prepared by conventional means and recrystallized from petroleum ether, had m.p. 60–62° (lit.[37] 60–62°).

3,5-Dibromobenzoic acid (from 1,3-dibromo-4-nitrobenzene): m.p. 219–220° (lit.[38] 219–220°); the amide, prepared by conventional means, had m.p. 184–186° (lit.[39] 187°).

2,4-Dibromobenzoic acid (from 1,3-dibromo-5-nitrobenzene): m.p. 163–167° (lit.[37] 168–169°); the amide, prepared by conventional means, had m.p. 195–196° (lit.[39] 195°).

2,5-Dibromobenzoic acid (from 1,4-dibromo-2-nitrobenzene): m.p. 151–153° (lit.[40] 157°); the mixed m.p. with an authentic sample (from permanganate oxidation of Eastman Kodak 2,5-dibromotoluene) of m.p. 156° was 152–155°.

***m*-Bromobenzoic acid** (from 1-bromo-2-nitrobenzene): m.p. 151–153°; mixed m.p. with an authentic sample (Eastman Kodak) was 152–155°.

Products from Reactions of Nitrosobenzene.—The reaction of nitrosobenzene with 2.6 g. of potassium cyanide in 25 cc. of 48% ethanol for one hour at 155° furnished a small crop of red needles which, after crystallization from ethanol, weighed 0.3 g. and had m.p. 65–66°. These were recognized as azobenzene (m.p. 68°) by reduction (tin and hydrochloric acid) to benzidine (m.p. 117–120°) which did not depress the mixed m.p. with an authentic sample.

The run in 75% dioxane yielded a yellowish neutral material of m.p. 29–31°; the mixed m.p. with an authentic sample of azoxybenzene (m.p. 31.5–32.2°) was 30–31.5°.

Experiments with Deuterium-labeled Compounds.—A tube was charged with 5.0 g. of nitrobenzene, 5.0 g. of anhydrous potassium cyanide, 5 cc. of the ethanol-O-*d* preparation described above, and 5 cc. of heavy water. It was sealed, heated one hour at 150–160°, and cooled. By our usual procedure, about 3 g. of nitrobenzene were recovered, and 0.380 g. of benzoic acid was obtained. After crystallization from common distilled water, and then sublimation, the acid showed m.p. 120.5–121°. It was quantitatively diluted with repurified reagent grade benzoic acid, and the mixture was sublimed to give the analytical sample.

At Reed, a tube containing 2.2 g. of deuterium-labeled 1-chloro-4-nitrobenzene, 5 g. of potassium cyanide and 30 cc. of 48% ethanol was sealed and heated at 160–170° for 75 minutes. The tube exploded as it was being opened, but a good deal of the product could be isolated from the lower part of the tube which did not shatter. The *m*-chlorobenzoic acid product, m.p. 151–152°, was isolated in the usual way and purified by crystallization from water. It was quantitatively diluted with repurified Eastman Kodak *m*-chlorobenzoic acid, and the mixture was recrystallized from water to give the analytical sample. At North Carolina, essentially the same procedure was followed except that a lower ratio of cyanide to nitro compound was employed.

The deuterium analyses were done in the Division of Steroid Biochemistry, Sloan-Kettering Institute for Cancer Research, by Josephine Leong under the supervision of Dr. David K. Fukushima and Dr. Thomas F. Gallagher.

Acknowledgments.—We thank the Research Corporation for support of this research during its early stages, and the Office of Ordnance Research, U. S. Army, for financial assistance more recently. We are also grateful to Dr. David K. Fukushima for his interest and advice.

CHAPEL HILL, N. C.

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[38] M. T. Bogert and W. F. Hand, THIS JOURNAL, **25**, 942 (1903).

[39] J. J. Sudborough, *J. Chem. Soc.*, **67**, 594 (1895).

[40] S. A. Koopal, *Rec. trav. chim.*, **34**, 148 (1915).

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY OF THE UNIVERSITY OF ROCHESTER]

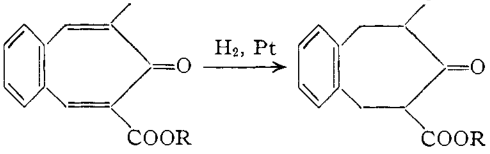
A Rearrangement Involving Aromatization. The Condensation of Δ^4-Tetrahydrophthalaldehyde with Diethyl Acetonedicarboxylate[1]

BY D. S. TARBELL AND BERNARD WARGOTZ[2]

RECEIVED JUNE 2, 1954

The condensation of Δ^4-tetrahydrophthalaldehyde with diethyl acetonedicarboxylate in the presence of piperidine acetate yields, by a rearrangement involving aromatization, 5,8-dihydro-2-hydroxy-3-carbethoxy-1-naphthaleneacetic acid ethyl ester (IX). The structure of this product has been established by converting it to the following compounds, which have been synthesized: the lactone of 2-hydroxy-1-naphthaleneacetic acid (XIII), 2-hydroxy-3-carbethoxy-1-naphthaleneacetic acid ethyl ester and 5,6,7,8-tetrahydro-2-hydroxy-3-carbethoxy-1-naphthaleneacetic acid ethyl ester. The ultraviolet and infrared spectra of the compounds are in agreement with the assigned structures, and the mechanism of the aromatization is discussed. An improved procedure for preparing Δ^4-tetrahydrophthalaldehyde is described, which involves the lithium aluminum hydride reduction of N,N,N',N'-tetramethyltetrahydrophthalamide. It is found that a basic ion-exchange resin is a good catalyst for the condensation of phthalaldehyde and diethyl acetonedicarboxylate.

The condensation of phthalaldehyde with diethyl acetonedicarboxylate leads to the dicarbethoxybenzocycloheptadieneone[3] I, and a similar reaction between phthalaldehyde and hydroxy- or methoxyacetone yields β,γ-benzotropolone[4] or its methyl ether.[5] The use of Δ^4-tetrahydrophthalaldehyde in similar condensation reactions might be expected to lead to compounds offering interesting possibilities for further synthetic operations in the tropolone and colchicine fields. The present paper reports a study of the condensation product from tetrahydrophthalaldehyde and diethyl acetonedicarboxylate; it is shown that the product does not contain a seven-membered ring, as expected, but is actually a dihydronaphthalene derivative. The condensation reaction therefore involves a molecular rearrangement with the formation of a benzenoid instead of a seven-membered ring.



I VII

The preparation of Δ^4-tetrahydrophthalaldehyde by addition of butadiene to maleic or fumaric dialdehyde was described previously.[6] A more convenient method has been found to be the lithium

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[1] This research was aided by a grant from the National Cancer Institute of the National Institutes of Health, Public Health Service.

