyth.[6] The constants in the equation: $C = C_0 + C_v\epsilon$ were determined by measurements of the capacity of the cell when filled with purified benzene and chlorobenzene as reference substances.[7] To secure greater accuracy in measurement of the small capacities involved with these liquids, a heterodyne beat apparatus of the type described by Chien[8] was used, together with a calibrated General Radio Type 722N Precision Condenser. It was found that $C_0 = 1.80 \pm 0.01$ μμf and $C_v = 3.800 \pm 0.005$ at all temperatures from 15 to 35°. Determination of C_v was also carried out at each of the temperatures studied by measurements at 1 mc. with the Twin-T Bridge of the capacity of the cell when filled with purified methanol and water. The values of Albright and Gosting[9] for the dielectric constants of these substances were used. In this manner also a value of $C_v = 3.800 \pm 0.005$ was obtained, independent of temperature in the 15 to 35° range.

At 10 mc. the inductance of the cell and residual

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(1) Based on research performed for the U. S. Army Signal Corps, Fort Monmouth, N. J. under contracts W36-039-sc-32265 and W36-039-sc-38184.

(2) Walden, *Z. physik. Chem.*, **46**, 175 (1903).

(3) Burdun and Kantor, *Doklady Akad. Nauk. S. S. S. R.*, **67**, 985 (1949).

(4) Vasenko, *J. Phys. Chem. (U. S. S. R.)*, **21**, 361 (1947).

(5) Sinclair, *Proc. Inst. Radio Eng.*, **28**, 310 (1940).

(6) Conner, Clarke and Smyth, THIS JOURNAL, **64**, 1379 (1942).

(7) Davies, *Phil. Mag.*, **21**, 1, 1008 (1936).

(8) Chien, *J. Chem. Ed.*, **24**, 494 (1947).

(9) Albright and Gosting, THIS JOURNAL, **68**, 1062 (1946).

impedances in the Bridge cause a considerable error in the observed readings. Correction for these errors was made empirically by measuring various liquids and liquid mixtures of low conductivity at 25° at both 1 mc. and 10 mc. using 650 $\mu\mu$f as the initial setting of the precision condenser in all cases. Assuming the 1 mc. measurements to be negligibly affected by the error sources mentioned, the difference between the 1 mc. and 10 mc. values for a given cell filling was plotted as a function of the 10 mc. value to give a smooth curve from which the correction to be applied to a given 10 mc. reading could be determined to within ± 0.1 $\mu\mu$f. Sufficient points were determined to accurately define the curve. In order to extend the curve to capacities as high as those involved in the working cell when filled with formamide, it was necessary to use a second cell (Cell No. 2), identical with Cell No. 1 except for the fact that the central electrode was $^1/_4$ in. longer, making its constants $C_0 = 2.0$ $\mu\mu$f and $C_v = 7.6$. It was assumed that the inductance of this second cell was essentially the same as that of Cell No. 1 and that the corrections determined with it were applicable to Cell No. 1. This appeared to be justified by the fact that the corrections determined with Cell No. 2 agreed closely with those from Cell No. 1 in the region of lower capacities where either cell could be used.

Water, methanol, benzene and chlorobenzene were purified by standard methods. The latter three were tested for purity either by density or melting point determination. Commercial formamide, supplied by the du Pont Co., was treated with calcium oxide (5 g./liter and distilled under a pressure of 1 mm. or less in a still affording essentially no fractionation. Two successive distillations of the middle fractions, treated each time with calcium oxide gave a colorless product having a m.p. of 2.3 to 2.4°. This material was subjected to three static crystallization steps in a container well protected from carbon dioxide and water. The final purified formamide had freezing points in the range 2.45 to 2.51° (lit. 2.55°)[10] and a specific conductivity of 4×10^{-6} ohm^{-1} cm.$^{-1}$ at 25°. The conductivity increased within 5 or 6 hours to about 1×10^{-5}. Its conductivity during measurements was less than 0.8×10^{-5} in all cases.

The observed values for the dielectric constant of formamide at 10 mc. are shown in Table I.

TABLE I

THE DIELECTRIC CONSTANT OF FORMAMIDE

Temp., °C.	ϵ
15.0	113.5
20.0	111.5
25.0	109.5
30.0	107.5
35.0	105.6

The above data, because of the short temperature range involved show a linear variation with temperature and can be represented by the equation: $\epsilon = 113.5 - 0.40\,(t - 15)$. It is estimated that the probable error of each of the reported values is ±0.2. As shown by Burdun and Kantor,[3] dielectric constants of formamide determined at 10 mc. can be regarded as equivalent to the limiting low frequency values.

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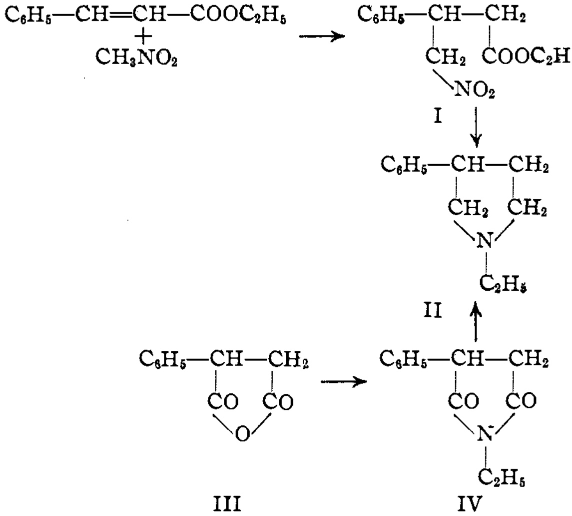
[10] Smith, *J. Chem. Soc.*, 3257 (1981).

Reductive Cyclization. Synthesis of 1-Ethyl-3-phenylpyrrolidine

BY NELSON J. LEONARD, ALLEN B. SIMON AND DONALD L. FELLEY

Past experience in this Laboratory has shown that the reductive cyclization of γ-nitroaliphatic esters to dialkylpyrrolidines can be accomplished by hydrogenation over copper chromite catalyst at high temperature and pressure.[1] It was of interest to learn whether the reaction could be extended to aryl-substituted γ-nitro esters for the preparation of aryl-substituted pyrrolidines. A representative ester of this type, namely, ethyl β-phenyl-γ-nitrobutyrate (I), accordingly has been made and has been found to yield 1-ethyl-3-phenylpyrrolidine (II) when subjected to the reductive cyclization process.



The precursor ester I was obtained by the addition of nitromethane to ethyl cinnamate in the presence of benzyltrimethylammonium butoxide in butanol solution, and was hydrogenated over copper chromite catalyst at 265° and 250 atm. in dioxane solution. The attendant N-alkylation, with the production of 1-ethyl-3-phenylpyrrolidine (II), has been observed previously in similar reductive cyclizations.[1] The identity of the product (II), obtained in 40% yield, was established by an alternative synthesis which actually proved to be the preferable method of preparation. In the second synthesis, phenylsuccinic anhydride (III) was converted to 1-ethyl-3-phenylsuccinimide (IV) by treatment with ethylamine, and the imide (IV) was reduced to 1-ethyl-3-phenylpyrrolidine (II) in 71% yield by the action of lithium aluminum hydride. The properties of the bases obtained by the two methods of synthesis were in every way identical, as were those of their corresponding derivatives.

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[1] N. J. Leonard and K. M. Beck, THIS JOURNAL, **70**, 2504 (1948); N. J. Leonard and W. V. Ruyle, *ibid.*, **71**, 3094 (1949); N. J. Leonard and E. Barthel, Jr., *ibid.*, **72**, 3632 (1950).

Experimental

Ethyl β-Phenyl-γ-nitrobutyrate.—To a stirred solution of 48.8 g. (0.8 mole) of nitromethane and 15 g. of benzyltrimethylammonium butoxide solution in butanol (Rohm and Haas Company) was added 35.2 g. (0.2 mole) of ethyl cinnamate. While the reaction mixture was stirred for 68 hours at 65–70°, additional 5-g. portions of catalyst were added at 24-hour intervals. The mixture was acidified with 1 *N* hydrochloric acid, an equal volume of ethylene dichloride was added, and the ethylene dichloride layer was washed with water. The solvent was removed and the residual oil was fractionally distilled in vacuum. Unchanged ethyl cinnamate (18.0 g.) was recovered at 100–110° (1 mm.), and the ethyl β-phenyl-γ-nitrobutyrate was collected as a light yellow oil; b.p. 156–158° (1 mm.); $n^{20}\text{D}$ 1.5085; $d^{20}{}_4$ 1.162; yield 17.6 g. (76% based on unrecovered ethyl cinnamate).

Anal. Calcd. for $C_{12}H_{15}NO_4$: N, 5.90; *MR*D, 61.40. Found: N, 5.90; *MR*D, 60.91.

1-**Ethyl-3-phenylpyrrolidine** by **Reductive Cyclization.**—A solution of 3.2 g. (0.014 mole) of ethyl β-phenyl-γ-nitrobutyrate in 34 ml. of dioxane was hydrogenated in the presence of 3 g. of copper chromite catalyst at 265° and 250 atm. during 3 hours. After removal of the catalyst and solvent in the usual manner,[1] the residue was fractionally distilled, and the product boiling at 64.5° (0.12 mm.) was collected; $n^{19}\text{D}$ 1.5238; yield 0.8 g. (40%).

Anal. Calcd. for $C_{12}H_{17}N$: N, 7.99. Found: N, 8.13.

1-Ethyl-3-phenylpyrrolidine Picrate (**Picrate** 1).—Prepared in ether and recrystallized from methanol, the picrate formed yellow elongated prisms, m.p. 153–155°.

Anal. Calcd. for $C_{18}H_{20}N_4O_7$: C, 53.46; H, 4.99; N, 13.86. Found: C, 53.41; H, 5.23; N, 14.00.

1-**Ethyl-3-phenylpyrrolidine Picrolonate** (**Picrolonate** 1).—Prepared in ethanol and recrystallized from methanol, the picrolonate formed yellow microcrystals, m.p. 149.5–151.5°.

Anal. Calcd. for $C_{22}H_{25}N_5O_5$: C, 60.13; H, 5.73; N, 15.94. Found: C, 59.90; H, 5.82; N, 16.20.

1-**Ethyl-3-phenylsuccinimide.**—A mixture of 35.0 g. (0.20 mole) of phenylsuccinic anhydride[2] and 25.6 g. (0.40 mole) of 70% aqueous ethylamine was heated gradually under a reflux air condenser to 280°. When the temperature had reached 280°, the reaction mixture was maintained there for 1 hour, then cooled and distilled twice *in vacuo* using a short-path apparatus; b.p. 140–146° (1.5-2.5 mm.); $n^{20}\text{D}$ 1.5501; $d^{20}{}_4$ 1.1574; yield 25.9 g. (65%).

Anal. Calcd. for $C_{12}H_{13}NO_2$: C, 70.91; H, 6.45; N, 6.89. Found: C, 70.95; H, 7.17; N, 6.95.

The infrared spectrum indicated the absence of any absorption due to N–H, and the presence of carbonyl absorption similar to that exhibited by succinimide.[3]

1-**Ethyl-3-phenylpyrrolidine** by **Lithium Aluminum** Hydride **Reduction.**—The procedure which was followed was identical with that described by Nystrom and Brown[4] for the reduction of amides by their lithium aluminum hydride reagent. The product was a colorless liquid, b.p. 77–78° (1.4–1.5 mm.); $n^{20}\text{D}$ 1.5240; $d^{20}{}_4$ 0.9608; yield 71%.

Anal. Calcd. for $C_{12}H_{17}N$: C, 82.23; H, 9.78; N, 7.99; *MR*D, 55.97. Found: C, 82.11; H, 9.82; N, 8.13; *MR*D, 55.82.

The picrate (Picrate 2), m.p. 153–155°, was undepressed on mixing with the picrate of 1-ethyl-3-phenylpyrrolidine obtained by reductive cyclization (Picrate 1).

Anal. Calcd. for $C_{18}H_{20}N_4O_7$: C, 53.46; H, 4.99; N, 13.86. Found: C, 53.50; H, 5.28; N, 13.91.

The picrolonate (Picrolonate 2), m.p. 149.5–151°, was undepressed on mixing with Picrolonate 1.

Anal. Calcd. for $C_{22}H_{25}N_5O_5$: C, 60.13; H, 5.73; N, 15.94. Found: C, 60.19; H, 5.92; N, 16.10.

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(2) P. E. Verkade and H. Hartman, *Rec. trav. chim.*, **52**, 945 (1933).

(3) Infrared analysis by Miss Elizabeth M. Petersen.

(4) R. F. Nystrom and W. G. Brown, THIS JOURNAL, **70**, 3738 (1948).

The Molar Absorbancy Indices of Some 2,4-Dinitrophenylhydrazones

BY E. E. LOCKHART, M. C. MERRITT AND C. D. MEAD[1]

The molar absorbancy indices of several 2,4-dinitrophenylhydrazones of saturated aliphatic aldehydes have already been published.[2,3] However, for a continuing investigation of the carbonyl fraction of food products, it became necessary to prepare and study the spectral characteristics of hydrazones of other members of the aliphatic series. The results of this study are reported here (Table I), to provide a more complete picture of this group of compounds.

TABLE I

MOLAR ABSORBENCY INDICES OF SOME 2,4-DINITROPHENYLHYDRAZONES

	Maximum		
Aldehyde	Primary $a_M \times 10^{-2}$	Secondary $a_M \times 10^{-2}$	Minimum $a_M \times 10^{-2}$
Isobutyr-	230	156	22
n-Valer-	231	157	22
Isovaler-	232	160	21
n-Capro-	238	161	21
n-Capryl-	218	149	21
n-Nonyl-	217	146	21
n-Decyl-	216	146	19
n-Dodecyl-	216	148	20

Our results agree essentially with those previously reported, with respect to wave lengths of maximum and minimum absorption. We were unable, however, to obtain any indication that a third or fourth absorption band might be present in the spectra studied, as suggested by Braude and Jones.[2] The resolution possible with their equipment may account for this discrepancy. With the exception of the formaldehyde hydrazone, all maxima occur at 224–226 mμ (secondary) and 357–358 mμ (primary). The minima are located at 282–283 mμ.

A portion of this study included a repetition of the earlier work. The results obtained, together with those reported here, seemed to indicate that the length of the alkyl chain has some small effect on the intensity of resonance. There is a relatively regular increase in the molar absorbancy indices with increase in chain length, until a maximum is reached at $C_5 \cdot CH=$. Chain lengths greater than this seem to have a damping effect on resonancy. The significance of this effect is being tested by a study of other carbonyl series.

Experimental.—The 2,4-dinitrophenylhydrazones were prepared according to the method of Allen.[4] They were recrystallized from 95% ethyl alcohol until a constant melting point was obtained. A Beckman model DU ultraviolet spectrophotometer and 1.000-cm. silica cells were used throughout this work. The absorption data were obtained from solutions containing uniformly 0.0125 mg. of hydrazone per ml. The solvent was 95% U.S.P. ethyl alcohol (U.S.I. synthetic). Preliminary work indicated that heating solid–liquid mixtures to facilitate dissolution of the hydrazones caused decomposition. It was necessary, therefore, to dissolve the compounds at room temperature. The time required varied from several hours to several days.

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(1) C. D. Mead, S.B. Thesis, Dept. Food Tech., Mass. Inst. Tech., 1949.

(2) E. A. Braude and E. R. H. Jones, *J. Chem. Soc.*, 498 (1945).

(3) J. D. Roberts and C. Green, THIS JOURNAL, **68**, 214 (1946).

(4) C. F. H. Allen, *ibid.*, **52**, 2955 (1930); C. F. H. Allen and J. H. Richmond, *J. Org. Chem.*, **2**, 222 (1937-1938).

Solutions were apparently stable at room temperature for at least one week. Reproducible data were obtained only if this procedure was followed.

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DEPARTMENT OF FOOD TECHNOLOGY
MASSACHUSETTS INSTITUTE OF TECHNOLOGY
CAMBRIDGE, MASS. RECEIVED SEPTEMBER 25, 1950

Some Alkanesulfinic Acids and their Derivatives[1]

BY C. S. MARVEL AND N. A. MEINHARDT

In connection with a study of alkanesulfinic acids as activators in an oxidation-reduction type polymerization recipe[2] we have had occasion to prepare the C_8 to C_{18} even-numbered carbon straight-chain members of the alkanesulfinic acid series and have characterized them with derivatives. The methods of preparation for the acids and derivatives are those recently described for 1-dodecanesulfinic acid.[3]

1-Octanesulfinic acid and 1-decanesulfinic acid are low melting and rapidly become colored in air. They obviously oxidize and/or rearrange very quickly and they have only been prepared in a crude state. Their derivatives, however, have been obtained as pure crystalline compounds.

Experimental.—The magnesium salts of the alkanesulfinic acids were prepared by the method of Houlton and Tartar[4] and converted into the various derivatives by standard methods.[3] The results of the work are presented in the tables.

This series of compounds is unstable and decomposes on standing for a few days. This makes their analysis unsatisfactory.