[2] Abbott Laboratories Fellow, 1953–1954.

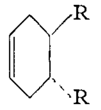
[3] J. Thiele and J. Schneider, *Ann.*, **369**, 287 (1909).

[4] D. S. Tarbell, G. P. Scott and A. D. Kemp, THIS JOURNAL, **72**, 379 (1950).

[5] (a) D. S. Tarbell and J. C. Bill, *ibid.*, **74**, 1234 (1952); (b) G. A. Nicholls and D. S. Tarbell, *ibid.*, **74**, 4935 (1952).

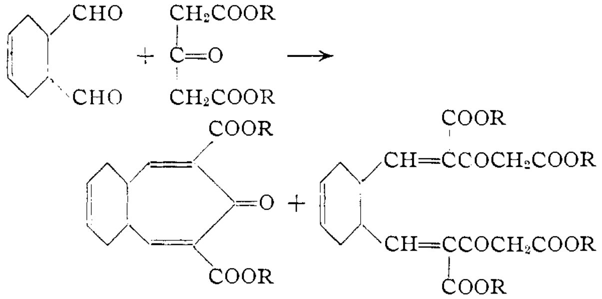
[6] D. L. Hufford, D. S. Tarbell and T. R. Koszalka, *ibid.*, **74**, 3014 (1952).

aluminum hydride reduction of N,N,N',N'-tetramethyl-Δ^4-tetrahydrophthalamide (II), which is readily prepared from Δ^4-tetrahydrophthalyl chloride.[7,8] The reduction leads to the formation of appreciable amounts of the diamine IV, if the lithium aluminum hydride is added rapidly to the diamide. The configurations of II, III and IV are regarded as *trans*, because the tetrahydrophthalyl chloride (precursor of II) is prepared[7] from butadiene and fumaryl chloride; furthermore, reduction of III to hexahydrophthalaldehyde, and oxidation of this with silver oxide, yields *trans*-hexahydrophthalic acid.[9]

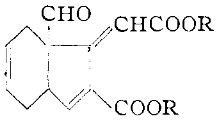


II. R = $CON(CH_3)_2$
III, R = CHO
IV, R = $CH_2N(CH_3)_2$

The condensation of III with diethyl acetonedicarboxylate yielded in the presence of piperidine acetate[10] a product, m.p. 126–127°, of the composition expected for V, along with a by-product, probably VI. The behavior of the main product did not, however, correspond to that expected for structure V; thus, dehydrogenation with chloranil in xylene[6,11] did not lead to Thiele's product I, and reduction with hydrogen and platinum in acetic acid gave an uptake of only one mole of hydrogen instead of three. It was shown that under the same conditions, Thiele's compound absorbed two moles of hydrogen in the seven-membered ring, forming VII. An alternative structure VIII for the condensation product was ruled out by showing that the material did not yield a carboxylic acid when treated with silver oxide[12] or with chromic acid in acetic acid.[13]

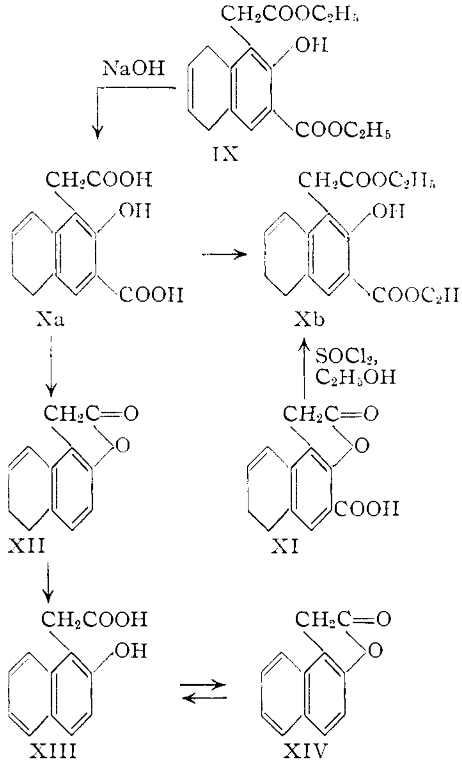


V VI, R = C_2H_5



VIII, R = C_2H_5

The structure of the condensation product was eventually shown to be 5,8-dihydro-2-hydroxy-3-carbethoxy-1-naphthaleneacetic acid ethyl ester (IX), by a combination of degradative, synthetic and spectral evidence. IX showed infrared absorption bands in carbon disulfide at 3090 (strongly associated hydroxyl), 1739 (normal ester carbonyl) and 1670 cm.$^{-1}$ (chelated ester carbonyl).[14] It gave a green ferric chloride color, was acetylated by acetic anhydride, and was converted by saponification to a dibasic acid Xa. The saponification of the diester IX was accompanied by isomerization of the double bond into conjugation with the benzenoid ring in Xa; re-esterification of Xa did not regenerate IX, but gave instead an isomer Xb, m.p. 113–114°. This compound was also formed from the lactone XI by treatment with thionyl chloride and alcohol. The ultraviolet spectra (see below) of IX and Xa and Xb confirm the shift of the double bond into a position of conjugation in Xa and derived compounds. The double bond may be in the 5,6- instead of the 7,8-position as shown.



The dibasic acid Xa was converted by heating to 230° to a lactone XI, which melted with decomposition at about 285°. The lactonic nature of XI was indicated by its composition and its behavior on titration; it consumed one mole of alkali in the cold, and a second one when heated. It showed infrared bands at 1797 (γ-lactone carbonyl) and 1667 cm.$^{-1}$ (carboxy carbonyl).

The decarboxylation of Xa with quinoline and copper powder yielded the neutral lactone XII, m.p. 127°, which was converted by palladium-on-charcoal in boiling biphenyl to the completely aromatic lactone XIII, m.p. 103–104°. This product

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[7] K. Alder and M. Schumacher, *Ann.*, **564**, 107 (1949).

[8] The reduction of N,N,N'N'-tetramethylphthalamide to phthalaldehyde is reported by F. Weygand and D. Tietjen, *Chem. Ber.*, **84**, 625 (1951).

[9] Lithium aluminum hydride does not invert carbon atoms adjacent to the group being reduced (D. S. Noyce and D. B. Denney, THIS JOURNAL, **72**, 5743 (1950).

[10] (a) R. Kuhn, W. Badstübner and C. Grundmann, *Ber.*, **69**, 98 (1936); (b) A. C. Cope, *et al.*, THIS JOURNAL, **63**, 3452, 3456 (1941).