TABLE I

ALKANESULFINIC ACIDS RSO_2H

Decane	Yield of acid from Mg salt, %	M. p., °C.	Analyses, % Carbon		Hydrogen		Sulfur	
			Calcd.	Found	Calcd.	Found	Calcd.	Found
1-Tetra-	65.5	48–48.4	64.12	64.46	11.43	11.51	12.2	12.06
1-Hexa-	58	54–55	66.21	65.90	11.71	11.58	11.05	11.15
1-Octa.	69.2	60–60.5	67.92	67.68	11.94	12.14	10.05	10.20

TABLE II

N,N-DI-(1-ALKANESULFONYL)-HYDROXYLAMINES $(RSO_2)_2NOH$

	Yield based on sodium salt, %	M. p., °C.	Analyses, % Carbon		Hydrogen		Nitrogen	
			Calcd.	Found	Calcd.	Found	Calcd.	Found
1-Octane	77.1	64–65	49.9	50.02	9.09	9.20	3.64	3.43
1-Decane	91.8	68–69	54.44	54.76	9.73	9.45	3.18	3.06
1-Tetradecane	90	74–75	60.75	60.77	10.68	10.77	2.53	2.45
1-Hexadecane	77	75–75.5	63.1	62.87	11.00	10.83	2.30	2.16
1-Octadecane	78.8	83–84	65.00	65.25	11.28	11.10	2.10	2.06

TABLE III

O-ACETYL-N,N-DI-(1-ALKANESULFONYL)-HYDROXYLAMINES $(RSO_2)_2NOCOCH_3$

	Yield based on hydroxylamine, %	M. p., °C.	Analyses, % Carbon		Hydrogen		Nitrogen	
			Calcd.	Found	Calcd.	Found	Calcd.	Found
1-Octane	65.6	24–25	50.58	50.19	8.66	8.6	3.29	3.00
1-Decane	72.3	43–45	54.66	54.45	9.31	9.66	2.90	2.69
1-Tetradecane	62	54–57.5	60.49	61.25	10.25	10.75	2.35	2.42
1-Hexadecane	65.9	74–75	62.66	63.05	10.59	11.32	2.14	2.19
1-Octadecane	70.4	78–79	64.5	65.10	10.89	11.39	1.98	2.27

TABLE IV

TRI-(1-ALKANESULFONYL)-AMINE OXIDES $(RSO_2)_3NO$

	M. p., °C.	Analyses, % Carbon		Hydrogen		Nitrogen	
		Calcd.	Found	Calcd.	Found	Calcd.	Found
1-Octane	39–40	51.3	51.14	9.26	8.90	2.49	2.76
1-Decane	47–48	55.8	55.86	9.77	9.57	2.17	2.35
1-Tetradecane	69–70	62.0	62.3	10.70	10.45	1.72	1.76
1-Hexadecane	74.5–76	64.25	64.3	11.02	11.25	1.56	1.74
1-Octadecane	76–77	66.06	66.10	11.31	11.49	1.43	1.64

TABLE V

1-ALKANESULFONYLACETIC ACIDS $RSO_2CH_2CO_2H$

	Yield based on sodium salt, %	M. p., °C.	Analyses, % Carbon		Hydrogen	
			Calcd.	Found	Calcd.	Found
1-Octane	82	95–96	50.9	51.2	8.47	8.57
1-Decane	52.6	102–103.5	54.6	54.73	9.09	9.09
1-Tetradecane	47.7	110–111	60.0	60.10	10.00	9.91
1-Hexadecane	47.5	113–114	62.1	62.18	10.34	10.43
1-Octadecane	45	116–117	63.8	64.49	10.62	10.69

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(1) This investigation was carried out under the sponsorship of the Office of Rubber Reserve, Reconstruction Finance Corporation, in connection with the U. S. Government Synthetic Rubber Program.

(2) Office of the Publication Board, U. S. Department of Commerce, Item P. B. No. 1636—Activation of Buna-S Polymerization in Mersolat Emulsion with Reducing Agents, Sherlock Swann, Jr., and N. M. Elias.

(3) C. S. Marvel and R. S. Johnson, *J. Org. Chem.*, **13**, 822 (1948).

(4) H. G. Houlton and H. V. Tartar, THIS JOURNAL, **60**, 544 (1938).

Mixed Diglycerides Containing 4-Arsonophenylglycine[1]

By Robert L. McGeachin and Robert E. Cox

The purpose of this investigation was the preparation of fat-soluble glycerides of 4-arsonophenylglycine, previously unreported in the literature. We have prepared and isolated the calcium salts of mixed diglycerides of myristic, lauric and stearic acids with 4-arsonophenylglycine.

The diglycerides were formed by the reaction of 4-arsonophenylglycine with fatty acid monoglycerides in the presence of diacetin. The free diglycerides formed were always contaminated with fatty acid monoglycerides and we were unable to separate these mixtures by use of any of the usual solvents. However, the calcium salts of the diglycerides were separated from the monoglycerides by extraction of the mixture with chloroform which removed the monoglycerides. It was found that the mixtures of the calcium salts and the monoglycerides must be thoroughly dried prior to the chloroform extraction to prevent formation of unseparable emulsions. All attempts to obtain the free acids from these calcium salts have been unsuccessful due to some hydrolysis of the ester bonds in the presence of acid.

Attempts to form the diglycerides by the reaction of fatty acids with α-4-arsonophenylglycylmonoglyceride were unsuccessful as were condensations of sodium salts of fatty acids with 1-(4-arsonophenylglycyl)-2-hydroxy-3-chloropropane.

Experimental

Fatty acid monoglycerides were prepared by a modification of the method of Hilditch and Rigg[2] using a five molar excess of glycerol and omitting the β-naphthalenesulfonic acid catalyst.

Reaction of Fatty Acid Monoglycerides with 4-Arsonophenylglycine.—Ten grams of 4-arsonophenylglycine, 15 g. of monoglyceride (myristoyl, lauroyl or stearoyl), 5 g. of diacetin and 0.1 g. of zinc chloride were heated at 150° for 4 hours at 20 mm. pressure. The mixture was dissolved in 50 ml. of 95% alcohol, charcoaled and filtered hot. Two hundred ml. of water was added to the filtrate and the mixture placed in the ice-box overnight. The precipitated solids were filtered off, washed with cold water and redissolved in 30 ml. of hot 95% alcohol. The solution was neutralized to a *p*H of 7 with sodium hydroxide and 20 ml. of 10% calcium chloride added, precipitating a white solid. The solid was centrifuged, washed with water and recentrifuged several times. This product was dried over calcium chloride *in vacuo* and extracted three times with chloroform. The yields were 4 to 5 g. (20–25%) of a white powder.

Anal.[3] Calcd. for $C_{46}H_{74}O_{16}N_2As_2Ca$: As, 13.6. Found: As, 13.4. *Anal.* Calcd. for $C_{50}H_{82}O_{16}N_2As_2Ca$: As, 13.0. Found: As, 12.7. *Anal.* Calcd. for $C_{58}H_{98}O_{16}N_2As_2Ca$: As, 11.8. Found: As, 11.5.

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[1] Taken from the M.S. thesis of Robert E. Cox.

[2] T. P. Hilditch and J. G. Rigg, *J. Chem. Soc.*, 1774 (1935).

[3] A modification of the method of F. E. Cislak and C. S. Hamilton, This Journal, **52**, 638 (1930), was used in the arsenic analyses.

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Esterification of Polyvinyl Alcohol with Trifluoroacetic Acid or Anhydride

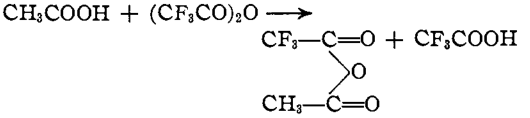
By Paul W. Morgan

The "impelling" action of chloroacetic acids and their anhydrides on the esterification of cellulose by other organic acids was described years ago by Malm and Clarke.[1] This reaction requires an additional catalyst but no esterification by the chloracetic acid takes place when a second carboxylic acid is present. Polyvinyl alcohol, on the other hand, reacts with a mixture of a carboxylic acid and monochloroacetic acid or its anhydride to form a soluble mixed ester[2] with or without the use of a catalyst. Very little esterification of polyvinyl alcohol is obtained with glacial acetic acid alone.

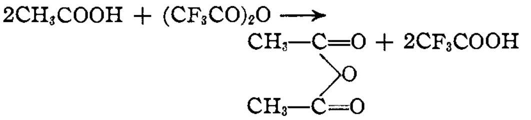
Trifluoroacetic acid or its anhydride differ from monochloroacetic acid because they promote the esterification of polyvinyl alcohol, or other alcohols, by a carboxylic acid without the introduction of trifluoroacetyl groups into the polymer and without the use of any other catalyst. Trifluoroacetic acid acts as an esterification catalyst.

Stacey and his co-workers[3] have described the esterification of various alcohols with carboxylic acids in the presence of relatively large amounts of trifluoroacetic anhydride. A mixed anhydride mechanism was suggested (see equations 1 and 3) but no evidence presented to support it. In their experiments an anhydride to alcohol ratio greater than one was required for good yields of ester. Their experiments seem to show a reaction by means of a mixed anhydride or the anhydride of the carboxylic acid and no, or at least low, catalytic activity on the part of the by-product trifluoroacetic acid.

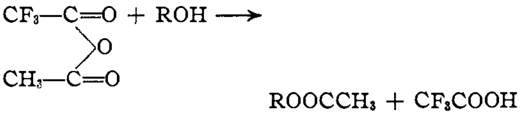
We have obtained evidence from freezing point depressions which indicates that when trifluoroacetic anhydride is added to glacial acetic acid a molecule of mixed anhydride and a molecule of trifluoroacetic acid are formed, in accordance with equation 1, rather than a molecule of new anhydride as shown by the second equation



$$CH_3COOH + (CF_3CO)_2O \longrightarrow \begin{matrix} CF_3—C{=}O \\ \quad \rangle O \\ CH_3—C{=}O \end{matrix} + CF_3COOH \quad (1)$$



$$2CH_3COOH + (CF_3CO)_2O \longrightarrow \begin{matrix} CH_3—C{=}O \\ \quad \rangle O \\ CH_3—C{=}O \end{matrix} + 2CF_3COOH \quad (2)$$



$$\begin{matrix} CF_3—C{=}O \\ \quad \rangle O \\ CH_3—C{=}O \end{matrix} + ROH \longrightarrow ROOCCH_3 + CF_3COOH \quad (3)$$

This supports the hypothesis that esterification of polyvinyl alcohol or other alcohols by a carboxylic acid in the presence of trifluoroacetic anhydride might proceed through the mixed anhydride to form the unhalogenated ester. However, high degrees of acetylation also are easily obtained by adding small amounts of trifluoroacetic acid or its anhydride to a slurry of polyvinyl alcohol in glacial acetic acid. In these cases the yield of ester must come from a direct esterification catalyzed by trifluoroacetic acid.

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[1] H. T. Clarke and C. J. Malm, U. S. Patent 1,880,808 (Oct. 4, 1932); British Patent 313,408 (Aug. 27, 1929).

[2] E. F. Izard and P. W. Morgan, *Ind. Eng. Chem.*, **41**, 619 (1949).

[3] M. Stacey, E. J. Bourne, J. C. Tatlow and T. M. Tedder, *Nature*, **164**, 705 (1949); *J. Chem. Soc.*, 2976 (1949).

In the absence of a second carboxylic acid, polyvinyl alcohol is quite readily esterified with anhydrous trifluoroacetic acid, yielding trifluoroacetyl esters soluble in many common organic solvents. These esters have been found to lack hydrolytic stability, but form tough, flexible, transparent films, which are slightly plasticized by water and which have low flammability. The hydrolytic instability probably results from the catalytic effect of traces of trifluoroacetic acid. Polyvinyl trifluoroacetate has been made previously by Howk and Jacobson by vinyl polymerization[4] and, except for the hydrolytic instability encountered here, the reported properties were quite similar.

Experimental

Esterification with Acetic Acid Plus Trifluoroacetic Acid.—High viscosity polyvinyl alcohol (Elvanol 91A–65 which was pretreated with dilute alkali to assure complete deacetylation; 5 g.) was heated at 90–100° for 2 hours in a mixture of 18 ml. of glacial acetic acid and 1 ml. of trifluoroacetic acid. At one hour a clear viscous solution was obtained. The viscosity dropped some during the second hour. The product was isolated by diluting the solution with acetone and casting a film. The plastic film was soluble in numerous organic solvents and was highly softened by water. The polymer contained no fluorine and was 74.3% substituted by acetyl groups. Trifluoroacetic anhydride, used in place of the trifluoroacetic acid, produced the same product in a somewhat shorter time.

In a similar reaction with glacial acetic acid alone polyvinyl alcohol remained as a white swollen mass and was still easily water soluble.

Esterification with Trifluoroacetic Acid or Anhydride.—Polyvinyl alcohol (5 g.) was mixed with 45 ml. of trifluoroacetic acid and heated under reflux by an oil-bath at 85° with only initial stirring. The powder dissolved in a very few minutes and esterifications were continued for the periods of time given in the table. The products were isolated by diluting the mixture with acetone, casting a film and washing the film with water. The films were freed of excess water and dried at 85°. They softened somewhat in air at 80° and were limp at 100°.

TABLE I

ANALYSIS FOR CF_3CO– GROUPS

Reacn. time, hours	Fluorine,[5] %	Substn. from F analysis, %	Substn. by sapon., %
0.5	36.6	58.3	58.3
1.5	39.9	70.0	69.5
4.0	44.1	89.7	90.2

Esterification of polyvinyl alcohol with trifluoroacetic anhydride or mixtures of anhydride and acid were more rapid than with the acid alone but the final products were similar in properties.

Tests for Interaction of Trifluoroacetic Anhydride and Acetic Acid.—Glacial acetic acid (10 g.) and trifluoroacetic anhydride (19 g., b.p. 40°) were mixed. Considerable heat was evolved but similar heats of mixing were noted for trifluoroacetic acid with acetic acid or acetic anhydride. The mixture was distilled slowly and distillation started at 73°, the boiling point of trifluoroacetic acid. The boiling point rose slowly to 115° and no definite fractions were obtained, although several cuts were made. The higher fractions had the odor characteristic of acetic anhydride. Titration of the fractions gave no indication of a definite composition. Distillation of mixtures of trifluoroacetic and acetic acids and of trifluoroacetic acid and acetic anhydride gave similar results with no indication of constant boiling fractions. Of course with the acids alone, no odor of anhydride was noted.

As a means of distinguishing between no reaction at all and those represented by equations 1 and 2, freezing point depressions in glacial acetic acid were determined, using a Beckmann thermometer and about 30 g. of additive per 1000 g. of acetic acid. A molal depression of 3.90° was used in the calculations.

TABLE II

MOLECULAR WEIGHTS DETERMINED IN GLACIAL ACETIC ACID

Additive	Molal depression	Mol. wt. Calcd.	Mol. wt. Obsd.
Acetic anhydride	3.68	102	108
Trifluoroacetic acid	3.74	114	119
	3.85		115
Trifluoroacetic anhydride	7.93	210	103
	7.34		112

Since the molal depression of trifluoroacetic anhydride is twice that expected from no reaction, equation 1 must represent the reaction. If equation 2 were correct, the freezing point depression would be three times the normal value.

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[4] B. W. Howk and R. A. Jacobson, U. S. Patent 2,436,144 (1948).

[5] Qualitative test: J. H. Simons and E. O. Ramler, THIS JOURNAL, 65, 391 (1943). Quantitative analysis: M. L. Nichols and J. S. Olsen, *Ind. Eng. Chem., Anal. Ed.*, 15, 342 (1943), and N. H. Furman, "Scott's Standard Methods of Chemical Analysis," 5th ed., Vol. I, D. Van Nostrand Co., Inc., New York, N. Y., 1939, p. 405.

Physical Properties of Some 1,1-Difluoro-2,2-dichloroethyl Alkyl Ethers[1,2]

BY J. D. PARK, CURTIS M. SNOW AND J. R. LACHER

We have previously reported on the base-catalyzed action of alkanols on $CF_2=CFCl$,[3] $CF_2—CF_2—CF=CF$[4] and $CF_2—CF_2—CCl=CCl$.[5]

The present study reports on some of the properties of some 1,1-difluoro-2,2-dichloroethyl alkyl ethers obtained by the reaction of $CF_2=CCl_2$ and some alkanols described above.[3,4,5] The

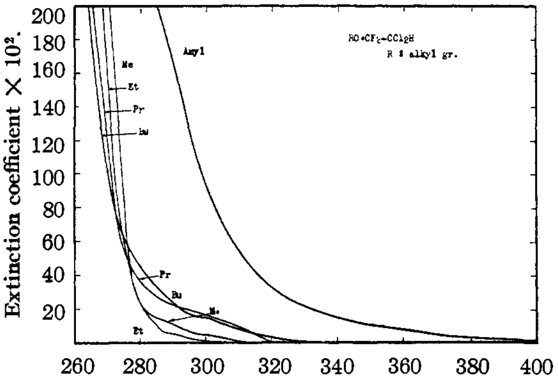

Fig. 1.—Ultraviolet absorption spectra of $ROCF_2–CCl_2H$, R is alkyl group.