[11] R. T. Arnold and C. Collins, *ibid.*, **61**, 1407 (1939).

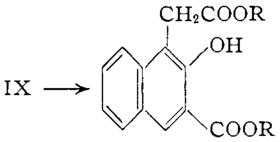
[12] K. Bernhauer and R. Forster, *J. prakt. Chem.*, **147**, 199 (1937).

[13] H. Koechlin and T. Reichstein, *Helv. Chim. Acta*, **30**, 1673 (1947).

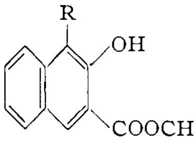
[14] (a) E. D. Bergmann, Y. Hirschberg and S. Pinchas, *J. Chem. Soc.*, 2351 (1950); (b) I. M. Hunsberger, THIS JOURNAL, **72**, 5626 (1950).

was shown to be identical with the known lactone of 2-naphthol-1-acetic acid (XIV) by comparison with synthetic samples[15] of both the lactone XIII and the naphtholacetic acid XIV, through mixed m.p. and comparison of spectra.

A further confirmation of structure IX for the condensation product was obtained by dehydrogenating it in xylene with chloranil; the product XV melted at 119–120°, and although it gave only a slight depression on mixed m.p. with the starting material IX, its ultraviolet spectrum was definitely different and indicated the presence of a naphthalene nucleus. The structure of XV was established by its synthesis from methyl 2-hydroxy-3-naphthoate; the steps involved were chloromethylation with chloromethyl ether in acetic acid[16] to yield methyl 1-chloromethyl-2-hydroxy-3-naphthoate[17] (XVIII), the conversion of this to the nitrile XIX, hydrolysis of the nitrile to the acid XVI, and esterification of the latter to form the diester XV. The synthetic product XV was shown to be identical with the sample obtained by chloranil dehydrogenation by mixed m.p. and comparison of spectra; the two acetates were also identical.



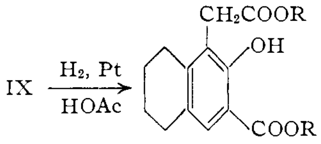
XV, R = C_2H_5
XVI, R = H



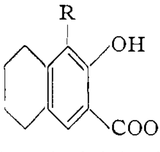
XVII, R = H
XVIII, R = CH_2Cl
XIX, R = CH_2CN

Compound IX was dehydrogenated and acetylated by selenium dioxide in boiling acetic anhydride to form 2-acetoxy-3-carbethoxy-1-naphthaleneacetic acid ethyl ester, which was identical with the acetylation product from synthetic XV.

The evidence given so far has established the structures of products obtained from IX by fairly drastic procedures, which might have involved molecular rearrangement of the original structure. A more conclusive proof of the structure was therefore provided by the synthesis of the dihydro compound XX, obtained from IX by catalytic reduction at room temperature.



XX, R = C_2H_5
XXI, R = H



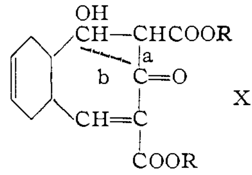
XXII, R = H, R' = CH_3
XXIII, R = CH_2Cl, R' = CH_3
XXIV, R = CH_2CN, R' = CH_3
XXV, R = CH_2CN, R' = H

Methyl 2-hydroxy-3-naphthoate (XVII) was reduced to the 5,6,7,8-tetrahydro compound XXII with Raney nickel and hydrogen.[18,19] The tetrahydro compound XXII was converted to the chloromethyl derivative XXIII with chloromethyl ether and zinc chloride in petroleum ether, and the latter was converted to the nitrile ester XXIV; some of the corresponding acid XXV was obtained also. Treatment of the nitrile ester XXIV with alcoholic hydrogen chloride gave a crude sample of the diethyl ester XX, which was purified by saponification and re-esterification. The diester XX thus obtained was identical with the product formed by catalytic reduction of IX.

The main features of the ultraviolet spectra of the key compounds described, which were very useful in the structural work, are listed in Table I.

The evidence for the position assigned to the double bond in IX, and in the diacid Xa and its derivatives, is as follows. (1) The ultraviolet spectrum of IX is identical with that of its dihydro compound XX, indicating that the double bond in IX is not conjugated with the benzene ring. (2) Re-esterification of the diacid Xa yielded the diester Xb with an absorption band at 340 mμ, which is not shown[20] by IX.

The mechanism of the rearrangement involved in the formation of the aromatic ring in IX appears to present some novel features, and must involve some such process as the following, in which bond a is broken and bond b is formed, in structure XXVI or its equivalent.[21] The structure of IX is incompatible with the symmetrical cyclopropanone type of intermediate, which has been demonstrated in the alkaline rearrangement of α-haloketones,[22] because the carbonyl group in XXVI is not converted to a carboxyl. The aromatization reactions of tropolones, in which a seven-membered ring is aromatized under basic conditions,[23] present some points of similarity to the present reaction.



XXVI

A reasonably satisfactory picture of the rearrangement indicated in XXVI is the following, in

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[15] (a) M. Julia, *Bull. soc. chim. France*, **20**, 640 (1953); (b) A. H. Cook, J. Downor and B. Hornung, *J. Chem. Soc.*, 502 (1941).

[16] *Cf.* G. Vavon, J. Bolle and J. Calin, *Bull. soc. chim. France*, **6**, 1025 (1939); O. Gawron, THIS JOURNAL, **71**, 744 (1949).

[17] W. A. Jacobs and M. Heidelberger, *J. Biol. Chem.*, **20**, 682 (1915).

[18] R. T. Arnold, H. E. Zaugg and J. Sprung, THIS JOURNAL, **63**, 1314 (1941).

[19] The method of Papa, Schwenk and Breiger, *J. Org. Chem.*, **14**, 366 (1949), for the reduction of 2-hydroxy-3-naphthoic acid to the 5,6,7,8-tetrahydro compound with Raney alloy and alkali was unsatisfactory in our hands, giving mixtures and poor yields.

[20] The effect of the conjugated double bond on the spectrum of the benzenoid ring is analogous to that of the double bond in 3,4-dihydronaphthalene on the spectrum of tetralin (R. A. Friedel and M. Orchin, "Ultraviolet Spectra of Aromatic Compounds," John Wiley and Sons Inc., 1951; figs. 10 and 29). The ultraviolet spectrum of 3,4-dihydro-6-methoxynaphthalene is given by R. B. Woodward and R. H. Eastman, THIS JOURNAL, **66**, 674 (1944).

[21] It is possible that the rearrangement indicated in XXVI may take place before the seven-membered ring has been closed by the aldol condensation with the second aldehyde group of III; however, the driving force in the rearrangement is undoubtedly the stability of the aromatic ring, and hence the ring closure is probably at least simultaneous with the shift in the carbon skeleton.

[22] R. B. Loftfield, THIS JOURNAL, **73**, 4707 (1951); this article contains an excellent summary of the earlier work.

[23] *Cf.* the illuminating discussion by W. E. Doering and L. H. Knox, *ibid.*, **73**, 832 (1951).

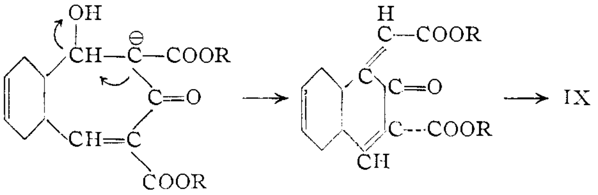
TABLE I

ULTRAVIOLET SPECTRA IN 95% ETHANOL

Maxima (mμ)	log ε
Dicarbethoxybenzocycloheptadienone (I)	
235	4.4
273	4.6
310 (shoulder)	3.99
Bis-condensation product VI from tetrahydrophthalaldehyde	
252	4.23
Bis-condensation product from phthalaldehyde	
253	4.13
5,8-Dihydro-2-hydroxy-3-carbethoxy-1-naphthaleneacetic acid ethyl ester (IX)	
216	4.35
252	3.84
320	3.57
5,6-Dihydro-2-hydroxy-3-carbethoxy-1-naphthaleneacetic acid ethyl ester (Xb)	
219	4.38
284	4.10
340	3.66
5,6-Dihydro-2-hydroxy-3-carboxy-1-naphthaleneacetic acid (Xa)	
284	3.85
326	3.48
5,6-Dihydro-2-hydroxy-3-carboxy-1-naphthalenacetic acid lactone (XI)	
226	4.34
280	4.19
318	3.62
5,6-Dihydro-2-hydroxy-1-naphthaleneacetic acid lactone (XII)	
228	4.17
255	3.79
262	3.85
272	3.74
300	3.15
2-Hydroxy-3-carbethoxy-1-naphthaleneacetic acid ethyl ester (XV)	
243	4.69
276	3.84
288	3.89
300	3.78
370	3.43
Diacid of XV (XVI)	
240	4.44
277	3.34
286	3.80
298	3.17
360	3.16
5,6,7,8-Tetrahydro-2-hydroxy-3-carbethoxy-1-naphthaleneacetic acid ethyl ester (XX)	
220	4.29
252	4.10
321	3.70
Diacid of XX (XXI)	
250	3.85
320	3.55
Methyl 5,6,7,8-tetrahydro-2-hydroxy-3-naphthoate (XXII)	
220	4.10
249	3.97
318	3.54
5,6,7,8-Tetrahydro-2-hydroxy-3-naphthoic acid[a]	
219	4.33
240	4.15
315	3.57

[a] The ester XXII absorbs at longer wave lengths than the corresponding acid in alcohol solution, as found by Bergmann, *et al.* (ref. 14a), for salicylic acid, 2-hydroxy-3-naphthoic acid and the corresponding esters.

which the anion XXVII, derived from XXVI by action of base, gives a nucleophilic displacement of the hydroxyl group by migration of the carbonyl carbon with its electron pair. This process, followed by shift of a hydride ion, leads to XXVIII, which gives IX by proton shifts.



XXVII XXVIII

An alternative scheme for the formation of IX, involving a series of cleavages and acylations, with the by-product VI as an intermediate, was shown to be improbable; VI did not yield IX when treated under the conditions of the original condensation.

Experimental[24]

N,N,N′,N′-Δ^4-Tetramethyltetrahydrophthalamide (II).—Crude Δ^4-tetrahydrophthalyl chloride[7] (96 g.) in 1 l. of dry ether was chilled in a Dry Ice–acetone-bath, and 118 g. of anhydrous dimethylamine was added with vigorous stirring over a period of 20 min., through a tube extending below the surface of the solution. After addition was complete, the solution was stirred for 1 hr., the dimethylamine hydrochloride was removed by filtration and the filter cake was washed with dry ether. The combined filtrates were dried and concentrated *in vacuo*, giving 100 g. of crude product; recrystallization of this material from hexane gave 93 g. of II, m.p. 53–56°, which was raised to 55–56° by further crystallization from hexane.

Anal. Calcd. for $C_{12}H_{20}N_2O_2$: C, 64.25; H, 8.99; N, 12.49. Found: C, 64.30; H, 9.20; N, 12.30.

The corresponding **N,N,N′,N′-tetraethylamide** was prepared in a similar manner. The analytical sample was prepared by three distilllations through a short path still and did not crystallize; it had $n^{20}D$ 1.4975.

Anal. Calcd. for $C_{16}H_{28}N_2O_2$: C, 68.53; H, 10.07; N, 9.99. Found: C, 68.66; H, 10.12; N, 9.84.

Δ^4-Tetrahydrophthalaldehyde (III).—To a cold (0°) solution of 38.0 g. of tetramethyltetrahydrophthalamide (II) in a mixture of 700 cc. of ether and 200 cc. of tetrahydrofuran, 9.0 g. of finely powdered lithium aluminum hydride was added in small portions, while the reaction mixture was stirred under nitrogen. The addition required 30 min., and after stirring for an additional 2.5 hr. at 0–5°, the reaction mixture was then allowed to stand overnight at room tem-

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[24] Melting points of all compounds exhibiting a transition at the m.p. were taken on the hot stage; all m.p.'s are corrected. Microanalyses are by Misses Claire King, Viola Williams, Annette Smith and Microtech Laboratories. We are indebted to Mr. Carl Whiteman for the infrared spectra. In chromatographic procedure, unless otherwise indicated, Davidson silica gel, mesh size "Through 200" was used; the petroleum ether used for elution was of b.p. 30–60°. Solvents were of C.P. or analytical grades, and solvent mixtures were made up on a volume per cent. basis.