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[1] This paper represents part of a thesis submitted by Curtis M. Snow to the Graduate School, University of Colorado, in partial fulfillment of the requirements for the degree Doctor of Philosophy, February, 1950.

[2] This work was supported in part by a grant from the Office of Naval Research, contract N6-onr-231, Task Order 6, project No. NR-056-105.

[3] J. D. Park, D. K. Vail, K. R. Lea and J. R. Lacher, THIS JOURNAL, 70, 1550 (1948).

[4] J. D. Park, M. L. Sharrah and J. R. Lacher, *ibid.*, 71, 2337 (1949).

[5] J. D. Park, C. M. Snow and J. R. Lacher, Abstract of Papers, 118th Meeting of the American Chemical Society, Division of Ind. and Eng. Chemistry, p. 22L.

starting olefin was obtained by dehydrochlorination of $CF_2Cl-CHCl_2$ using a previously described pyrolysis method,[6a,b,c] which consisted of passing $CF_2Cl-CHCl_2$ through a Pyrex tube (65 cm. × 9 mm. i.d.) heated to 650° to give yields of 60–75% of $CF_2{=}CCl_2$ per pass at a contact time of 8–10 seconds.

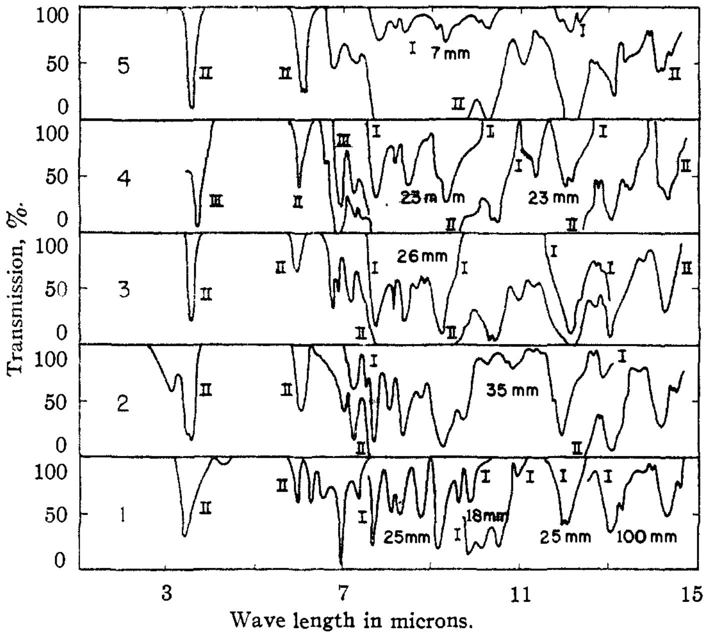

Fig. 2.—The infrared absorption spectrograms at room temperature: I in a 10–cm. gas cell at ind., press., II in a 0.025 mm. liquid cell, and III in a 0.1 mm. liquid cell of (1) $CH_3-O-CF_2CHCl_2$, (2) $C_2H_5-O-CF_2CHCl_2$, (3) $C_3H_7-O-CF_2CHCl_2$, (4) $n-C_4H_9-O-CF_2CHCl_2$, and (5) $n-C_5H_{11}-O-CF_2CHCl_2$.

Some of the physical properties of the ethers are listed in Table I.

TABLE I

PHYSICAL PROPERTIES OF 1,1-DIFLUORO-2,2-DICHLOROETHYLALKYL ETHERS, $R—O—CF_2—CHCl_2$.

R	F.p.	B.p., °C.	B.p., Mm.	d^{20}_4	$n^{25}d$	$M_r{}^a$	$M_r{}^b$	A_rF^c
$-CH_3{}^d$		104	760	1.4226	1.3864	27.26	27.29	1.01
$-C_2H_5{}^e$	Glass	120	760	1.3461	1.3895	31.51	31.91	0.83
$-C_3H_7$	Glass	136.5	760	1.2636	1.3968	36.79	36.53	1.16
$-C_4H_9$	Glass	153	760	1.2184	1.4029	41.79	41.15	1.19
$-C_5H_{11}$	Glass	172.5	760	1.1817	1.4157	49.51	48.74	1.41

R	Chlorine, % Calcd.	Chlorine, % Found	Molecular weight Calcd.	Molar susceptibility × 10^6 Calcd.	Molar susceptibility × 10^6 Found
$-CH_3$	42.99	42.76	164.99	− 97.53	− 80.68
$-C_2H_5$	39.61	39.61	179.02	−109.39	− 96.13
$-C_3H_7$	36.73	36.48	193.05	−121.25	−107.19
$-C_4H_9$	34.24	34.28	207.08	−133.11	−119.48
$-C_5H_{11}$	32.07	31.88	221.11	−144.97	−129.84

[a] M_r denotes the molecular refraction calculated by the Lorentz–Lorenz formula. [b] M_r denotes the molecular refraction calculated by adding the customary increments for C, H, O, F and double bond (F = 1.03). [c] A_rF is the atomic refraction of fluorine, obtained from M_ra by subtracting the customary increments for C, H, O and the double bond. [d] W. T. Miller, E. W. Fager and P. H. Griswold, THIS JOURNAL, **70**, 431 (1948). [e] T. B. Gowland, British Patent 523,449; *C.A.*, **35**, 6265 (1941).

The ultraviolet absorption spectra of the ethers were measured with a Beckman quartz spectrophotometer model DU. The measurements were made on the pure liquids with an empty reference cell. The quartz cells were 1 cm. long. The extinction coefficient, E, defined by $\log I/I_0 = -El$ was measured; l is the length of the cell in cm. (unity in the present case). The results are given in Fig. 1.

The infrared absorption spectra were measured using an automatic recording Perkin–Elmer infrared spectrometer, model 12B with beam chopper attached. The samples were run in a 0.1 mm. liquid cell, a 0.025 mm. liquid cell or in a 10 cm. gas cell. The results are given in Fig. 2 where per cent. transmission is plotted against wave length in microns. Some qualitative assignments of the peaks are possible using the data of Barnes, *et al.*[7] The strong absorption appearing at 3.37–3.68 microns is due to C–H stretching in alkyl groups. A C–H bending absorption appears at 6.78–6.93. The absorption due to C–O stretching in a saturated ether is strong in the region 9.22–9.32 and is characteristic. The molar diamagnetic susceptibilities measured by the Quincke tube method[8] show a fairly constant deviation from the additive values obtained using Pascal's constants. This deviation is probably due to interaction forces between non-bonded atoms directed along the edges of a tetrahedron.[8,9]

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[6] (a) P. Torkington and H. W. Thompson, *Trans. Faraday Soc.*, **41**, 236 (1945); (b) F. B. Downing, A. F. Benning and R. C. McHarness, U. S. Patent 2,387,247; (c) A. F. Benning, F. B. Downing and J. D. Park, U. S. Patent 2,406,794.

[7] R. B. Barnes, R. C. Gore, R. W. Stafford and V. Z. Williams, *Anal. Chem.*, **20**, 402 (1948).

[8] J. R. Lacher, R. E. Scruby and J. D. Park, THIS JOURNAL, **71**, 1797 (1949).

[9] J. R. Lacher, *ibid.*, **69**, 2067 (1947).

Aromatization of Cyclic Compounds by Solid Potassium Perchlorate

BY SAUL PATAI AND LEON RAJBENBACH

In the course of a study of heterogeneous oxidation processes by solid inorganic oxidants[1] we have investigated the reaction of solid potassium perchlorate with aromatic hydrocarbons such as toluene, naphthalene and phenanthrene. Such compounds are generally oxidized without difficulty to the corresponding acids or quinones by various oxidants. Although potassium perchlorate is a powerful oxidizing agent, heating at 370–440° left the mixtures practically unchanged apart from the production of small amounts of potassium chloride and some carbonaceous material. At higher temperatures, approaching the decomposition temperature of potassium perchlorate (510°[2]), very rapid reaction takes place resulting in the explosion of the glass ampoules used.

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[1] Patai and Hoffmann, THIS JOURNAL, **72**, 5098 (1950).

[2] Marvin and Woolaver, *Ind. Eng. Chem., Anal. Ed.*, **17**, 474 (1945).

TABLE I

DEHYDROGENATION BY SOLID POTASSIUM PERCHLORATE

Organic compound, grams	$KClO_4$, g.	Reaction time, hr.	Reaction temp., °C.	Product (identification)	Yield,[a] % A	Yield,[a] % B
4.8 Tetralin	10	18	370	Naphthalene (picrate)	94	87
1.75 Decalin	4.4	18	380	Naphthalene (picrate)	58	92
4.1 Cyclohexene	5	24	350	Benzene (*m*-dinitrobenzene)	5[b]	13[b]
1.9 Cyclohexanol	7.5	14	380	Phenol (tribromophenol)	4.8	22
1.9 Cyclohexanone	7.5	9	375	Phenol (tribromophenol)	2.5	2.5
1.8 3-Methylcyclohexanone	7.5	13	375	*m*-Cresol (tribromocresol)	17	14

[a] Yield A calculated on basis of the organic starting material, yield B calculated on basis of the amount of potassium perchlorate which decomposed (determined as chloride). [b] Dinitration of benzene in the presence of cyclohexene gave poor yields. The actual yield of benzene was probably much higher than the stated value.

In an attempt to obtain phthalic acid from tetralin instead of naphthalene, the reaction surprisingly produced an excellent yield of naphthalene only.

The same reaction, *i. e.*, dehydrogenation to the corresponding aromatic compound, was observed on allowing potassium perchlorate to react at 350–380° with decalin, cyclohexene, cyclohexanol, cyclohexanone and 3-methylcyclohexanone. All reactions were carried out in heavy-walled Pyrex tubes, using an excess of potassium perchlorate (200 mesh). The closed tubes were inserted in iron tubes and heated in an electric furnace behind a steel protecting plate, as heavy explosions may occur due to accidental overheating or to faulty ampoules. The results of preliminary experiments are summarized in Table I. No systematic effort has been made to improve the yields.

The reaction of alicyclic compounds with solid potassium perchlorate appears to be a new route to the corresponding aromatic compounds. The mechanism of the reaction, as well as its possible synthetic applications are now being investigated.

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RECEIVED JULY 10, 1950

Studies on Lignin and Related Products. IV.[1] Separation of Syringaldehyde and Vanillin by Chromatography[2]

BY IRWIN A. PEARL AND EDGAR E. DICKEY

For many years the quantitative separation of syringaldehyde and vanillin from the bisulfite-soluble fractions of angiosperm lignin reaction mixtures has offered a problem to the lignin chemist. Hibbert and co-workers[3] have proposed a number of methods based upon differential solubilities of their potassium and ammonium salts in ethanolic solution and upon fractional sublimation in high vacuum. Bland[4] has reported recently the qualitative separation of syringaldehyde and vanillin by paper partition chromatography but this method is limited to very small quantities and its quantitative adaptation presents numerous difficulties. The present paper reports a relatively simple chromatographic procedure for the quantitative separation of these two aldehydes. The procedure is a modification of a general chromatographic method originally employed by McNeely, Binkley and Wolfrom[5] for the separation of sugar acetates. An acid washed Magnesol[6] absorbent and a petroleum ether–ethanol developer successfully separated these two aldehydes. The colorless zones were located by five streak reagents which were applied with capillary-tipped pipets in a manner similar to the brush technique. With these pipets it was possible to apply a narrow, uniform streak to the extruded columns.

All melting points are uncorrected.

Acid-washed Magnesol.[7]—A mixture of Magnesol and Celite No. 535[8] (5:1 by weight) was prepared and suspended with mechanical stirring in sufficient dilute hydrochloric acid (1:3) to form a free-flowing slurry. The slurry was filtered on a Büchner funnel and washed with distilled water until free of chloride ions (by the silver nitrate test). The water was displaced with acetone, and the adsorbent was air dried at room temperature overnight and then at 110° for an additional 18 hours.

Separation of Vanillin and Syringaldehyde.—A solution of 23.4 mg. of syringaldehyde and 25.2 mg. of vanillin in 5 ml. of benzene was adsorbed on a column (18 mm. in diameter and 140 mm. long) of acid-washed Magnesol, and the

TABLE I

STREAK REAGENTS APPLIED TO CHROMATOGRAMS OF SYRINGALDEHYDE AND VANILLIN

Reagent	Behavior with syringaldehyde	Behavior with vanillin
2,4-Dinitrophenylhydrazine (satd. solution in 2 *N* HCl)	Deep orange	Deep orange
Potassium permanganate (1% $KMnO_4$ in 10% aqueous NaOH)	Fast reduction	Slow reduction
Phloroglucinol (satd. solution in concd. HCl)	Orange-red	Orange-red
Ferric chloride (5% $FeCl_3$ in water)	Very light gray	No reaction
Mäule test (satd. chlorine water followed in 2 min. by 5% aqueous sodium sulfite)	Cerise	No reaction

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[1] For Part III of this series, see THIS JOURNAL, **72**, 2309 (1950).

[2] This paper represents a portion of the results obtained in the research program sponsored by the Sulphite Pulp Manufacturers' Research League and conducted for the League by The Institute of Paper Chemistry. Acknowledgment is made by the Institute for permission on the part of the League to publish these results.

[3] (a) M. J. Hunter and H. Hibbert, THIS JOURNAL, **61**, 2190 (1939). (b) J. J. Pyle, L. Brickman and H. Hibbert, *ibid.*, **61**, 2198 (1939). (c) R. H. J. Creighton, J. L. McCarthy and H. Hibbert, *ibid.*, **63**, 3049 (1941).

[4] D. E. Bland, *Nature*, **164**, 1093 (1949).

[5] W. H. McNeely, W. W. Binkley and M. L. Wolfrom, THIS JOURNAL, **67**, 525 (1945).

[6] A synthetic hydrated magnesium acid silicate manufactured by Westvaco Chlorine Products Company, South Charleston, West Virginia.

[7] This procedure was developed by one of the authors (E. E. D.) in the laboratory of Dr. M. L. Wolfrom at The Ohio State University.

[8] A siliceous filter-aid manufactured by Johns-Manville Company, New York, N. Y.

chromatogram was developed with 100 ml. of 50:1 petroleum ether (65–110°)-ethanol. The column was extruded and streaked with the reagents as shown in Table I, using capillary-tipped pipets which were drawn from about 10-cm. lengths of thick-walled 8-mm. (o.d.) Pyrex tubing. The tips were ground with emery until an orifice of approximately 0.1 mm. was formed, and the pipets were operated with 1-ml. medicine dropper bulbs.

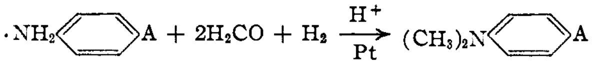
Syringaldehyde occupied a well-defined zone between 39 and 65 mm. from the top of the chromatographic column, and vanillin an equally well-defined zone at 97 to 124 mm. Each zone was eluted with 50 ml. of acetone, the solvent was evaporated under a current of air on a steam-bath, and the recovered crystalline substances were air dried and weighed. Vanillin melting at 76–79° and syringaldehyde melting at 108–110.5° were recovered in yields of 99 and 98%, respectively. Single recrystallizations from water of these recovered aldehydes yielded vanillin melting at 81–82° and syringaldehyde melting at 111–112°, which were identical with those of the original materials.

INSTITUTE OF PAPER CHEMISTRY
APPLETON, WISCONSIN
RECEIVED AUGUST 28, 1950

Reductive Methylation of Amines

BY D. E. PEARSON AND J. D. BRUTON

Reductive methylation is seldom used as a means of preparation of tertiary aromatic amines because of facile nuclear condensation.[1] However, it has been possible in this Laboratory to accomplish the following reductive methylations of which the first two (I and II) are much the preferred methods of preparation



A = $COCH_3$, yield 70% I
A = COOH, yield 87% II
A = H, yield 74% III (as picrate)

Also, the reductive methylation of glycine yielded 79% N,N-dimethylglycine.

The essential feature of the first two preparations was the avoidance of an excess of formaldehyde. The essential feature of the third preparation was the use of a slowly-generating source of formaldehyde, trioxane, as well as a limited concentration of the same.