perature. The complex and excess lithium aluminum hydride were decomposed with 100 cc. of 10% sulfuric acid followed by ice-water. The inorganic salts were removed by filtration, the filter cake washed with ether and the combined filtrates concentrated *in vacuo*. The concentrate was taken up in ethyl acetate and the solution was washed a few times with dilute hydrochloric acid, with sodium carbonate solution, and then with water until neutral. Drying and removal of solvent from the ethyl acetate solution gave 10.2 g. of crude dialdehyde, which yielded, on distillation, 7.8 g. of material, with the following constants: b.p. 70–74° (1.2 mm.), $n^{23}\text{D}$ 1.4960. The reported values[6] for Δ^4-tetrahydrophthalaldehyde are $n^{20}\text{D}$ 1.4940; b.p. 56° (0.3 mm.). The dialdehyde obtained by the above procedure yielded the same bis-dinitrophenylhydrazone reported previously[6]; reduction with hydrogen and palladium, followed by oxidation with silver oxide, yielded *trans*-hexahydrophthalic acid, as described previously.[6]

4,5-Bis-dimethylaminomethylcyclohexene (IV).—This diamine is also formed by the reduction of the tetramethylphthalamide, in yields depending on the rate of addition of lithium aluminum hydride to the cold solution. Thus, fractional distillation with a spinning band column of the crude reduction product from 20.0 g. of the diamide, without first washing with dilute acid, gave 3.5 g. of the diamine IV, b.p. 78° (2.5 mm.), $n^{20}\text{D}$ 1.4780.

The **dipicrate**, after three crystallizations from methanol, melted at 206–207°.

Anal. Calcd. for $C_{24}H_{40}N_3O_{14}$: C, 44.04; H, 4.62; mol. wt., 655. Found: C, 44.26; H, 4.94; mol. wt.,[25] 667.

The **methiodide**, after three crystallizations from methanol, melted at 263–264°.

Anal. Calcd. for $C_{14}H_{30}I_2N_2$: C, 35.01; H, 6.30. Found: C, 34.87; H, 6.40.

5,8-Dihydro-2-hydroxy-3-carbethoxy-1-naphthaleneacetic Acid Ethyl Ester (IX) by Condensation of Tetrahydrophthalaldehyde and Diethyl Acetonedicarboxylate.—A solution of 7.0 g. of tetrahydrophthalaldehyde (prepared by reduction of the diamide II, $n^{23}\text{D}$ 1.4960), 9.9 g. of redistilled diethyl acetonedicarboxylate,[26] 0.87 cc. of acetic acid, and 0.23 cc. of dry piperidine in 25 cc. of dry benzene was refluxed for 18 hr.; the water formed was collected in a water separator.[10b] Removal of the benzene under diminished pressure gave a viscous oil, to which 25 cc. of alcohol was added, and the solution seeded[27] with a sample of IX. The solution deposited after 3 hr. 2.5 g. of crystals of m.p. 125–126°, and an additional 290 mg. of product, m.p. 123–124°, was obtained from the mother liquors. The mother liquors were then chromatographed on 50 g. of silica gel; elution with 10% ether–petroleum ether gave an additional 1.6 g. of crude product, m.p. 117–118° after recrystallization from ethanol. The analytical sample, after recrystallization from ethanol, melted at 126–127°, and gave a green ferric chloride test.

Anal. Calcd. for $C_{17}H_{20}O_5$: C, 67.09; H, 6.62. Found: C, 67.35; H, 6.62.

The Bis-condensation Product VI.—From a condensation reaction carried out essentially as described above on 2.8 g. of the dialdehyde III and 3.8 g. of diethyl acetonedicarboxylate, 1.8 g. of crystalline product IX, m.p. 125–126°, was obtained; the mother liquors were chromatographed on 50 g. of silica gel, and elution with 10% ether–petroleum ether gave 640 mg. additional of crude IX. The bis-condensation product VI (710 mg.) was obtained by elution with 30% ether–petroleum ether; after three crystallizations from alcohol, it melted at 180–182°, and gave a reddish-violet ferric chloride color.

Anal. Calcd. for $C_{26}H_{34}O_{10}$: C, 61.65; H, 6.77. Found: C, 61.31; H, 6.74.

5,8-Dihydro-2-acetoxy-3-carbethoxy-1-naphthaleneacetic Acid Ethyl Ester.—Acetylation of the diester IX (105 mg.) by refluxing with acetic anhydride and *p*-toluenesulfonic acid for 4.5 hr. yielded 121 mg. of crude product, after working up in the usual way. Chromatography on 10 g. of silica gel and elution with 40% ether–petroleum ether gave 28 mg. of oil, which crystallized when treated with ethanol–water. A further crystallization from the same solvents gave material of m.p. 40–41°. It showed infrared bands at 1745 and 1706 cm.$^{-1}$.

Anal. Calcd. for $C_{19}H_{22}O_6$: C, 65.88; H, 6.40. Found: C, 65.91; H, 6.29.

5,6-Dihydro-2-hydroxy-3-carboxy-1-naphthaleneacetic Acid (Xa).—Saponification of 500 mg. of the diester IX by heating with 100 cc. of 10% sodium hydroxide on the steam-bath for 2 hr., followed by acidification with 12 *N* hydrochloric acid, precipitated the diacid Xa; after filtration and washing with water, 370 mg. of crystals was obtained. Two recrystallizations from ethyl acetate followed by one crystallization from methanol–water gave a product melting with transition at 233°, with subsequent melting with decomposition at 300°.

Anal. Calcd. for $C_{13}H_{12}O_5$: C, 62.90; H, 4.87; neut. equiv., 124. Found: C, 63.24; H, 4.93; neut. equiv., 127.

5,6-Dihydro-2-hydroxy-3-carboxy-1-naphthaleneacetic Acid Lactone (XI) from the Corresponding Diacid Xa.—The diacid Xa (160 mg.) was heated to 230–240° for 10 min., and the product was sublimed in high vacuum at 210°; the sublimate (108 mg. of white solid) was recrystallized three times from acetone, and melted at 294–295° with dec.

Anal. Calcd. for $C_{13}H_{10}O_4$: C, 67.82; H, 4.38. Found: C, 67.82; H, 4.30.

Titration in the cold of 0.4366 mmole of the compound XI consumed 0.3722 mmole of base; addition of excess alkali, heating on the steam-bath for 30 min. and back titration showed the consumption of an additional 0.3988 mmole of base. A sample of the lactone XI was warmed with 5% alkali, acidified and recrystallized from methanol–water to give a product of m.p. (with transition) 230–232°, final m.p. with dec. 281–282°. It appeared to be identical with the starting diacid X.

5,6-Dihydro-2-hydroxy-3-carbethoxy-1-naphthaleneacetic Acid Ethyl Ester (Xb).—The diacid Xa (60 mg.) was esterified by refluxing for 12 hr. with ethanol and mineral acid. The crude product (31 mg.) was chromatographed on silica, and elution with 10% ether–petroleum ether gave the crystalline diester, m.p. 113–114°, unchanged by recrystallization from alcohol–water. The same product was obtained by treating the lactone XI with thionyl chloride and alcohol.