It is interesting to note that previous attempts to prepare *p*-dimethylaminoacetophenone (I) have been quite frustrating,[2] the best yield reported being 3%.[3]

Experimental[4]

***p*-Dimethylaminoacetophenone** (I).—*p*-Aminoacetophenone (0.1 mole, Eastman Kodak Co. White Label) was dissolved in a mixture of 80 ml. of 95% ethyl alcohol and 5 ml. of concd. hydrochloric acid and cooled to 5°. In another flask, 15 ml. of formalin (40%, W. H. Curtin Co., 0.2 mole) was similarly cooled. The contents of both flasks were mixed in a Burgess–Parr reduction container with 0.15 g. of pre-reduced Adams catalyst and reduced at 45 lb. total hydrogen pressure in the usual manner. About 88 to 95% of the theoretical hydrogen was absorbed in 45 minutes; the ketone group was apparently not subject to hydrogenation under these conditions. The solution was then filtered, neutralized to color change,[5] and diluted with water to incipient cloudiness. After refrigeration, I was removed by filtration. Further dilution of the filtrate yielded more I. After air-drying, I was recrystallized from petroleum ether (b.p. 69–70°); 11.5 g., 70%; m.p. 102–104°; reported,[3] m.p. 105.5°; mixed m.p. with *p*-aminoacetophenone, 67–73°. The following variations lowered the yield: (1) delay in reducing after mixing all components,[6] (2) increase in molar ratio of formalin, (3) decrease in acid concentration, (4) re-use of Adams catalyst.

***p*-Dimethylaminobenzoic Acid** (II).—*p*-Aminobenzoic acid (recrystallized, 0.1 mole) was reductively methylated exactly as above. Despite the fact that the mixture was heterogeneous, the reduction went smoothly to completion in 1 hour. The solution was then made slightly basic with ammonium hydroxide, filtered to remove the catalyst, concentrated to one-third its volume and acidified while still hot. Refrigeration, filtration and air-drying yielded II, 14.4 g., 87%; m.p. 236.5–237.5°; reported, m.p. 233°. The above preparation is mentioned in the patent literature.[7]

Dimethylaniline (III).—Though of no preparative value in this specific case, reductive methylation of aniline revealed no evidence of nuclear condensation products under the following conditions. Aniline hydrochloride (Baker and Adamson, 13 g., 0.1 mole) was dissolved in a solution of water (50 ml.), sulfuric acid (50 ml.) and alcohol (50 ml.). The solution was cooled to 0° and poured into the container of a Burgess–Parr hydrogenation apparatus over pre-reduced Adams catalyst (0.15 g.). Trioxane (6.5 g., 0.072 mole, Eastman Kodak Co. Practical) was added and reduction at 45 lb. total pressure of hydrogen was begun. After an initial lag until the solution had warmed, the reduction proceeded at a slow rate and was discontinued after 7 hours when 88% of the theoretical amount of hydrogen had been absorbed. The solution was then filtered, made alkaline and extracted with ether. The ether was removed by distillation and the residue dissolved in 100 ml. of methyl alcohol containing 0.1 mole of picric acid. Refrigeration and filtration yielded dimethylaniline picrate (26.1 g., 74%; m.p. 156–158°). This included crops from the mother liquor.

N,N-Dimethylglycine.—Glycine (7.5 g., 0.1 mole) was dissolved in 40 ml. of water, 5 ml. of concentrated hydrochloric acid and 20 ml. of formalin (40%, 0.26 mole) and reduced as described. The solution was filtered to remove the catalyst, treated with 30 ml. of concd. hydrochloric acid and concentrated to a thick sirup. On cooling, the resultant crystals were filtered and recrystallized from glacial acetic acid. Yield of N,N-dimethylglycine hydrochloride was 22.2 g., 79%; m.p. 185–187°; reported, m.p. 183–184°. A similar preparation is reported but no yield given.[8]

DEPARTMENT OF CHEMISTRY
VANDERBILT UNIVERSITY
NASHVILLE 4, TENN.
RECEIVED SEPTEMBER 5, 1950

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[1] W. S. Emerson in Adams, "Organic Reactions," Vol. IV, John Wiley and Sons, Inc., New York, N. Y., 1949, p. 194.

[2] C. D. Hurd and C. N. Webb, THIS JOURNAL, **49**, 551 (1927); J. Klingel, *Ber.*, **18**, 2694 (1885).

[3] H. Staudinger and N. Kon, *Ann.*, **384**, 111 (1911).

[4] All melting points were taken with partial immersion thermometer, A. S. T. M. specification.

[5] The mixture serves as its own indicator: red in acid; yellow in basic solution.

[6] F. C. Wagner, THIS JOURNAL, **55**, 724 (1933).

[7] A. Skita and W. Stuhmer, German Patent 716,668; *C. A.*, **38**, 2345 (1945).

[8] R. E. Bowman and H. H. Stroud, *J. Chem. Soc.*, 1342 (1950).

Preparation of α,α-Diphenylpropionitrile[1]

BY P. L. PICKARD AND E. F. ENGLES[2]

While the literature contains several references[3,4,5,6,7] to the preparation of α,α-diphenylpropionic acid, no method suitable for the synthesis of large quantities of the corresponding nitrile are given. The ease of methylation of phenylace-

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[1] This work was done with the support of the Office of Naval Research.

[2] Presented as a portion of a dissertation in partial satisfaction of the requirements for the Ph.D. in chemistry at the University of Oklahoma.

[3] C. Bottinger, *Ber.*, **14**, 1595 (1881).

[4] H. Meerwein, *Ann.*, **396**, 260 (1913).

[5] W. Thorner and Th. Zincke, *Ber.*, **11**, 1993 (1878).

[6] H. Staudinger and P. Meyer, *Helv. Chim. Acta*, **5**, 670 (1922).

[7] D. E. Bateman and C. S. Marvel, THIS JOURNAL, **49**, 2917 (1927).

tonitrile using sodamide[8] suggested a similar preparation from diphenylacetonitrile. The proposed alkylation was carried out with methyl iodide, using sodium hydride as the alkylating catalyst. The yield on several preparations varied between 80–90%. The product was identified by its physical constants, by analysis, and by hydrolysis to the corresponding amide and acid.

Experimental.—To 32.5 g. (1.35 moles) of sodium hydride and 175 ml. of anhydrous diethyl ether in a three-necked round-bottom flask was added 262 g. (1.35 moles) of diphenylacetonitrile dissolved in 375 ml. of dry benzene and 100 ml. of diethyl ether. Addition was dropwise over a period of 3 hours. The mixture was refluxed for 30 hours. To the cooled reaction mixture was added 192 g. (1.35 moles) of methyl iodide in 100 ml. of benzene dropwise over a period of 6 hours. Sodium iodide was precipitated immediately. After cooling, the mixture was washed with cold 10% acetic acid to destroy any unreacted sodium hydride. The product was extracted with benzene and ether and dried over calcium chloride. Distillation yielded a highly colored fraction boiling constantly at 135° at 1 mm. pressure. This fraction was dissolved in 500 ml. of ether and treated with 80 g. of adsorption alumina, filtered and redistilled. The product boiling constantly at 142° at 2 mm. pressure weighed 227 g. (1.096 moles, 80.7%); $n^{20}\text{D}$ 1.5744, $d^{20}{}_4$ 1.0671; $MR\text{D}$ 64.13 (calcd. $MR\text{D}$ 64.03).

Anal. Calcd. for $C_{15}H_{13}N$: N, 6.76. Found: N, 6.94.

To 14 g. of potassium hydroxide in sufficient absolute ethanol to effect solution was added 5 g. of α,α-diphenylpropionitrile, and the solution refluxed for 168 hours. Slight evolution of ammonia was detected during the hydrolysis. The reaction mixture was poured into 200 ml. of water and 4 g. of crude amide recovered. Recrystallization from *n*-heptane produced a material melting at 103–104°.[9] Acidification of the filtrate from the crude product produced a small amount of α,α-diphenylpropionic acid melting at 173–174°.[10]

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[8] H. Adkins and G. M. Whitman, THIS JOURNAL, **64**, 150 (1942).

[9] H. Wieland and E. Dorrer, *Ber.*, **63B**, 407 (1930), report the m.p. as 103-104°. Bateman (ref. 7) gives m.p. as 149°.

[10] Thorner and Zincke (ref. No. 7) report the m.p. as 173-174°.

DEPARTMENT OF CHEMISTRY AND THE RESEARCH INSTITUTE
THE UNIVERSITY OF OKLAHOMA
NORMAN, OKLAHOMA
RECEIVED OCTOBER 2, 1950

Studies in Silico-organic Compounds. XI. Products Resulting from the Action of Benzylmagnesium Chloride on Triethoxysilane[1]

BY ALBERT L. REILLY AND HOWARD W. POST

Incidental to the study of certain other reactions, benzylmagnesium chloride was allowed to react with triethoxysilane in different molar ratios. Benzyldiethoxysilane, dibenzylethoxysilane and tribenzylsilane were formed.

Triethoxysilane (25 g., 0.15 mole) in 150 cc. of anhydrous ether was treated, with stirring, with 147 cc. of a 1.02 *M* solution of benzylmagnesium chloride in anhydrous ether (0.15 mole). After standing overnight at reflux temperature, the solid residue was separated and the ethereal layer was fractionated. Benzyldiethoxysilane was isolated, 3.9 g., 12% yield, b.p. 108–109° (5 mm.), $n^{25}\text{D}$ 1.4666, $d^{25}{}_{25}$ 0.9782.

Anal. Calcd. for $C_{11}H_{18}SiO_2$: Si, 13.3; silane hydrogen (caustic treatment), 0.477; *MR*, 61.06. Found: Si, 12.9; silane hydrogen, 0.454; *MR*, 59.63.

Using double the relative amount of benzylmagnesium chloride, dibenzylethoxysilane was formed, 8 g., 20% yield, b.p. 141–143° (5 mm.), $n^{25}\text{D}$ 1.5370, $d^{25}{}_{25}$ 0.9945.

Anal. Calcd. for $C_{16}H_{20}SiO$: Si, 11.9: silane hydrogen, 0.390; *MR*, 80.08. Found: Si, 11.6; silane hydrogen, 0.380; *MR*, 80.38.

When 0.042 mole of triethoxysilane was allowed to react with 0.153 mole of benzylmagnesium chloride as above, tribenzylsilane was formed, 3 g., 23% yield, m.p. found 90–91°, literature[2,3] 91°.

Anal. Calcd. for $C_{21}H_{22}Si$: Si, 9.3; silane hydrogen, 0.331. Found: Si, 9.1; silane hydrogen, 0.320.

A greater degree of purity could not be attained for benzyldiethoxysilane in spite of careful fractionation and careful attention to the purity of reagents. Triethoxysilane was prepared in accordance with a method already in use.[4]

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[1] This work was made possible by a grant from the Office of Naval Research, under contract.

[2] Evison and Kipping, *J. Chem. Soc.*, 2830 (1931).

[3] Jenkins and Post, *J. Org. Chem.*, **15**, 552 (1950).

[4] Havill, Joffe and Post, *ibid.*, **13**, 280 (1948).

THE UNIVERSITY OF BUFFALO
BUFFALO 14, N. Y.
RECEIVED AUGUST 4, 1950

1,1-Bis-(*p*-methoxyphenyl)-1-propene

BY KURT RORIG

From the aluminum chloride catalyzed reaction of propionyl chloride with anisole in carbon disulfide solvent, Gattermann[1,2] has isolated a by-product melting at 100 to 101° in addition to the expected *p*-methoxypropiophenone. Because this by-product gave *p,p'*-dimethoxybenzophenone upon chromic oxide oxidation, Gattermann considered it to be 1,1-bis-(*p*-methoxyphenyl)-1-propene. Gattermann rationalized its formation by assuming that the first-formed *p*-methoxypropiophenone condensed with a second molecule of anisole to give 1,1-bis-(*p*-methoxyphenyl)-1-propene and a molecule of water.

Much later, Skraup and Freundlich[3] prepared 1,1-bis-(*p*-methoxyphenyl)-1-propene by an unequivocal synthesis from *p,p'*-dimethoxybenzophenone and ethylmagnesium bromide. They found that the propene so prepared also melted at 101. However this propene differed in all other respects from the product they obtained by a repetition of Gattermann's experiment. Therefore they concluded that Gattermann had been in error.

By a repetition of Gattermann's work we were able to show that he was indeed correct in formulating the Friedel–Crafts product $C_{17}H_{18}O_2$, m. p. 100–101°, as 1,1-bis-(*p*-methoxyphenyl)-1-propene.

Experimental

Sixty grams of anhydrous aluminum chloride was added, as rapidly as the exothermic reaction allowed, to a solution of 50 g. of anisole and 50 g. of propionyl chloride in 100 ml. of carbon disulfide. After allowing the mixture to stand one-half hour it was carefully decomposed with water and extracted with ether. Upon evaporation of the dried ether extract 62 g. of yellow, semi-crystalline material remained. After two crystallizations from 95% ethanol this gave 23.5 g. of faintly yellowish plates melting 99.5–100.5°.

Anal. Calcd. for $C_{17}H_{18}O_2$: C, 80.28; H, 7.13; OCH_3, 24.41. Found: C, 80.40; H, 7.22; OCH_3, 24.50.

This product gave a deep-red color when dissolved in concentrated sulfuric acid. The melting point of a mixture of this product, m.p. 99.5–100.5°, with some of the 1,1-bis-(*p*-methoxyphenyl)-1-propene, m.p. 99–100°, prepared by Skraup's Grignard synthesis[3] was 99.5–100.5°.

RESEARCH LABORATORIES
G. D. SEARLE AND COMPANY
SKOKIE, ILLINOIS
RECEIVED SEPTEMBER 5, 1950

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[1] L. Gattermann, *Ber.*, **22**, 1129 (1889).

[2] L. Gattermann, R. Ehrhardt and H. Maisch, *ibid.*, **23**, 1199 (1890).

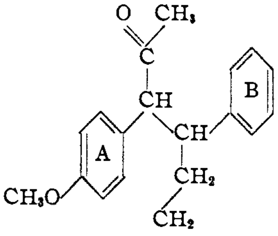
[3] S. Skraup and L. Freundlich, *Ann.*, **431**, 269 (1923).

3-(*p*-Methoxyphenyl)-4-phenyl-2-hexanone and Derivatives

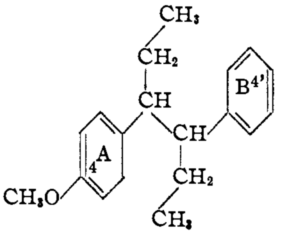
BY DANIEL R. SATRIANA, ATHANASIOS LOTER AND MANUEL M. BAIZER

Hager and Burgison[1] have reported the synthesis of 4,4′-bis-(acetoxyacetyl)-α,α′-diethylstilbene as part of a study of synthetic analogs of the adrenal cortical hormones.

In related work whose objective is the preparation of "open model" aromatic compounds which have a keto group in a position corresponding formally to the 11-oxygen function of corticosterone and its important derivatives (*e. g.*, Kendall's compounds A, E and F), we have prepared and characterized one of the *dl*-forms of 3-(*p*-methoxyphenyl)-4-phenyl-2-hexanone (I) and certain of its derivatives.



I



II

Brownlee and Duffin[2] claim the successful introduction of an acetyl or substituted acetyl group into the 4′-position of II by a Friedel–Crafts reaction between II and an appropriate acyl halide; 4-methoxy-4′-glycolyl-α,α′-diethyldibenzyl, so prepared, is claimed to have corticosterone-like activity.[3]

When I in carbon disulfide was treated with acetylglycolyl chloride and excess anhydrous aluminum chloride,[4] 83% of starting material was recovered unchanged and no other identifiable product was obtained. With chloroacetyl chloride, I yielded *ca.* 35% of a halogen-containing product (III) melting at 78–80°. However, analysis of III indicated that the desired product, if formed at all, was present in only small quantity.

The presence of a carbonyl group is known to impede the Friedel–Crafts reaction.[5] In view of the fact, however, that compounds in which the carbonyl group is separated (by one or more methylenes) from the ring-to-be-substituted have been successfully acylated,[6] the deactivation of ring B of I is surprising. Investigation of the reactivity of the other *dl*-form of I might clarify the respective roles of the carbonyl group and of steric factors in this impedance.

Acknowledgment.—We wish to express our appreciation to Dr. W. G. Bywater, S. B. Penick and Co., for many helpful discussions.

Experimental

***p*-Methoxy-α-cyanostilbene (IV).**—This compound was obtained in 67.5% yield by the condensation of benzaldehyde and *p*-methoxybenzyl cyanide.[7]

α-(*p*-Methoxyphenyl)-β-phenylvaleric Acid (V).—The reaction of IV with ethylmagnesium bromide followed the procedure used by Hunter and Korman[8] in a similar case. The mixture of isomeric α-(*p*-methoxyphenyl)-β-phenylvaleronitriles was obtained in 98–100% crude yield. A mixture of 23.5 g. of sodium hydroxide, 46.5 ml. of water and 78.3 g. of these nitriles was heated under reflux for 46 hours. The reaction mixture was diluted with 700 ml. of water and filtered hot. The filtrate was chilled, acidified with dilute hydrochloric acid and extracted with three 150-ml. portions of ether. The combined ethereal extracts were extracted with three 150-ml. portions of 2.5% sodium hydroxide. Acidification of the alkaline solution caused the precipitation of 11.6 g. of crude V, m.p. 174–177°; ether extraction of the filtrate followed by evaporation of the ether and recrystallization of the residue (56 g.) from 95% ethanol yielded an additional 14 g. of similar material. Recrystallization of crude V from 95% ethanol provided the analytical sample, m.p. 180–181°.

Anal.[9] Calcd. for $C_{18}H_{20}O_3$: C, 76.03; H, 7.09. Found: C, 76.03; H, 7.25.

From the alcoholic mother liquors there was isolated *ca.* 12 g. of the other isomeric acid, which, after two recrystallizations from 95% ethanol, melted at 147–148°.

Anal. Calcd. for $C_{18}H_{20}O_3$: C, 76.03; H, 7.09. Found: C, 76.04; H, 7.19.

3-(*p*-Methoxyphenyl)-4-phenyl-2-hexanone (I).—The acid chloride from 19.9 g. (0.07 mole) of V was allowed to react in dry benzene with dimethylcadmium prepared from 12.84 g. (0.07 mole) of anhydrous cadmium chloride.[10] After a two-hour reflux period, the reaction mixture was cooled and poured into 250 ml. of dilute hydrochloric acid. The organic layer was separated; the aqueous solution was extracted with three 100-ml. portions of ether. The organic solutions were combined, washed with water, dried and distilled to dryness. The residue was heated under reflux for 90 minutes with 250 ml. of 1% sodium hydroxide. The solution was cooled and extracted three times with ether. From the alkaline solution 4.9 g. of crude V was recovered. The ether solution on evaporation to dryness yielded 15.9 g. of solid which after recrystallization from 95% ethanol gave 5.9 g. of I, m.p. 95–99°. An additional 0.7 g. of I was recovered from the alcoholic mother liquor by evaporating to dryness and distilling the residue at 168–170° (4 mm.). The sample for analysis was recrystallized from 95% ethanol; m.p. 104–105°.

Anal.[9] Calcd. for $C_{19}H_{22}O_2$: C, 80.81; H, 7.90. Found: C, 80.36; H, 8.13.

The dinitrophenylhydrazone was prepared in the usual manner,[11] and recrystallized from 90% ethanol; m.p. 145–147°.

Anal.[9] Calcd. for $C_{25}H_{26}O_5N_4$: C, 64.86; H, 5.67; N, 12.12. Found: C, 65.17; H, 5.89; N, 11.67.

3-(*p*-Hydroxyphenyl)-4-phenyl-2-hexanone.—A mixture of 2.0 g. of I, 20 ml. of glacial acetic acid and 8.0 ml. of 48% hydrobromic acid was heated under reflux for 6 hours, cooled and poured into water. The aqueous solution was extracted with three 75-ml. portions of ether. The combined ether extracts were washed with water, sodium bicarbonate and then water. Washings were discarded. The ethereal solution was extracted with 5% sodium hydroxide, the alkaline solution acidified and extracted with ether.

---

[1] G. P. Hager and R. M. Burgison, *J. Am. Pharm. Assn., Sci. Ed.*, **39**, 7 (1950).

[2] G. Brownlee and W. M. Duffin, U. S. Patent 2,376,415, May 22, 1945.

[3] W. R. Biggerstaff and A. L. Wilds, THIS JOURNAL, **71**, 2132 (1949), synthesized the very closely related 3-(*p*-acetoxyacetylphenyl)-4-(*p*-acetoxyphenyl)-hexane and found it inactive at 2-mg. daily doses in life-maintenance tests on adrenalectomized rats; *cf.* W. C. J. Ross, *J. Chem. Soc.*, 538 (1945).

[4] In this and subsequently attempted Friedel-Crafts reactions a large excess of catalyst was used in order to compensate for the quantity that was expected to be bound by the keto-group of I. *Cf.* Gilman, "Organic Chemistry, an Advanced Treatise," Vol. I, second edition, John Wiley and Sons, Inc., New York, N. Y., 1943, p. 184.

[5] Berliner, in Adams, "Organic Reactions," Vol. V, John Wiley and Sons, Inc., New York, N. Y., 1949, p. 233.

[6] W. Borsche and F. Sinn, *Ann.*, **553**, 260 (1942).

[7] J. B. Niederl and A. Ziering, THIS JOURNAL, **64**, 885 (1942).

[8] J. H. Hunter and J. Korman, *ibid.*, **70**, 3424 (1948).

[9] Schwarzkopf Microanalytical Laboratory, Middle Village, L. I., N. Y.

[10] *Cf.* W. R. Biggerstaff and A. L. Wilds, THIS JOURNAL, **71**, 2136 (1949).

[11] Shriner and Fuson, "Identification of Organic Compounds," second edition, John Wiley and Sons, Inc., New York, N. Y., 1940, p. 143.

The ethereal solution, upon washing, drying, and evaporating left 1.21 g. of solid which, after recrystallization from ethanol–benzene–ligroin, yielded 0.18 g. of the phenolic ketone, m.p. 184–186°.

Anal.[9] Calcd. for $C_{18}H_{20}O_2$: C, 80.58; H, 7.53. Found: C, 80.52; H, 7.83.

The acetoxy derivative was prepared in the usual manner.[12]

Anal.[9] Calcd. for $C_{20}H_{22}O_3$: C, 77.41; H, 7.15. Found: C, 77.59; H, 7.54.

Attempts to Acylate I by a Friedel–Crafts Reaction. (a) **With Acetylglycolyl Chloride.**—A solution of 2.00 g. of I (0.007 mole) and 1.06 g. (0.007 mole) of acetylglycolyl chloride in 50 ml. of carbon disulfide was chilled to 5°. Over a period of 20 minutes 2.77 g. (0.021 mole) of anhydrous aluminum chloride was added with mechanical stirring. The mixture was allowed to come to room temperature and then heated under reflux for 5 hours. It was then cooled and poured into 40 ml. of 10% hydrochloric acid. The layers were separated, the aqueous solution was extracted twice with carbon disulfide. The combined organic layers were dried and evaporated. The residue (1.8 g.), after recrystallization from ethanol, yielded 1.66 g. of solid, m.p. 98–100°, giving no depression in a mixture melting point with I.

(b) **With Chloroacetyl Chloride.**—The reaction was carried out as described above. The residue (1.8 g.) remaining after the evaporation of the carbon disulfide was heated *in vacuo* to distill out unchanged I. The residual sirup, after several crystallizations from alcohol–water, yielded 0.88 g. of III, m.p. 78–80°, giving a positive Beilstein halogen test. Analysis showed 3.50% of chlorine instead of the anticipated 9.88%.

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(12) Reference 11, p. 138.

THE NEW YORK QUININE & CHEMICAL WORKS, INC.
BROOKLYN, NEW YORK
RECEIVED SEPTEMBER 14, 1950

Some Amides of Tuberculostearic Acid

BY DAVID A. SHIRLEY AND GUSTAV A. SCHMIDT[1]

Tuberculostearic acid or 10-methyloctadecanoic acid is a naturally occurring fatty acid of unique structure isolated by Anderson and Chargaff[2] from the human tubercle bacillus. In an earlier paper[3] we have described an improved method of synthesis of *dl*-tuberculostearic acid.

As a part of a general program of examination of certain derivatives of long chain fatty acids as anti-tubercular chemotherapeutic agents, we have introduced the *dl*-tuberculostearic acid fragment into several biologically active amines such as *p*-aminosalicylic acid and 4,4′-diaminodiphenyl sulfone.

Biological evaluation of these amides is being conducted by the Eli Lilly Co. of Indianapolis and we are grateful to Dr. R. G. Jones for arranging the tests.

We would also like to express appreciation to the Research Corporation of New York for a grant which supported this work.

Experimental[4]

p,p′-**Bis-(10-methyloctadecanamido)-diphenyl Sulfone.**—Four grams (0.0135 mole) of *dl*-10-methyloctadecanoic acid was converted to the acid chloride by thionyl chloride as mentioned previously.[3] To the acid chloride was added a solution of 1.6 g. (0.0065 mole) of *p,p′*-diaminodiphenyl sulfone in 15 ml. of pyridine. The mixture was refluxed for 4 hours, cooled and poured into 200 ml. of water. The precipitated solid was dissolved in acetone, decolorized with charcoal and recrystallized from ethanol to give 4.5 g. of product melting in the range 80–86.5°. Two additional recrystallizations from ethanol and one from a mixture of benzene and petroleum ether (b. p. 60–80°) gave 1.0 g. (20%) of the amide melting at 86.5–88°.

Anal. Calcd. for $C_{50}H_{84}N_2O_4S$: N, 3.46; C, 74.4; H, 10.2. Found: N, 3.48, 3.54; C, 74.2; H, 10.2.

p-**(10-Methyloctadecanamido)-salicylic Acid.**—The acid chloride from 2.0 g. (0.0068 mole) of 10-methyloctadecanoic acid was added to a solution of 1.0 g. (0.0067 mole) of *p*-aminosalicylic acid in 20 ml. of pyridine. After standing 1 hour, the reaction mixture was poured into excess water and acidified with hydrochloric acid. The precipitated material solidified on standing and was separated and recrystallized once from ethanol, two times from 70% aqueous ethanol and two times from benzene to give 1.4 g. (48%) of the amide melting at 170–172°.

Anal. Calcd. for $C_{26}H_{43}NO_4$: N, 3.23; C, 72.2; H, 9.93. Found: N, 3.30; C, 72.0; H, 9.95.

1,4-Bis-(10′-methyloctadecanamido)-benzene.—The acid chloride from 2.5 g. (0.0084 mole) of 10-methyloctadecanoic acid and 0.4 g. (0.0037 mole) of *p*-phenylenediamine was treated in general accordance with the procedures used above except an overnight reflux period was used. There was obtained 1.0 g. (40%) of the diamide, m. p. 155–156°.

Anal. Calcd. for $C_{44}H_{80}N_2O_2$: N, 4.19; C, 79.1; H, 12.0. Found: N, 4.14; C, 79.1, 78.9; H, 12.1, 12.1.

4-(*p*-Nitrobenzenesulfonamido)-acetanilide.—Nine grams (0.0407 mole) of *p*-nitrobenzenesulfonyl chloride was added to a solution of 5.5 g. (0.037 mole) of *p*-aminoacetanilide in 30 ml. of anhydrous pyridine. After standing 1 hour, the mixture was poured into excess water and the precipitated solid (8.0 g.) recrystallized three times from ethanol. The product melted at 242–242.5° and weighed 6.0 g. (48%).

Anal. Calcd. for $C_{14}H_{13}N_3O_5S$: N, 12.54. Found: N, 12.60.

4-(*p*-Nitrobenzenesulfonamido)-aniline.—The acetanilide derivative above (1.6 g. or 0.0048 mole) was hydrolyzed by a two hour reflux with 30 ml. of 6*N* hydrochloric acid and 15 ml. of ethanol. The mixture was filtered and the filtrate neutralized with sodium acetate. The precipitated amine (1.1 g. or 80%) was recrystallized once from ethanol to give small plates, m. p. 201–202°.

Anal. Calcd. for $C_{12}H_{11}N_3O_4S$: N, 14.33. Found: N, 14.40.

4-*p*-Nitrobenzenesulfonamido)-1-(10′-methyloctadecanamido)-benzene.—Reaction of 1.0 g. (0.0034 mole) of the above amine with the acid chloride from 1.4 g. of 10-methyloctadecanoic acid in general accordance with the procedures used above gave 0.8 g. (42%) of the amide, m. p. 170.5–172°. The product was recrystallized four times from ethanol and once from a 1:1 mixture of benzene and hexane.

Anal. Calcd. for $C_{31}H_{47}N_3O_5S$: N, 7.35. Found: N, 7.55.

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[1] Frederick G. Cottrell Research Fellow, 1949-1950.

[2] Anderson and Chargaff, *J. Biol. Chem.*, **85**, 77 (1929).

[3] Schmidt and Shirley, THIS JOURNAL, **71**, 3804 (1949).

[4] All melting points reported were taken on a Fisher melting point block and are uncorrected.

Replacement of Vitamin B_{12} by Desoxynucleotides in Promoting Growth of Certain Lactobacilli

BY WILLIAM SHIVE, MARGARET E. SIBLEY AND LORENE L. ROGERS[1]

Thymidine,[2a,b] hypoxanthine desoxyriboside[3] and other purine desoxyribosides[4,5,6] replace vitamin

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[1] Eli Lilly and Co. Post-doctorate Fellow.

[2] (a) Shive, Ravel and Eakin, THIS JOURNAL, **70**, 2614 (1948); (b) Wright, Skeggs and Huff, *J. Biol. Chem.*, **175**, 475 (1948).

[3] Shive, papers presented at Conference on Development and Uses of Antimetabolites, New York Acad. Sci., Feb., 1949, *Ann. N. Y. Acad. Sci.*, **52**, 1212 (1950).

[4] Kocher and Schindler, *Intern. Z. Vitaminforschl.*, **20**, 441 (1949).

[5] Kitay, McNutt and Snell, *J. Biol. Chem.*, **177**, 993 (1949).

[6] Hoff-Jorgensen, Abstr. 1st Intern. Congr. Biochem., 292 (Cambridge, 1949).

B_{12} in promoting growth of *Lactobacillus lactis* and *Lactobacillus leichmanni;* however, these desoxyribosides do not replace this vitamin in reversing the toxicity of sulfanilamide for *Escherichia coli* under conditions such that methionine synthesis is the limiting factor for growth.[3] In the present investigation the phosphorylated derivatives of the desoxyribosides have been found to be approximately as effective as the desoxyribosides for the Lactobacilli. Also, the desoxynucleotides (100 γ per 10 cc.) are inactive for *Escherichia coli* under the conditions for assay of vitamin B_{12}.[3] Desoxycytidylic acid frequently stimulated greater early growth of the lactobacilli than did the other desoxynucleotides. This suggests the possibility that desoxycytidylic acid is more closely related to the immediate product of the functioning of vitamin B_{12} in the biosynthesis of desoxyribosides than are the other desoxynucleotides; however, the delay in obtaining a maximal response with certain desoxynucleotides, particularly desoxyadenylic acid and thymidylic acid, may be the result of the inhibitory activity of these compounds on related systems.

Although vitamin B_{12} is approximately 10,000 to 30,000 times as effective as the desoxynucleotides in stimulating growth of the lactobacilli in test-tubes, the effect of the desoxynucleotides cannot be accounted for on the basis of contamination with vitamin B_{12}, because the desoxynucleotides are inactive in the *Escherichia coli* assay, are, relative to vitamin B_{12}, more effective in plate assays than in tube assays with the lactobacilli, and migrate differently on paper chromatograms.

On paper chromatograms in several different solvents the desoxynucleotides were found to move much more slowly than the corresponding desoxyribosides. Since the R_f values for these phosphorylated compounds fall within the range of those for vitamin B_{12}, these substances may give abnormally high values when the vitamin B_{12} content of natural materials is determined by paper chromatographic methods.

The results of the studies are indicated in Table I.

TABLE I

REPLACEMENT OF VITAMIN B_{12} BY DESOXYNUCLEOTIDES

Supplements	Quantity γ per 10 cc.	R_f[a] Value	Galvanometer readings[b] *Lactobacillus leichmanni*	Galvanometer readings[b] *Lactobacillus lactis*	Plate method[c] *Lactobacillus lactis*
None			4	3.5	13.2
Vitamin B_{12}	0.0001	0.17–0.29	27	28	
	.0002		41	41	
	.0005		55	60	
	.001		62	70	
	.002				15.8
	.005				17.6
	.01				20.3
	.02				22.7
	.05				25.2
Desoxycytidylic acid	.3	.14–0.16	11	8	
	1		22	22	19.7
	3		44	52	23.4
	10		56	73	27.8
Desoxythymidylic acid	0.3	.21–0.29	7.5	7	
	1		17	12	18.7
	3		33	29	22.6
	10		53	39	26.8
Desoxyguanylic acid	0.3	.12–0.16	12	9	
	1		22	30	20.2
	3		43	47	24.5
	10		56	73	28.5
Desoxyadenylic acid	0.3	.16–0.23	10	6	
	1		23	19	20.4
	3		38.5	41	24.0
	10		52	61	27.9
5-Methyldesoxycytidylic acid	0.3	.10–0.18	10	11	
	1		21	24	
	3		35	44	
	10		50	60	
Thymidine	0.3	.73–0.88	14	9	
	1		26	19	19.4
	3		45	40	24.6
	10		54	65	28.5

[a] Paper chromatographs with 2,6-lutidine. [b] A measure of culture turbidity; distilled water reads 0, an opaque object, 100. [c] Diameter of zones of growth in mm. Paper disc is 13.1 mm. in diameter.

Experimental

The desoxynucleotides used in this work were kindly supplied by Drs. Waldo E. Cohn[7] and C. E. Carter.

The organisms used in this work were *Lactobacillus leichmanni* 313 and *Lactobacillus lactis* Dorner 8000.

The tube assays were carried out on either the medium described by Shive, *et al.*,[2a] and Wright, *et al.*,[2b] or a modification of the medium described by Caswell, Koditschek and Hendlin.[8] In the latter case, two grams of Tween 80 per liter of final medium was added, and the phosphate content was increased. The organisms responded equally well on either medium, but that of Caswell, *et al.*,[8] was used preferentially because of its definite chemical composition.