Anal. Calcd. for $C_{17}H_{20}O_5$: C, 67.09; H, 6.62. Found: C, 67.12; H, 6.65.

Refluxing the diacid Xa with alcoholic hydrogen chloride for 36 hr. gave a product which apparently contained some of the completely aromatic diester XV, because it showed absorption at 365 mμ (log ε 3.32).

Decarboxylation of the Diacid Xa to 5,6-Dihydro-2-hydroxy-1-naphthaleneacetic Acid Lactone (XII).—The diacid Xa (520 mg.) was heated in 3.0 cc. of pure quinoline with 10–20 mg. of copper powder at 200–235° for a few min., the heating being continued after ebullition had ceased. The product was taken up in ether, the copper powder was removed by filtration, the ether solution was washed a few times with 10% hydrochloric acid, was dried, and the solvent was removed *in vacuo*. The crude crystalline residue was chromatographed on 50 g. of silica gel; elution with benzene yielded 140 mg. of the lactone XII, m.p. 123–125°, which, after three recrystallizations from ethanol, melted at 126–127°.

Anal. Calcd. for $C_{12}H_{10}O_2$: C, 77.40; H, 5.41. Found: C, 77.10; H, 5.55.

Dehydrogenation of XII to 2-Hydroxy-1-naphthaleneacetic Acid Lactone (XIII).—A sample of 860 mg. of crude XII, prepared as above, was heated with 3.0 g. of biphenyl and 300 mg. of 10% palladium charcoal for 5 hr. at 240–260°. The product was cooled and taken up in hexane, the catalyst was removed by filtration and the solvent was removed *in vacuo*. The residue was taken up again in ether, the solution was washed with dilute sodium carbonate solution, then with water and was dried. The solution was concentrated, and the resulting oil was chromatographed on 50 g. of silica gel. Elution with petroleum ether gave biphenyl; elution with 10% ether–petroleum ether gave 125 mg. of 2-hydroxy-1-naphthaleneacetic acid lactone, m.p. 101–103°, and an additional 98 mg., m.p. 95–100° from later fractions. Recrystallization from alcohol raised

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[25] Determined spectrophotometrically following K. G. Cunningham, W. Dawson and F. S. Spring, *J. Chem. Soc.*, 2305 (1951).

[26] R. Adams and H. M. Chiles, "Organic Syntheses," Coll. Vol. I, 2nd Ed., John Wiley and Sons, Inc., New York, N. Y., p. 237.

[27] Prepared in preliminary studies by Dr. D. L. Hufford.

the m.p. to 103–104.5°, giving no depression on mixed m.p. with a synthetic sample of the lactone prepared from 2-methoxynaphthalene by the published procedure.[15a,b]) The infrared spectra of the samples of XII obtained by synthesis and degradation were identical, as were also the samples of 2-hydroxy-1-naphthaleneacetic acid derived from the two samples of lactone.

Dehydrogenation of 5,8-Dihydro-2-hydroxy-3-carbethoxy-1-naphthaleneacetic Acid Ethyl Ester (IX) to the Aromatic Compound XV.—The diester IX (300 mg.) was refluxed for 4 hr. in 15 cc. of dry xylene with 500 mg. of chloranil. After standing overnight, the chloranil and its hydroquinone were removed by filtration, washed with dry benzene, and the filtrates were combined, dried and concentrated *in vacuo*. The residue was taken up in ether, washed with 5% alkali, then with water and was dried. Concentration of the solution under reduced pressure gave 355 mg. of crude product, which, after several crystallizations from alcohol, melted at 119–120°. A mixed m.p. with the starting material IX gave only a small depression (m.p. 115–117°), but the ultraviolet spectrum of the dehydrogenation product clearly showed that a change had occurred. The fact that the dehydrogenation product was identical with synthetic XV, prepared as described below, was shown by mixed m.p. and by the correspondence of the ultraviolet and infrared spectra of the two samples.

Anal. Calcd. for $C_{17}H_{18}O_5$: C, 67.54; H, 6.00. Found: C, 67.90; H, 6.16.

Methyl 1-Chloromethyl-2-hydroxy-3-naphthoate (XVIII).—To a solution of 14 g. of chloromethyl ether in 200 cc. of acetic acid[16] was added rapidly with efficient stirring at 10–15° a solution of 19 g. of methyl 2-hydroxy-3-naphthoate[28] in 80 cc. of acetic acid. After the addition was complete, the reaction mixture was stirred an additional hour, the ice-bath was removed, and 20 g. of the chloromethyl compound XVIII, m.p. 163–164°, crystallized out. Recrystallization from toluene raised the m.p. to 164–165°; the reported[17] m.p. is 164.5–166°.

Methyl 1-Cyanomethyl-2-hydroxy-3-naphthoate (XIX).—To a solution of 1.8 g. of the chloromethyl compound XVIII in 45 cc. of acetone was added rapidly with vigorous stirring a solution of 1.0 g. of potassium cyanide in 25 cc. of water. After standing 1 hr. at 20–30° after the addition was complete, the solution was concentrated on the steam-bath under reduced pressure to remove the acetone, and water was added to restore the original volume. Cautious acidification with 6 *N* hydrochloric acid gave a yellow precipitate of the cyanomethyl compound XIX, which was collected, washed with water and dried; the yield was 1.2 g. of material of m.p. 178–185°. Several crystallizations from acetone gave the analytical sample, m.p. 190–191.5°. In later experiments, it was found convenient to use the crude nitrile directly without recrystallization.

Anal. Calcd. for $C_{14}H_{11}NO_3$: C, 69.70; H, 4.59. Found: C, 69.71; H, 4.71.

2-Hydroxy-3-carbethoxy-1-naphthaleneacetic Acid Ethyl Ester (XV).—The crude cyanomethyl compound (8.0 g.) was hydrolyzed by heating for 7 hr. at 180° in an oil-bath with a mixture of 65 cc. of concd. sulfuric acid, 50 cc. of acetic acid and 50 cc. of water. The crude diacid XVI (7.2 g.) was obtained by cooling the reaction mixture and collecting the precipitate. To 2.0 g. of the crude diacid in 60 cc. of absolute alcohol was added 2 cc. of concd. sulfuric acid, and the mixture was refluxed for 2 days. From the neutral product was obtained 627 mg. of an oil which was chromatographed on 10 g. of silica gel. Elution with 20% ether–petroleum ether gave 216 mg. of the diester XV, m.p. 116–118°, which was raised to 119.5–120.5° by crystallization from ethanol. As mentioned above, this product was identical with the chloranil dehydrogenation product of IX.