For the plate assays, 10-cc. portions of the above sterilized medium containing 2% agar and inoculated with *Lactobacillus lactis* were poured into sterile Petri dishes and alowed to harden. A 13.1 mm. disc of filter paper was laid with forceps on the hardened medium, and an aliquot (an amount just sufficient to moisten the entire disc) of the proper dilution of each substance to be tested was delivered to the paper disc from a special pipet delivering a constant volume of 0.1 cc. Four different dilutions were usually assayed on each plate. After the plates were incubated for 16 hours at 37°, diameters of zones of growth were determined.

The capillary ascent method of Williams and Kirby[9] was employed for the paper chromatograms, 65% 2,6-lutidine being the solvent used. The resulting filter paper strips were dried and placed on a hardened agar medium identical with that used for the plate assays. After 15 to 30 minutes the paper strips were removed and the plates were incubated for 16 hours at 37°. The R_f values were calculated from the position of the zones of growth.

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(7) Volkin, Khym and Cohn, unpublished work, Oak Ridge National Laboratory.

(8) Caswell, Koditschek and Hendlin, *J. Biol. Chem.*, **180**, 126 (1949); Shorb, *Science*, **107**, 397 (1948).

(9) Williams and Kirby, *Science*, **107**, 481 (1948).

The Mutual Solubility of Mercury and Gallium

BY WILLIAM M. SPICER AND HENRY W. BARTHOLOMAY

Little is known about the mutual solubility of gallium and mercury. Ramsay[1] in a study of the

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(1) W. Ramsay, *J. Chem. Soc.*, **55**, 521 (1889).

molecular weights of metals dissolved gallium in boiling mercury to the extent of 0.7855%. However, he did not attempt to determine the solubility. Puschin, Stepanovic and Stajic[2] investigated the mutual solubilities by means of freezing point lowering and concluded that the metals are at their freezing points either insoluble or very slightly soluble in one another. Davies and Keeping,[3] in a study of the magnetic susceptibility of some amalgams, made an amalgam containing 0.2436% gallium at 18.9°. Gilfillan and Bent,[4] on the basis of freezing point lowering, concluded that at the freezing points the solubility of gallium in mercury is about 0.13%, while that of mercury in gallium is immeasurably small.

In view of the uncertainty in these data, it was decided to determine the mutual solubilities at 35° and at 100° by the following direct method: The liquids were mixed and allowed to equilibrate. Weighed samples were removed from each layer and the gallium dissolved out by hydrochloric acid. The remaining mercury was weighed. Our results indicate that the solubilities are considerably greater than had been thought.

Experimental.—The gallium was obtained from the Aluminum Co. of America and was said to be better than 99.95% gallium. This high purity was confirmed by qualitative spectrographic analysis. The mercury was purified by washing with nitric acid and water, drying and distilling.

Gallium wets glass and oxidizes rapidly when exposed to air. It was found, however, that when it is placed under a weakly acidic (with HCl) solution of gallium chloride its surface apparently remains free of oxide and it no longer wets glass. It was felt that the presence of this film of oxide may have caused previous investigators to obtain low results for the solubility. Therefore, the gallium was always kept under such a solution.

Weighed portions of the metals (approximately 3.5 g. Ga and 7.0 g. Hg) were placed in a glass tube under the gallium chloride solution and allowed to equilibrate, with frequent shaking, in a bath maintained at constant temperature.

The interface between the two phases could not be seen. In order to locate it, a steel shot of somewhat smaller diameter than the tube was added and forced to the bottom of the mixture of metals by means of a small glass rod. When released the shot rose to what was assumed to be the interface. That the shot would stop at the interface is reasonable in view of the densities which are: Hg = 13.6, Fe = 7.5 and Ga = 5.9.

Several small samples were taken from each layer and weighed. (Samples were removed from the lower mercury-rich layer through a stopcock on the lower end of the tube, and from the upper layer by means of a pipet.) To these, concentrated HCl was added to dissolve the gallium. As soon as all of the gallium had dissolved as indicated by the discontinuance of gas evolution, the solution was decanted from the mercury, which was quickly dried with filter paper and reweighed. Gallium reacts only slowly with hydrochloric acid and the gallium-rich samples required several days for complete reaction even when heated on a water-bath. In spite of this long time, that no mercury dissolved was proved by spectrographic analysis of the acid solution.

Furthermore, the validity of the method of analysis was demonstrated by applying it to a mercury–gallium mixture of known composition.

The results are given in Table I. In order to eliminate the possibility that the metals were simply dispersed in one another, two of the determinations were made after the metals had stood in contact for approximately two months. These are indicated in the table by an asterisk.

TABLE I

LIQUID–LIQUID EQUILIBRIA DATA FOR THE SYSTEM GALLIUM MERCURY

Run no.	Layer rich in	Wt. of sample, g.	Wt. of mercury, g.	Hg, %	Ga, %
		At 35°			
1	Hg	0.4671	0.4615	98.8	1.2
2	Hg	.4659	.4594	98.6	1.4
3	Hg	.4083	.4036	98.8	1.2*
4	Hg	.7873	.7774	98.7	1.3*
5	Ga	.3138	.0189	6.0	94.0
6	Ga	.2022	.0135	6.7	93.3
7	Ga	.3687	.0241	6.6	93.4*
8	Ga	.1007	.0067	6.7	93.3*

Average: mercury-rich layer, 98.7% Hg; gallium-rich layer, 6.5% Hg. In terms of atom per cent.: solubility of gallium in mercury is 3.6% and solubility of mercury in gallium is 2.0%.

Run no.	Layer rich in	Wt. of sample, g.	Wt. of mercury, g.	Hg, %	Ga, %
		At 100°			
1	Hg	0.8370	0.8258	98.6	1.4
2	Hg	.8200	.8090	98.6	1.4
3	Hg	.8518	.8400	98.6	1.4
4	Ga	.2133	.0183	8.5	91.5
5	Ga	.2944	.0250	8.5	91.5
6	Ga	.5042	.0443	8.8	91.2

Average: mercury-rich layer, 98.6% Hg; gallium-rich layer, 8.6% Hg. In terms of atom per cent.: solubility of gallium in mercury is 3.9% and solubility of mercury in gallium is 3.2%.

In view of the small increase in solubility with temperature, it is doubtful that a critical solution temperature exists in this system at one atmosphere pressure.

The low mutual solubilities of these metals are not surprising in view of the large difference in their internal pressures. Taking the boiling point of gallium as 2300°K. as given by Harteck[5] and using the Hildebrand rule[6] for estimating internal pressures one computes 38,800 atm. for mercury and 196,000 atm. for gallium.

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[2] N. A. Puschin, S. Stepanovic and V. Stajic, *Z. anorg. Chem.*, **209**, 329 (1932).

[3] W. G. Davies and E. S. Keeping, *Phil. Mag.*, [7] **7**, 145 (1929).

[4] E. S. Gilfillan, Jr., and H. E. Bent, THIS JOURNAL, **56**, 1661 (1934).

[5] P. Harteck, *Z. physik. Chem.*, **134**, 1 (1928).

[6] J. H. Hildebrand, "Solubility of Non-Electrolytes," second edition, Reinhold Publishing Corp., New York, N. Y., 1936, p. 103.

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Some Fluorine Containing Isosteres of Sulfa Drugs

BY AUGUST SVEINBJORNSSON AND CALVIN A. VANDERWERF

Investigation of the effect on the chemotherapeutic properties of various medicinals produced by the substitution of fluorine atoms for other groups in the molecule has been extended by the herein reported study of the synthesis and bacteriostatic action of a number of analogs of familiar sulfa drugs in which the amino group is replaced by the isosteric fluorine atom. Several *p*-fluorobenzamides have also been synthesized, as compounds of considerable interest from a bacteriological standpoint because of their relationship to *p*-aminobenzoic acid.

Experimental

***p*-Fluorobenzenesulfonamide.**—This compound, m.p. 123.1–124.0°, was prepared in 92% yield from *p*-fluorobenzenesulfonyl chloride and ammonia.

2-(*p*-Fluorobenzenesulfonamido)-pyrimidine.—To a 125-ml. conically shaped flask, equipped with a mechanical stirrer, a condenser and a dropping funnel, and containing 9.5 g. (0.1 mole) of 2-aminopyrimidine[1] in 30 ml. of dry pyridine, 19.4 g. (0.1 mole) of *p*-fluorobenzenesulfonyl chloride was added with stirring. The mixture was heated at 120° for 2 hours and a solution of 4.4 g. (0.11 mole) of sodium hydroxide in 25 ml. of water was then added slowly with continued heating. The pyridine was removed by distillation under reduced pressure, water being added from time to time to maintain the volume approximately constant. The product which separated was filtered, washed well with water, and air-dried. The yield of pure 2-(*p*-fluorobenzenesulfonamido)-pyrimidine, m.p. 184.5–185.0°, was 14.6 g. (57.7%).

Anal. Calcd. for $C_{10}H_8O_2N_3SF$: N, 16.6. Found: N, 16.5.

2-(*p*-Fluorobenzenesulfonamido)-thiazole.—This compound was prepared by the method used for 2-(*p*-fluorobenzenesulfonamido)-pyrimidine except that 10.0 g. (0.1 mole) of 2-aminothiazole was substituted for the 2-aminopyrimidine. The crude material was recrystallized from glacial acetic acid to yield 15.5 g. (60.1%) of product melting at 171.2–172.0°,

Anal. Calcd. for $C_9H_7O_2N_2SF$: N, 10.9. Found: N, 10.7.

2-(*p*-Fluorobenzenesulfonamido)-pyridine.—This product was prepared by the method described for 2-(*p*-fluorobenzenesulfonamido)-pyrimidine, except that 9.4 g. (0.1 mole) of 2-aminopyridine was used in place of 2-aminopyrimidine. The crude product (23 g.) was recrystallized repeatedly from glacial acetic acid to give 5.3 g. (21.0%) of pure material, melting at 151.2–151.7°.

Anal. Calcd. for $C_{11}H_9O_2N_2SF$: N, 11.1. Found: N, 11.0.

***p*-Fluorobenzoic Acid.**—This product, m.p. 184.1–184.7°,[2] was prepared in 70% yield from *p*-fluorotoluene[3] according to the directions given by Clark and Taylor[4] for the oxidation of *o*-chlorotoluene to *o*-chlorobenzoic acid.

2-(*p*-Fluorobenzamido)-pyridine.—This compound was prepared from 2-aminopyridine and *p*-fluorobenzoyl chloride[5] by the general method described for 2-(*p*-fluorobenzenesulfonamido)-pyrimidine. The crude material was recrystallized from alcohol–water. The yield of pure product, m.p. 123.6–124.3°, was 62%.

Anal. Calcd. for $C_{12}H_9ON_2F$: N, 12.9. Found: N, 12.7.

2-(*p*-Fluorobenzamido)-thiazole.—Prepared by the usual method, this compound, m.p. 186.2–186.8° after recrystallization from alcohol–water, was obtained in 75% yield.

Anal. Calcd. for $C_{10}H_7ON_2FS$: N, 12.6. Found: N, 12.5.

2-(*p*-Fluorobenzamido)-pyrimidine.—To a mixture of 2.7 g. (0.028 mole) of 2-aminopyrimidine, 5.4 g. (0.028 mole) of powdered potassium carbonate, and 50 ml. of dry ether contained in a 200-ml. conically shaped 3-necked flask, fitted with a mechanical stirrer, a reflux condenser, and a dropping funnel, 4.4 g. of *p*-fluorobenzoyl chloride was added dropwise with stirring. The mixture was heated under reflux on a steam-bath for 3 hours. The solid remaining after removal of the ether and addition of 50 ml. of water was filtered and air dried to give 5.6 g. (91%) of crude material. This was dissolved in benzene, extracted with 5% hydrochloric acid and the benzene solution dried over anhydrous sodium sulfate. Addition of Skellysolve C to the benzene solution gave 4.8 g. (80.0%) of a colorless product, m.p. 224.4–226.0°.

Anal. Calcd. for $C_{11}H_8ON_3F$: C, 60.8; H, 3.7. Found: C, 60.6; H, 3.7.

Discussion.—The compounds were tested *in vitro* as antagonists of the growth of *Staphylococcus aureus*, using Klinger medium and of *Escherichia coli*, using MacLeod medium. The organisms were inoculated, at the peak of their growth curves, into Klett–Summerson tubes containing standard drug concentrations. The tubes were incubated at 37° for 24 hours, and growth was determined by means of a Klett–Summerson photoelectric colorimeter. The minimal effective concentrations necessary to inhibit completely the growth of the organism are shown in Table I. Data for sulfathiazole and sulfasuxadine are added for comparison purposes.

TABLE I

Compound	Minimal effective concentration, *M* *E. coli*	*S. aureus*
p-Fluorobenzenesulfonamide	1×10^{-2}	
2-(*p*-Fluorobenzenesulfonamido)-pyridine	1×10^{-3}	
2-(*p*-Fluorobenzenesulfonamido)-pyrimidine	1×10^{-3}	
2-(*p*-Fluorobenzenesulfonamido)-thiazole	1×10^{-3}	1×10^{-4}
p-Fluorobenzoic acid	1×10^{-2}	1×10^{-2}
p-Fluorobenzamide[a]	1×10^{-1}	1×10^{-2}
Sulfathiazole	1×10^{-4}	4×10^{-6}
Sulfasuxadine	2×10^{-2}	

[a] Prepared by the method of J. H. Slothouwer, *Rec. trav. chim.*, **33**, 324 (1914).

It is noteworthy that the inhibition of growth on *Escherichia coli* produced by *p*-fluorobenzoic acid was not reversed by its isostere *p*-aminobenzoic acid, but was reversed by tyrosine. The *p*-fluorobenzamides of 2-aminopyridine, 2-aminopyrimidine and 2-aminothiazole were not sufficiently soluble in the media to be tested.

Acknowledgment.—These studies were aided by a contract between the Office of Naval Research, Department of Navy, and the University of Kansas.

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[1] Obtained through the kindness of the Calco Chemical Division of the American Cyanamid Co.

[2] G. Schiemann and W. Winkelmüller, "Organic Syntheses," Coll. Vol. II, John Wiley and Sons, Inc., New York, N. Y., 1943, p. 299, reported 186°.

[3] B.p. 114-115° at 728 mm. Prepared in 71% yield by diazotization of *p*-toluidine in anhydrous hydrogen fluoride, followed by decomposition of the resulting diazonium fluoride in refluxing hydrogen fluoride.

[4] H. T. Clarke and E. R. Taylor, ref. 2, p. 135.

[5] Prepared by reaction of *p*-fluorobenzoic acid with thionyl chloride.

The Mechanism of Addition of Grignard Reagents to Ketones

BY C. GARDNER SWAIN AND HENRY B. BOYLES

By testing a prediction from a mechanism based on kinetic studies of a model system which did not involve diisopropyl ketone at all, we have succeeded in increasing the yield of addition product in the reaction of *n*-propylmagnesium bromide with diisopropyl ketone from 36[1] to 65%.

This prediction was based on a consideration of the difference between the most probable mechanism for *addition of Grignard reagents to ketones* and the most probable mechanism for *reduction*, which is the principal competing side reaction. From other simple mechanisms which might be assumed to hold for these two processes, one would have predicted either no effect or a lower yield of addition by the new procedure; hence, the

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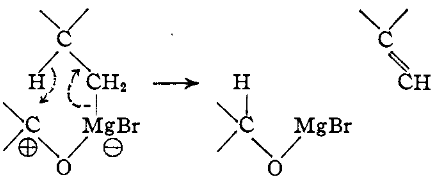
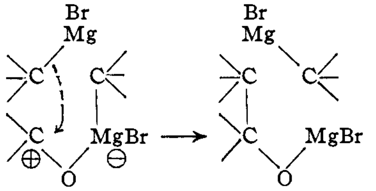
[1] Whitmore and George, THIS JOURNAL, **64**, 1239 (1942).

success of the prediction is evidence for the correctness of the mechanisms originally assumed. These are outlined briefly below.

The mechanism for *reduction* involves an internal *cyclic* rearrangement of a complex.[2]



However, the mechanism for *addition of Grignard reagents to ketones* must be different for reasons previously given[3] and appears to involve reaction of the Grignard-ketone complex with a *second* molecule of Grignard reagent.



This mechanism unambiguously predicts that one should be able to increase the yield of addition to a hindered ketone at the expense of reduction by the simple expedient of adding magnesium bromide to the ketone prior to addition of the Grignard reagent. Magnesium bromide is a slightly stronger Lewis acid than the Grignard reagent and should complex preferentially with the ketone, polarizing it even more strongly than would a Grignard reagent. Thus it would tend to play the role of the first molecule of Grignard reagent (which complexes with the ketone) in the normal Grignard-ketone addition mechanism. The magnesium bromide–ketone complex would be incapable of reduction by intramolecular rearrangement, but possibly even more susceptible than a Grignard-ketone complex to attack by an external molecule of Grignard reagent.

To test this prediction we selected the reaction of *n*-propylmagnesium bromide with diisopropyl ketone, which was reported by Whitmore and George to give 36% addition, 60% reduction and 2% enolization when carried out in the normal way.

n-Propylmagnesium bromide was added to diisopropyl ketone (1) with nothing else added, to check the results of Whitmore and George,[1] (2) after mixing an ether solution of more than equivalent magnesium bromide with the ketone to complex with it, and (3) after adding only ether, to show that the effect produced in (2) was not one of dilution. The reaction conditions were identical and the products were hydrolyzed in the same manner in each case. The yields found were (1) 30% addition, 63% reduction, 3% enolization; (2) 65% addition, 26% reduction, 1% enolization; (3) 29% addition, 66% reduction, 2% enolization. Evidently the addition of magnesium bromide in (2) favors the addition reaction at the expense of the reduction reaction.

The success of this prediction is additional evidence for the correctness of the mechanism on which it was based.

We plan to test the synthetic utility of this technique in even more hindered cases, such as the Grignard synthesis of triisopropyl- and tri-*t*-butylcarbinols. It may prove advantageous to substitute magnesium iodide or other Lewis acids for the magnesium bromide.

Experimental

Reagents.—*n*-Propylmagnesium bromide was made by adding 185 g. (1.50 moles) of freshly distilled *n*-propyl bromide slowly to 38 g. (1.56 moles) of magnesium turnings in 450 cc. of dry ether. After settling overnight the supernatant liquid was siphoned into 200-cc. narrow-mouth screw-cap bottles under a nitrogen atmosphere. The bottles were stored at 5°.

Diisopropyl ketone was redistilled through a four-foot column packed with glass helices at a reflux ratio of 20:1, b.p. 122.9–123.2°, $n^{20}\text{D}$ 1.4001, $n^{25}\text{D}$ 1.3980 (reported[1,4] b.p. 123.7°, $n^{20}\text{D}$ 1.4002).

Diisopropylcarbinol was redistilled through the same column, b.p. 139–140°, $n^{20}\text{D}$ 1.4229, $n^{25}\text{D}$ 1.4209 (reported[4] b.p. 140°, $n^{20}\text{D}$ 1.4226).

Analysis of Mixtures of Diisopropylcarbinol and Diisopropyl Ketone.—The per cent. carbinol in the distilled *s*-carbinol–ketone fraction of the reaction products was determined by refractive index, by comparison with a plot of composition *vs.* refractive index prepared from standard mixtures of the pure components.

Reaction with Ketone, Magnesium Bromide and Grignard Reagent.—Bromine (113 g., 0.71 mole) was added slowly with continuous stirring to 17.2 g. (0.71 mole) of magnesium and 210 cc. of ether using a sealed nichrome wire stirrer and a slight positive static pressure of dry nitrogen. Finally, the bromine color disappeared. The magnesium bromide was not all in solution, since its solubility in ether is less than 0.2 *M*.[5] Diisopropyl ketone (35.9 g., 0.314 mole) was added over a period of 1 hour with stirring, and stirred 1 hour more. Then *n*-propylmagnesium bromide (0.6 mole in 210 cc. of ether) was added to the mixture over 1 hour, and stirred 1 hour more. The mixture was hydrolyzed by adding it slowly to 830 cc. of 10% sodium carbonate solution at 0° with good stirring. The ether was distilled from the ether layer and 600 cc. of ether extracts in a Claisen flask, and the residue (43.9 g.) was distilled at 115 mm. through an 18-inch column packed with small stainless steel helices at a reflux ratio of 15:1. The fractions obtained were 10.1 g. of a mixture of diisopropyl ketone and diisopropylcarbinol, b.p. 80–90° at 115 mm., and 32.5 g. (0.205 mole) of *n*-propyldiisopropylcarbinol, b.p. 121–122° at 115 mm. The separation was very sharp, with less than 1 cc. distilling between 95 and 115°. The mixture had a refractive index $n^{20}\text{D}$ 1.4200, hence contained 9.7 g. (0.083 mole, 26%) of diisopropylcarbinol and 0.4 g. (0.003 mole, 1%) of diisopropyl ketone. The *n*-propyldiisopropylcarbinol (65% yield) was identified by boiling point, refractive index $n^{25}\text{D}$ 1.4401 and analysis.

Anal. Calcd. for $C_{10}H_{22}O$: C, 75.88; H, 14.01. Found: C, 75.62; H, 13.92.

Reactions without Magnesium Bromide.—*n*-Propylmagnesium bromide (0.6 mole in 210 cc. ether) was added in the same way to either pure diisopropyl ketone or 33.4 g. (0.292 mole) of the ketone mixed with 210 cc. of ether. The products were worked up as before. In the latter case they totaled 37.0 g., and were separated into 23.0 g. of a mixture of diisopropylcarbinol and diisopropyl ketone, b.p. 78–85° at 110 mm., and 13.5 g. (0.0874 mole) of *n*-propyldiisopropylcarbinol, b.p. 104° at 60 mm. The mixture had

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[2] The mechanism pictured is consistent with the findings of Kharasch and Weinhouse (*J. Org. Chem.*, **1**, 209 (1936)). Although solvation of magnesium is not shown here, it is understood that the magnesium atom of the reactant is coördinated with an ether molecule, and that the attack of a second ether molecule may contribute to the rupture of the Mg-C bond.

[3] Swain, This Journal, **69**, 2306, 2308 (1947); *cf.* also Swain and Kent, *ibid.*, **72**, 518 (1950).

[4] Poletaeff, *Ber.*, **24**, 1309 (1891).

[5] Menshutkin, *Z. anorg. Chem.*, **49**, 34 (1906).

$n^{25}D$ 1.4202, hence contained 22.4 g. (0.193 mole, 66%) of diisopropylcarbinol and 0.6 g. (0.005 mole, 2%) of diisopropyl ketone. The *n*-propyldiisopropylcarbinol (29%) was identified by b.p. and refractive index $n^{25}D$ 1.4400.

DEPARTMENT OF CHEMISTRY
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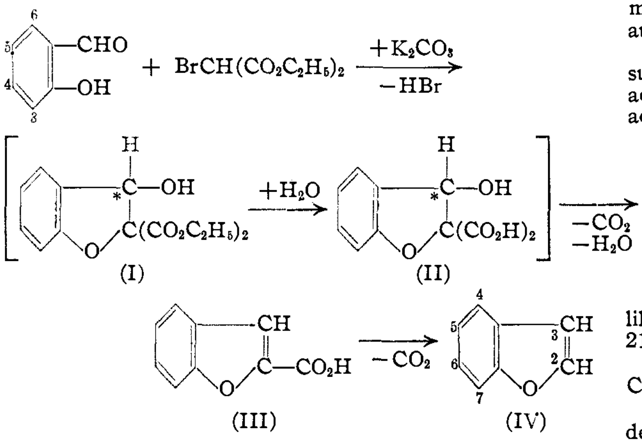
Coumarones from *o*-Hydroxyaldehydes and Bromomalonic Ester

BY SANAE TANAKA

This paper describes the results obtained in substituting ethyl bromomalonate for ethyl bromoacetate in the coumarone synthesis from *o*-hydroxyaldehydes.[1,4] The reaction is given in the scheme



Salicylaldehyde and ethyl bromomalonate refluxed in methyl ethyl ketone[2] in the presence of potassium carbonate condense to give DL-3-hydroxycoumaran-2,2-dicarboxylic acid ester (I). This product was converted without isolation to DL-3-hydroxycoumarandicarboxylic acid (II), which in turn was converted to coumarilic acid (III) on decarboxylation and dehydration. The salicylaldehyde has been replaced with its 4-methoxy, 5-methoxy and 4,5-dimethoxy derivatives. The yields of crude coumarilic acid and its derivatives range from 72–90%. The coumarilic acids have been decarboxylated in quinoline with copper powder[3] and gave coumarone (IV) and the corresponding derivatives, isolated in some cases as their picrates, in 80–93% yields. With *o*-hydroxyacetophenone a 38% yield of 3-methylcoumarilic acid was obtained. It has been shown previously[4] that isolation of the intermediate products I and II decreases over-all yields.

Experimental

Coumarilic Acid (III).—Salicylaldehyde (2.5 g.), ethyl bromomalonate[5] (5 g.), anhydrous potassium carbonate (2.5 g.) and methyl ethyl ketone (10 ml.) were mixed together and the whole was refluxed for 5 hours on a steam-bath. After distilling off the main part of the solvent, the residue was mixed with water and acidified with dilute sulfuric acid and then extracted with ether. The ethereal extract, after removal of the solvent, was dissolved in alcoholic potash (alcohol 20 ml., potassium hydroxide 2 g.) and then refluxed on a steam-bath for 1 hour. After concentrating to a small volume the residue was dissolved in water and acidified with dilute sulfuric acid. The colorless crystals thus formed were collected, washed with water and dried. Recrystallization from benzene gave colorless long plates; yield 2.5 g. (76%); m.p. 192–193°.[6]

Anal. Calcd. for $C_9H_6O_3$: C, 66.66; H, 3.70. Found: C, 66.45; H, 3.67.

Coumarone (IV).—Coumarilic acid (0.5 g.) and copper powder (0.1 g.) were refluxed in quinoline (10 ml.) for 30 minutes. After cooling ether was added, the mixture filtered from copper, then washed several times with 2 *N* hydrochloric acid, then with water to remove quinoline. This ethereal extract, when freed from the solvent, gave coumarone as an oil which possesses a guaiacol-like odor. It was warmed with picric acid. The coumarone picrate thus obtained was recrystallized from dilute alcohol; yield 0.75 g. (80%) yellow columns; m.p. 102–103°.[7] No melting point depression was observed when mixed with an authentic specimen.

6-Methoxycoumarilic Acid.—4-Methoxysalicylaldehyde[4b] substituted for salicylaldehyde gives 6-methoxycoumarilic acid in 90% yield, m.p. 206°,[8] recrystallized from ethyl acetate.

Anal. Calcd. for $C_{10}H_8O_4$: C, 62.48; H, 4.19. Found: C, 62.31; H, 3.98.

6-Methoxycoumarone.—6-Methoxycoumarilic acid was decarboxylated by the technique described above. The product was isolated in its picrate, m.p. 64°.[9]

Anal. Calcd. for $C_9H_8O_2 \cdot C_6H_3O_7N_3$: N, 11.14. Found: N, 10.93.

5-Methoxycoumarilic Acid.—5-Methoxysalicylaldehyde[10] likewise gives 5-methoxycoumarilic acid in 72% yield, m.p. 212–213°, recrystallized from acetone.

Anal. Calcd. for $C_{10}H_8O_4$: C, 62.48; H, 4.19. Found: C, 62.61; H, 4.29.

5-Methoxycoumarone.—5-Methoxycoumarilic acid upon decarboxylation gave 5-methoxycoumarone in 93% yield, m.p. 32–33°, b.p. 120–125° (30 mm.).

Anal. Calcd. for $C_9H_8O_2$: C, 72.97; H, 5.45. Found: C, 73.25; H, 5.49.

5,6-Dimethoxycoumarilic Acid.—4,5-Dimethoxysalicylaldehyde[11] similarly gave 5,6-dimethoxycoumarilic acid, in 80% yield, m.p. 245° (dec.), recrystallized from alcohol.

Anal. Calcd. for $C_{11}H_{10}O_5$: C, 59.46; H, 4.50. Found: C, 59.48; H, 4.65.

5,6-Dimethoxycoumarone.—5,6-Dimethoxycoumarilic acid through decarboxylation gave 5,6-dimethoxycoumarone in 90% yield, m.p. 53–54°.

Anal. Calcd. for $C_{10}H_{10}O_3$: C, 67.41; H, 5.62. Found: C, 67.31; H, 5.66.

3-Methylcoumarilic Acid.—*o*-Hydroxyacetophenone, when condensed with ethyl bromomalonate, afforded 3-methylcoumarilic acid in 38% yield, the melting point of which (188.5–189.5° from diluted alcohol) coincides with those given by Hantzsch[12] or Peter.[13]

Anal. Calcd. for $C_{10}H_8O_3$: C, 68.18; H, 4.54. Found: C, 68.36; H, 4.68.

Further attempts to attain 3-methylcoumarone were abandoned owing to the scarcity of the material.

Acknowledgment.—The author wishes to express his gratitude to Prof. Sin'iti Kawai, under whose suggestion this work was undertaken. He is also indebted to the research fund awarded for him from the Department of Education.

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(1) Kostanecki, *Ber.*, **42**, 901 (1909); **43**, 2155 (1910).

(2) Acetone can be used instead but somewhat poorer yields of coumarilic acid result.

(3) Shepard, THIS JOURNAL, **52**, 2083 (1930).

(4) (a) Kawai, Nakamura and Sugiyama, *Ber.*, **72**, 1146 (1939); (b) Kawai, Nakamura and Yoshida, *ibid.*, **73**, 581 (1940).

(5) "Organic Syntheses," Vol. VII, p. 34 (1927).

(6) Perkin [*J. Chem. Soc.*, **24**, 45 (1871)] gave m. p. 192-193°.

(7) Kraemer [*Ber.*, **23**, 3276 (1890)] described m.p. 102-103°.

(8) Robertson [*J. Chem. Soc.*, 787 (1940)] described m.p. 206°.

(9) Anderson [THIS JOURNAL, **60**, 1419 (1938)] described m.p. 64-65°.

(10) Rubenstein, *J. Chem. Soc.*, **127**, 1999 (1925).

(11) Robertson, *ibid.*, 2434 (1930).

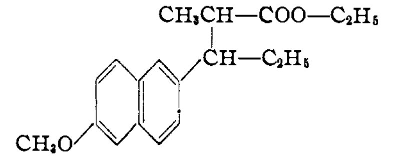
(12) Hantzsch, *Ber.*, **19**, 1292 (1886); m.p. 188-189°.

(13) Peter, *ibid.*, **41**, 832 (1908); m.p. 188°.

Intermediates for Synthetic Hormones

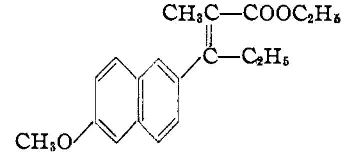
By Herbert E. Ungnade[1] and Norman L. Jennings[2]

In connection with another problem it became necessary to prepare the ester (I) of the allenolic acid which has been described by Jacques and Horeau[3] as an active estrogen.[4]



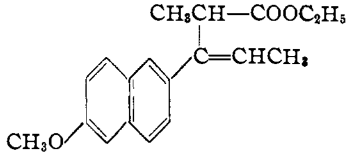
I

In the course of this investigation it has been possible to isolate the hitherto unknown unsaturated intermediates (II) and (III) which have been



II

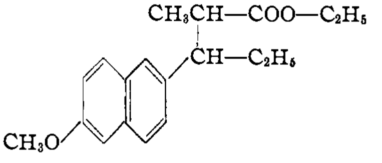
M. p. 103–104° and m.p. 94–96°



III

M.p. 78–80°

identified on the basis of their absorption spectra (Fig. 1).[5] Each of the three isomers has been hydrogenated over platinum catalyst, yielding the two expected racemates (IV). The order of the



IVa, m.p. 43–45°
IVb, m.p. 64–65°

hydrogenation rates of the isomers was (II) > (III). Hydrolysis of the esters (IV) gave oils with molecular formulas corresponding to $C_{17}H_{20}O_3$ which have failed to crystallize and have been used without further purification.

Model experiments have shown that (I) can be converted to the corresponding methyl ketone by treating its acid chloride with dimethylcadmium. The methoxyl group is cleaved during the reaction. When the phenolic ketone is reduced with Raney nickel catalyst as described recently,[6] the phenolic ring is saturated without the hydrogenolysis of the hydroxyl group which has been observed by other investigators.[6a,b]

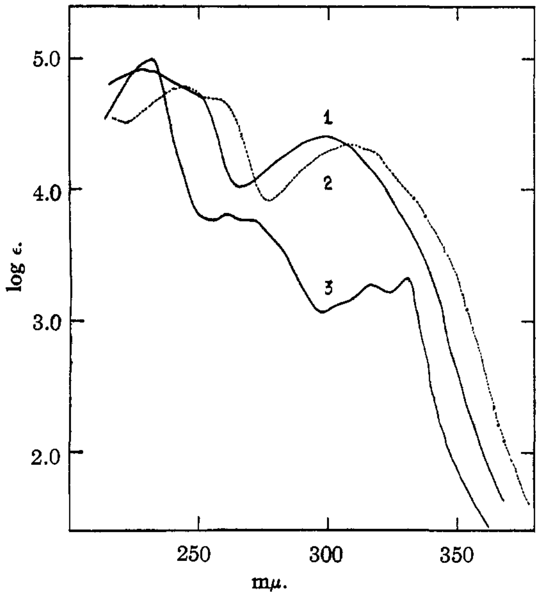


Fig. 1.—Ultraviolet absorption spectra (Beckman quartz spectrophotometer): curve 1, unsaturated ester (II) m.p. 94–96°; curve 2, unsaturated ester (II) m.p. 103–104°; curve 3, ester (III).