2-Hydroxy-3-carboxy-1-naphthaleneacetic Acid (XVI).—This was obtained by hydrolysis of 96 mg. of the synthetic diester XV described above with 10% alkali. Three re-recrystallizations from ethanol–water gave pure diacid XVI, m.p. 246–247° (with transition) and final melting with dec. at 302–303°.

Anal. Calcd. for $C_{13}H_{10}O_5$: C, 63.41; H, 4.09. Found: C, 63.53; H, 4.49.

2-Acetoxy-3-carbethoxy-1-naphthaleneacetic Acid. A. By Selenium Dioxide–Acetic Anhydride Dehydrogenation of IX.—A solution of 180 mg. of the diester IX in 10 cc. of acetic anhydride was refluxed for 4 hr. with 70 mg. of selenium dioxide. The selenium was removed by filtration while the mixture was still warm, and the deep red filtrate was concentrated *in vacuo;* the residue was chromatographed on 50 g. of silica gel. Elution with benzene gave 97 mg. of oil which was not further characterized; elution with 10% ether–benzene, followed by ether gave 33 mg. of clear oil, which crystallized on standing to a solid of m.p. 53–55°. The m.p. was raised to 55–56° by recrystallization from ethanol, and the infrared spectrum showed bands at 1757, 1730, 1706 and 1623 cm.$^{-1}$.

Anal. Calcd. for $C_{19}H_{20}O_6$: C, 66.27; H, 5.85. Found: C, 66.41; H, 5.84.

B. By Acetylation of Synthetic XV.—The synthetic diester XV described above (140 mg.) was acetylated with acetic anhydride–sodium acetate. The product was worked up in the usual way, and was purified by chromatography on 10 g. of silica gel; elution with 50% ether–petroleum ether gave 111 mg. of the acetoxy derivative, which crystallized to a solid of m.p. 54–55°. This product gave no depression on mixed m.p. with the product from selenium dioxide–acetic anhydride dehydrogenation described above.

5,6,7,8-Tetrahydro-2-hydroxy-3-carbethoxy-1-naphthaleneacetic Acid Ethyl Ester (XX).—The diester IX (250 mg.) was hydrogenated in 25 cc. of acetic acid with 125 mg. of platinum oxide at room temperature, until the uptake was negligible (about 1 mole). The catalyst was removed, washed with alcohol, and the filtrate was concentrated under reduced pressure to give the crude product, which, after two recrystallizations from methanol weighed 145 mg. and melted at 92–94°. Crystallization from pentane raised the m.p. to 96.5–97°; the product was identical with the synthetic compound described below, as shown by mixed m.p. and ultraviolet and infrared spectra comparisons.

Anal. Calcd. for $C_{17}H_{22}O_5$: C, 66.65; H, 7.22. Found: C, 66.37; H, 7.56.

5,6,7,8-Tetrahydro-2-hydroxy-3-carboxy-1-naphthaleneacetic Acid (XXI).—The diester XX (450 mg.) was saponified by refluxing with 10% alkali for 3 hr. The crude product was recrystallized from alcohol–water three times to give material melting with transition at 234–235°, final m.p. with dec. 293–294°. It showed infrared bands at 1694, 1651, 1613 and 1574 cm.$^{-1}$.

Anal. Calcd. for $C_{13}H_{14}O_5$: C, 62.39; H, 5.64; neut. equiv., 125. Found: C, 62.26; H, 6.02; neut. equiv., 125.

5,6,7,8-Tetrahydro-2-hydroxy-3-carbomethoxy-1-chloromethylnaphthalene (XXIII).—To a mixture of 10 g. of 5,6,7,8-tetrahydro-2-hydroxy-3-carbomethoxynaphthalene[18] (XXII) in 15 cc. of petroleum ether in a small pressure bottle, 9.0 g. of chloromethyl ether and 1.0 g. of zinc chloride were added and the contents were warmed gently on the steam-bath with swirling for 10 minutes, and were then shaken for 1 hour at room temperature on a shaker. The resulting insoluble precipitate was collected and dissolved in ether; the ethereal solution was washed with water until neutral, and was dried over calcium chloride. Concentration of the solution *in vacuo* yielded a product which gave after crystallization from ether–pentane, 5.5 g. of the chloromethyl compound XXIII, melting at 96–98°. An additional 800 mg. was obtained from the mother liquors. The compound gave a white precipitate when tested with 5% silver nitrate solution. The analytical sample, m.p. 97–98°, was prepared by recrystallization from ether–pentane.

Anal. Calcd. for $C_{13}H_{15}ClO_3$: C, 61.29; H, 5.93. Found: C, 61.37; H, 6.17.

5,6,7,8-Tetrahydro-2-hydroxy-3-carbomethoxy-1-cyanomethylnaphthalene (XXIV) and the Corresponding Acid XXV.—A solution of 1.7 g. of potassium cyanide in 45 cc. of water was added rapidly to a solution of 3.0 g. of the chloromethyl compound XXIII in 80 cc. of acetone. The temperature was maintained at 30–40° for 1 hour after the addition was complete. The mixture was cooled, acidified with 10% hydrochloric acid, and the resulting precipitate was collected; the yield was 2.8 g. of crude nitrile ester, m.p. 105–107°. Five recrystallizations from ethanol yielded the pure nitrile ester XXIV, m.p. 136–137°.

Anal. Calcd. for $C_{14}H_{15}NO_3$: C, 68.55; H, 6.16. Found: C, 68.14; H, 6.30.

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(28) Prepared from the acid with diazomethane, m.p., after crystallization from methanol, 75–76°; J. B. Cohen and H. W. Dudley, *J. Chem. Soc.*, **97**, 1748 (1910), give 73–74°.

From the mother liquors from the recrystallization of the nitrile ester XXIV was obtained the **nitrile acid XXV**, by fractional crystallization. Three crystallizations from benzene–pentane gave the analytical sample of the acid XXV, m.p. 204–205°.

Anal. Calcd. for $C_{13}H_{13}NO_3$: C, 67.52; H, 5.67. Found: C, 67.43; H, 5.77.

5,6,7,8-Tetrahydro-2-hydroxy-3-carbethoxy-1-naphthaleneacetic Acid Ethyl Ester (XX).—The crude nitrile ester and acid (XXIV and XXV, 900 mg.) was refluxed for 5 hours with 2% absolute ethanolic hydrogen chloride. The excess ethanol was removed *in vacuo*, 30 cc. of water was added to the residue and it was warmed gently for 25 minutes. The mixture was cooled, extracted with ether and the ether extracts were washed a few times with 5% sodium carbonate, followed by washing with water until the washes were neutral. The ether solution was dried, the ether was removed *in vacuo*, and the semicrystalline residue was chromatographed on 25 g. of silica gel. Elution with 10% ether–petroleum ether gave 350 mg. of product, m.p. 83–87° and an additional 150 mg. melting at 88–89°. Repeated recrystallization from pentane did not raise the m.p.