Experimental[7]

The unsaturated esters (II) and (III) were synthesized from 2-methoxy-6-propionaphthone[8] through the Reformatsky reaction and also by use of the Grignard reaction. Since the resultant hydroxy ester could not be crystallized, it was dehydrated in the crude state. The two procedures furnished different ratios of the unsaturated esters.

Reformatsky Reaction.—Ethyl α-bromopropionate (20 g.) was added to a boiling solution of 2-methoxy-6-propionaphthone (16 g.) in 100 ml. of benzene and 100 ml. of toluene containing 25 g. of granulated zinc. A crystal of iodine was added, the reaction was allowed to subside and the mixture was refluxed for 1 hour. The reaction mixture was decomposed with ice and dilute hydrochloric acid, extracted with benzene and the extract was dried and distilled. The oily residue consisting of hydroxy ester was heated with 20 g. of potassium bisulfate for 15 minutes at 190°. The mixture was treated with water and extracted with ether. The extract was dried and the solvent was displaced with Skellysolve B.[8a] The resultant solution was adsorbed on aluminum oxide. The Skellysolve B eluate contained 10.35 g. of (II), m. p. 103–104°.

Anal. Calcd. for $C_{19}H_{22}O_3$: C, 76.51; H, 7.38. Found: C, 76.53; H, 7.34.

The column contained two additional bands visible under ultraviolet light. The lower one yielded 0.35 g. of isomer (II), m. p. 94–96°.

Anal. Calcd. for $C_{19}H_{22}O_3$: C, 76.51; H, 7.38. Found: C, 76.40; H, 7.43.

The third isomer (III) was recovered from the top band. It melted at 78–80° and weighed 1.20 g.

Anal. Calcd. for $C_{19}H_{22}O_3$: C, 76.51; H, 7.38. Found: C, 76.27; H, 7.21.

Grignard Reaction.—Magnesium (2.3 g.) was activated by treating with ethyl iodide (1.2 ml.) and ether (20 ml.). The

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(1) New Mexico Highlands University, Las Vegas, New Mexico.

(2) From the master's thesis of N. L. Jennings, 1950.

(3) Jacques and Horeau, *Bull. soc. chim.*, 714 (1948).

(4) The racemate melting at 128–128.5° is reported to be active in doses of 100 γ.

(5) An analogous interpretation of the absorption spectra of similar unsaturated isomers was given by Johnson and Graber (This Journal, **72**, 929 (1950)).

(6) Ungnade and Morriss, *ibid.*, **72**, 2112 (1950).

(6a) Julia, Jacques and Horeau, *Compt. rend.*, **230**, 660 (1950).

(6b) Note added in proof: Analogous compounds have been reported more recently by Horeau and Jacques, *Compt. rend.*, **230**, 1667, 2029 (1950).

(7) All temperatures uncorrected. Analyses by R. Carpenter and J. S. Finney.

(8) Haworth and Sheldrick, *J. Chem. Soc.*, 864 (1934).

(8a) Petroleum ether, b. p. 60–80°.

solution was decanted and the residue was washed with dry ether. To the prepared magnesium was added 20 ml. of anhydrous ether, 13.6 g. of ethyl α-bromopropionate, 30 ml. of dry benzene and 16 g. of 2-methoxy-6-propionaphthone. The mixture was refluxed for 3 hours and decomposed with ice and hydrochloric acid. The reaction product was isolated and dehydrated as described above. The mixture of unsaturated esters was separated by chromatographic adsorption. The isomers obtained in 51% yield were identical with the substances described above: (II), m. p. 103–104°, yield 1.90 g.; (II), m. p. 94–96°, yield 8.45 g.; (III), m. p. 78–80°, yield 2.25 g.

Ethyl 2-Methyl-3-(6-methoxy-2-naphthalene)-pentanoate.—The unsaturated esters (1.75 g. each), dissolved in 80 ml. of acetic acid, were hydrogenated with 200 mg. of platinum oxide at room temperature. Under identical conditions (II), m. p. 103–104°, m. p. 94–96°, and (III) required 70, 15 and 360–480 minutes, respectively, to take up the theoretical amount of hydrogen.

The oily products, after removal of solvent and catalyst, were taken up in Skellysolve B and were chromatographed on aluminum oxide. Two bands were visible under ultraviolet light. They were cut apart and extracted with hot methanol. Crystallization from aqueous methanol yielded the racemate melting at 43–45° (IVa) from the lower band and the isomer, m. p. 64–65° (IVb) from the upper band (Table I).

TABLE I

HYDROGENATION RESULTS

Unsaturated ester	Yield (IVa), g.	Yield (IVb), g.	Total yield, %
II, m.p. 103–104°	1.32	0.25	90
II, m.p. 94–96°	0.25	1.40	95
III, m.p. 78–80°	0.75	0.65	80

Anal. Calcd. for $C_{19}H_{24}O_3$: C, 76.00; H, 8.00. Found: (IVa) C, 76.09; H, 8.07; (IVb) C, 76.10; H, 8.03.

2-Methyl-3-(6-methoxy-2-naphthalene)-pentanoic Acid.—The mixture of isomeric esters (IVa and IVb, 12.0 g.) was hydrolyzed by refluxing for 3 hours with 125 ml. of 30% aqueous sodium hydroxide and 300 ml. of propylene glycol. After cooling, 200 ml. of water was added, the mixture was acidified with hydrochloric acid and extracted with ether. The extract yielded 10.8 g. of a glassy product which resisted all attempts at crystallization.

Anal. Calcd. for $C_{17}H_{20}O_3$: C, 74.72; H, 9.80. Found: C, 74.39; H, 9.73.

Several attempts to obtain crystalline acids by hydrolyzing crystalline esters only gave non-crystallizable glassy substances.

3-Methyl-4-(6-hydroxy-2-naphthalene)-2-hexanone.—The glassy acid mixture (IV) (8.0 g.) was converted to the acid chloride with oxalyl chloride according to Wilds.[9] The acid chloride (7.8 g.), dissolved in 50 ml. of dry ether, was added to a solution of dimethylcadmium prepared from 1.0 g. of cadmium chloride and methylmagnesium iodide (from 1.0 g. of methyl iodide). After the reaction subsided, the mixture was warmed on a steam-bath for 1 hour. Dilute sulfuric acid was added to the cooled mixture until the white precipitate dissolved. The mixture was extracted with ether, separated, and the ether layer was washed successively with water, dilute base and water, dried and evaporated. Attempts to crystallize the resulting reddish oil failed. The oil was taken up in Skellysolve B and chromatographed on aluminum oxide. The single main band yielded 3.35 g. of oily product. Further purification by conversion to the oily oxime and hydrolysis only gave an oily ketone, yield 3.0 g.

Anal. Calcd. for $C_{17}H_{20}O_2$: C, 79.65; H, 7.81. Found: C, 79.49; H, 7.58.

Catalytic Hydrogenation.—The oily ketone (3 g.) was hydrogenated with Raney nickel (W-2, aged three weeks under absolute alcohol) at 240 atm. and 165° in sodium ethoxide solution containing 0.02 g. of sodium.[6] After removal of catalyst and solvent, the product was taken up in benzene and chromatographed on alumina. One single major band was eluted with the same solvent and yielded 2.7 g. of glassy product which was Folin-negative.

Anal. Calcd. for $C_{17}H_{28}O_2$: C, 77.27; H, 11.08. Found: C, 77.10; H, 10.86.

Absorption Spectra.—The ultraviolet absorption spectra of (II) and (III) were determined in 95% ethanol in concentrations of 6.29, 9.73 and 8.66 mg. per 25 ml.[10]

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RECEIVED JULY 5, 1950

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[9] Wilds and Shunk, THIS JOURNAL, **70**, 2427 (1948).

[10] Absorption spectra by Dr. E. E. Pickett, University of Missouri, Columbia, Missouri.

A Simple Acetolysis of Nitrate Esters[1]

BY M. L. WOLFROM, R. S. BOWER AND G. G. MAHER

The nitrate esters of carbohydrates may be effectively denitrated by any of several methods involving metallic agents such as alkali metal hydrosulfides,[2] aluminum and mercuric chloride,[3] Devarda's alloy in a highly alkaline medium,[4] and iron dust (or zinc and iron dust) in glacial acetic acid.[5,6] A combined denitration and acetylation can be produced with zinc and anhydrous hydrogen chloride (or dry pyridine) in acetic anhydride.[7] A catalytic regeneration of the original alcohol from a nitrate ester has been effected by high pressure hydrogenolysis[8] and by the employment of hydrazine.[9] All of these methods employ reducing agents.

This report concerns a very simple acetolysis applicable to nitrate esters of small carbohydrate units. It has been developed from the observations of Kuhn[10] that ethyl nitrate in cold sulfuric acid produces considerable amounts of NO_2^+ and from the observations of Wolfrom and Montgomery[11] that in cold absolute sulfuric acid carbohydrate sulfate esters are converted to the acetates in the presence of acetic anhydride. The nitrate ester is dissolved in a small amount of sulfuric acid–acetic anhydride reagent in the cold and after subsequent hydrolysis of excess reagent, the acetate is separated by extraction of the hydrolyzate with some suitable solvent. No reducing environment is needed. Acetate derivatives were obtained in good yield (Table I) from the nitrates of cellobiose, D-glucose, pentaerythritol, erythritol, D-mannitol and levoglucosan (1,6-anhydro-β-D-glucopyranose). These acetolysis conditions are similar to those employed to anomerize β-acetates to the α-forms.[12,13] Thus the isolation of members of the α-D-series is to be expected. Our procedure is somewhat related to that of Clémente and Rivière[14] for producing cellulose acetate from cellulose nitrate. These authors employed acetic acid, acetic anhydride and

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[1] This work was carried out under a contract (W33-019ord-6279; supervising agency, Ballistic Research Laboratory, Aberdeen Proving Ground, Maryland) between the Ordnance Department and The Ohio State University Research Foundation (Project 313).

[2] H. de Chardonnet, German Patent 56,655 (1890).

[3] B. Rassow and E. Dörr, *J. prakt. Chem.*, **216**, 113 (1924).

[4] A. Devarda, *Z. anal. Chem.*, **33**, 113 (1894).

[5] J. W. H. Oldham, *J. Chem. Soc.*, **127**, 2840 (1925).

[6] J. Dewar and G. Fort, *ibid.*, 492, 496 (1944); J. Dewar, G. Fort and N. McArthur, *ibid.*, 499 (1944).

[7] D. O. Hoffman, R. S. Bower and M. L. Wolfrom, THIS JOURNAL, **69**, 249 (1947).

[8] L. P. Kuhn, *ibid.*, **68**, 1761 (1946).

[9] L. P. Kuhn, *Abstracts Papers Am. Chem. Soc.*, **117**, 2-0 (1950).

[10] L. P. Kuhn, THIS JOURNAL, **69**, 1974 (1947).

[11] M. L. Wolfrom and R. Montgomery, *ibid.*, **72**, 2859 (1950).

[12] Edna Montgomery and C. S. Hudson, *ibid.*, **56**, 2463 (1934).

[13] K. Freudenberg and K. Soff, *Ber.*, **69**, 1245 (1936).

[14] L. Clémente and C. Rivière, U. S. Patent 1,168,164 (1916).

TABLE I

ACETOLYSIS OF NITRATE ESTERS OF SUGARS AND SUGAR DERIVATIVES

Original substance	Yield, %[b]	Acetate derivative Found[a] M.p., °C.	$[\alpha]^{25}\mathrm{D}$, $CHCl_3$	Accepted M.p., °C.	$[\alpha]\mathrm{D}$, $CHCl_3$
Cellobiose octanitrate[c]	83[d]	224–226	+ 41°	229.5	+ 41°
β-D-Glucose pentanitrate[e]	85[f]	112-113	+101	114	+102
Levoglucosan (1,6-anhydro-β-D-glucopyranose) trinitrate	72[f]	104-107	+99.5	114	+102
Erythritol tetranitrate	88	86-88	*meso*	89	*meso*
Pentaerythritol tetranitrate	92	83-84	....	84	...
D-Mannitol hexanitrate	87	120-121.5	+25.5	120	+26

[a] On recrystallized material. [b] Unrecrystallized material of good purity. [c] W. R. Ashford, T. H. Evans and H. Hibbert, *Can. J. Research*, **B25**, 155 (1947). [d] α-Cellobiose octaacetate was the product. [e] G. Fleury and L. Brissaud, *Compt. rend.*, 222, 1051 (1946). [f] α-D-Glucose pentaacetate was the product.

sulfuric or benzenesulfonic acid and by this means cellulose nitrates of low nitrogen content were successfully acetolyzed.

Experimental

The following procedure for the preparation of D-mannitol hexaacetate from D-mannitol hexanitrate is typical of the acetolysis method in general. One gram of crystalline D-mannitol hexanitrate was dissolved in 25 ml. of a solution of acetic anhydride and 100% sulfuric acid, 10:1 by volume, at 0°. The solution was allowed to stand for 24 hours in an ice–salt-bath. It was then poured into 400 g. of ice and water to hydrolyze the excess acetic anhydride. The hydrolyzate was extracted with five 40-ml. portions of chloroform. The extract, after washing with a saturated water solution of sodium bicarbonate and then with water, was dried over anhydrous calcium chloride. Evaporation of the solvent left a crude residue; yield 0.85 g. The residue was recrystallized from 95% ethanol and its physical constants were determined (Table I).

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Chromatography of Sugars and Their Derivatives; Aldonamides[1]

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In a previous publication on the chromatography of sugars and their derivatives a general method for separations was described and a table or classification was established in which the following principal groups appeared: (I) sugars, sugar alcohols and glycosides; (II) acetylated sugars; and (III) methylated sugars.[2] To this list there may now be added a fourth group, the aldonamides. These are readily available derivatives of the aldonic acids. Using the same adsorbent as before, Silene EF–Celite in admixture, and dioxane as a developer a number of such amides have been zoned and put into classes. As a continuation of the aforementioned classification this new group appears in Table I. To test the subdivision a single pair, L-fuconamide and D-gluconamide, were separated, with good recovery of each effected. Coleman[3] has developed a related chromatographic separation on silicic acid of aldonamides as their O-*p*-azophenylbenzoates.

TABLE I[a]

CHROMATOGRAPHIC ADSORPTION SERIES OF SOME SUGARS AND DERIVATIVES (ARRANGED IN DECREASING ORDER OF ADSORPTIVE STRENGTH)

Adsorbent, 0.9 x 10 cm.[b] of 5:1 Silene EF[c]–Celite[d]; adsorbate soln., noted with group heading; developer, noted with class heading.

Group IV. Aldonamides (0.5 cc. of 90%[e] dioxane[f] followed immediately by a solution of 2 mg. of substance in 0.2 cc. of 90% dioxane).

Class 1. (10 cc. of 90% dioxane)	D-Gluco-D-*gulo*-heptonamide D-Galactonamide, D-gluconamide
Class 2. (5 cc. of 90% dioxane)	D-Lyxonamide D-Ribonamide L-Fuconamide

[a] Designed as an addition to Table I of ref. 2. [b] Column dimensions are those of the adsorbent. [c] Product of the Columbia Chemical Division, Pittsburgh Plate Glass Co., Barberton, Ohio. [d] Celite 535, a product of Johns-Manville Co., New York, N.Y. [e] Prepared by diluting 90 cc. of absolute dioxane with 10 cc. of water. [f] Purified by the procedure of K. Hess and H. Frohm, *Ber.*, 71B, 2627 (1938), as modified by L. F. Fieser, "Experiments in Organic Chemistry," D. C. Heath and Co., New York, N. Y., 1941, p. 369.

Experimental

The general techniques of the previously cited work were followed. D-Gluconamide and L-fuconamide, 400 mg. of each in 40 cc. of 90% dioxane, were placed on a column of Silene EF–Celite (5:1 by wt.) prewet with 50 cc. of 90% dioxane. Development was made with 450 cc. of 90% dioxane. The column was extruded and the zones detected by a brush streak[4] with a freshly prepared 1% solution of potassium permanganate in 2.5 N sodium hydroxide. Zones were located at 60–92 mm. and 115–150 mm. from the column top. The zones were eluted and their organic substituents purified as described previously.[2] From the upper zone a 74% recovery of D-gluconamide was effected; m.p. 143–144.5°, $[\alpha]^{18}\mathrm{D}$ +30.5° (*c* 4, water), accepted values 145° and $[\alpha]^{20}\mathrm{D}$ +31°. From the lower zone L-fuconamide was recovered in 66% yield, m.p. 179.5–180.5°, $[\alpha]^{18}\mathrm{D}$ −31° (*c* 4, water), accepted values 180.5° and $[\alpha]^{20}\mathrm{D}$ −31°.

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[2] L. W. Georges, R. S. Bower and M. L. Wolfrom, THIS JOURNAL, **68**, 2169 (1946).

[3] G. H. Coleman, private communication.

[4] This is best effected by holding the solution in a medicine-dropper whose tip is drawn to a fine capillary and bent nearly at a right angle.