The crude ester XX (350 mg.) was saponified by refluxing for 5 hr. with 10% alkali to yield 260 mg. of the crude diacid XVI, which after recrystallization from aqueous alcohol, melted with transition at 233–234°, final m.p. 294–295° dec. Esterification of 147 mg. of the crude acid with 2% alcoholic hydrogen chloride, followed by purification on silica gel and elution with 5% ether–petroleum ether gave 70 mg. of the diester XV, m.p. 96–97°. This was identical with the product obtained by hydrogenation of IX, as shown by mixed m.p. and the identity of the ultraviolet spectra.

4,5-Benzo-2,7-dicarbethoxycycloheptadienone (I) and By-product.—Phthalaldehyde (3.0 g.), 4.56 g. of diethyl acetonedicarboxylate, 0.2 cc. of dry piperidine and 0.8 cc. of acetic acid were refluxed in 15 cc. of dry benzene until 0.8 cc. of water (3.5 hr.) had collected in the water separator. The benzene was evaporated, 10 cc. of ethanol was added to the residue, and after standing some time, 4.3 g. of I, m.p. 96–97°, was obtained; the reported[3] m.p. is 95.5°. The mother liquors deposited 440 mg. of the by-product, m.p. 146–148°, unchanged by recrystallization from ethanol. The analysis corresponded to that of the benzenoid analog of VI.

Anal. Calcd. for $C_{26}H_{30}O_{10}$: C, 62.14; H, 6.02. Found: C, 61.89; H, 6.28.

The condensation to form I using a basic ion-exchange resin as catalyst was carried out as follows.[29] To a solution of 2 g. of phthalaldehyde dissolved in 30 cc. of dry benzene, were added 2.9 g. of diethyl acetonedicarboxylate and 500 mg. of Amberlite IR 4-B resin (washed with acetone and air-dried). The mixture was refluxed for 4 hours; after cooling, the catalyst was removed and washed a few times with dry benzene. The filtrates were combined and concentrated *in vacuo* to give a green oil, which was dissolved in alcohol, treated with norite and filtered. Concentration of the filtrate gave 1.8 g. of I, m.p. 93–96°.

4,5-Benzo-2,7-dicarbethoxycycloheptanone (VII).—To 250 mg. of prereduced Adams catalyst in 30 cc. of acetic acid was added 500 mg. of 4,5-benzo-2,7-dicarbethoxycycloheptadienone (I), and the mixture was hydrogenated until slightly over 2 moles of hydrogen was absorbed. The catalyst was removed, washed with ethanol, the filtrates were combined and the solvents removed *in vacuo*, to give 520 mg. of crude crystalline material. The product was chromatographed on 40 g. of silica gel, and elution with 30% ether–petroleum ether gave 103 mg. of the tetrahydro product VII, m.p. 99–102°. The m.p. was raised to 109–110° by three crystallizations from hexane; the infrared spectrum showed bands at 1731 (ester carbonyl) and 1690 cm.$^{-1}$ (keto carbonyl).

Anal. Calcd. for $C_{17}H_{20}O_5$: C, 67.09; H, 6.62. Found: C, 67.22; H, 6.73.

Treatment of the By-product VI with Piperidine Acetate.—The by-product VI (630 mg.) was refluxed for 24 hours with 0.2 cc. of piperidine and 0.82 cc. of acetic acid. The solvent was removed *in vacuo*, the residue was taken up in ethanol, and the solution deposited 250 mg. of VI after standing. The m.p. of the product was raised to 180–182° by recrystallization from ethanol. The combined mother liquors were chromatographed on 50 g. of silica gel, and eluted with 10% ether–petroleum ether, which would have yielded the dihydronaphthalene IX if it was present. Elution with 30% ether–petroleum ether gave an additional 195 mg. of VI, m.p. 178–180°. Further elution with 40 and 50% ether–petroleum ether gave 28 mg. of non-crystallizable oil. Elution with 70% ether–petroleum ether gave 100 mg. of product, m.p. 188–190°; the m.p. was not raised by crystallization from ethanol. A mixed m.p. with VI gave a slight depression, 174–176°. The 190° compound gave a single absorption peak at 250 mμ, similar to VI. The total recovery of material from the reaction was 573 mg.

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[29] For a review of the use of ion-exchange resins as catalysts in the Claisen and Knoevenagel condensations, see M. J. Astle and J. A. Zaslowsky, *Ind. Eng. Chem.*, **44**, 2867 (1952).

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[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, UNIVERSITY OF MISSOURI]

The Action of Aluminum Chloride on Alkylbenzenes. IV

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When 1,3-dimethyl-4-*n*-butylbenzene, 1,3-dimethyl-4-*sec*-butylbenzene and 1,3-dimethyl-4-isobutylbenzene are warmed with aluminum chloride, the butyl group migrates to the 5-position without isomerization. The alkylation of *m*-xylene with *n*-butyl chloride yields a mixture of 1,3-dimethyl-5-*n*-butylbenzene and 1,3-dimethyl-5-*sec*-butylbenzene. The alkylation of *m*-xylene with *sec*-butyl chloride yields 1,3-dimethyl-5-*sec*-butylbenzene.

In a previous publication from this Laboratory,[2] it was shown that the acetylation of *p*-di-*n*-butylbenzene and *p*-di-*sec*-butylbenzene by means of aluminum chloride in refluxing carbon disulfide yielded 2,4-di-*n*-butylacetophenone and 2,4-di-*sec*-butylacetophenone as the principal dialkylacetophenones. The fact that the migrating butyl groups were not isomerized led us to repeat the earlier rearrangement experiments of the senior author with the 1,3-dimethyl-4-butylbenzenes.[3]

It has now been established by both chemical and spectroscopic evidence that the principal changes which take place when these trialkylbenzenes are warmed on a steam-bath with aluminum chloride are

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[1] Abstracted from a portion of the dissertation to be submitted by J. M. Shackelford for the degree of Doctor of Philosophy.

[2] D. V. Nightingale and H. B. Hucker, *J. Org. Chem.*, **18**, 1529 (1953).

[3] D. V. Nightingale and L. I. Smith, THIS JOURNAL, **61**, 101 (1939).