Anal. Calcd. for $C_{17}H_{15}NO_3$: C, 81.92; H, 6.02; N, 5.62. Found: C, 81.64; H, 5.89; N, 5.55.

Oxidation of 2-Methyl-3-benzyl-4-hydroxyquinoline (X) to 2-Methyl-3-benzoyl-4-hydroxyquinoline (IX).—Five grams of the benzylquinoline (X) was dissolved in 50 cc. of glacial acetic acid and the mixture was treated with 7 g. of chromic acid in small amounts at a time. The reaction mixture was warmed at 70° for about 20 minutes. It was cooled and then decomposed with ice-cold water and left in the refrigerator overnight. The solid that had separated was filtered off. It was digested with 5% solution of warm sodium hydroxide and filtered free from the unreacted quinoline. The filtrate was acidified with hydrochloric acid and the precipitate after crystallization from glacial acetic acid proved to be 2-methyl-3-benzoyl-4-hydroxyquinoline (IX) as shown by the mixed melting point determination; yield 1.8 g.

Methyl (or Ethyl) Benzoylacetoacetate.—The following procedure for the benzoylation of methyl (or ethyl) acetoacetate which is completed in a much shorter period of time, is to be preferred to that given in reference 13. Eleven and one-half grams (0.5 g. atom) of sodium metal was dissolved in 200 cc. of absolute ethanol. To 100 cc. of this solution was added 32.5 g. (0.25 mole) of ethyl acetoacetate with stirring and keeping the temperature below 5°. To this mixture was added dropwise 14 g. of benzoyl chloride dissolved in 50 cc. of toluene, maintaining the temperature below 5°. An additional 50 cc. of the sodium ethoxide solution was added and this was again followed by the addition of 7 g. of benzoyl chloride dissolved in 25 cc. of toluene. These additions were repeated once more in a similar fashion. After standing overnight, the reaction mixture was decomposed with ice-cold hydrochloric acid. The toluene layer was removed and the aqueous solution was further extracted with ether. The combined extracts were dried and after removal of the solvent yielded 35 g. (75%) of a colorless oil, b.p. 145–148° (6 mm.). The methyl ester, b.p. 142–145° (6 mm.), was also prepared similarly in 75–80% yield.

Condensation of Ethyl Benzoylacetoacetate and Aniline and Subsequent Cyclization to 2-Methyl-3-benzoyl-4-hydroxyquinoline (IX).—The condensation was carried out as described under methyl β-anilinocrotonate. After removal of benzene, the reaction mixture was diluted with petroleum ether. A small amount of a white crystalline solid separated out at this stage. This, after crystallization from ethanol as white needles, had m.p. 109–112°. The product was soluble in hydrochloric acid and could be recovered on neutralization or dilution. It could be distilled at atmospheric pressure completely unchanged and failed to undergo cyclization.

Anal. Found: C, 71.74; H, 6.90; N, 9.90.

The structure is unknown. The filtrate after removal of the solid was heated under vacuum to remove all the petroleum ether. The residual oil was cyclized in boiling diphenyl ether to give a 35–40% yield of 2-methyl-3-benzoyl-4-hydroxyquinoline.

When methyl benzoylacetoacetate was condensed with aniline and the oily condensation product was chromatographed over activated alumina and the column was eluted with petroleum ether, there was obtained a 20–25% yield of methyl β-phenyl-β-anilinoacrylate which after crystallization from petroleum ether into large stout cubic crystals had m.p. 89–90°.

Anal. Calcd. for $C_{16}H_{15}NO_2$: C, 75.90; H, 5.90; N, 5.50. Found: C, 75.68; H, 5.68; N, 5.93.

On cyclization in boiling diphenyl ether, it gave 2-phenyl-4-hydroxyquinoline, m.p. 255–257°, undepressed on admixture with an authentic sample.[4]

NEW DELHI, INDIA

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(13) "Organic Syntheses," Coll. Vol. II, John Wiley and Sons, Inc., New York, N. Y., pp. 266–267.

[CONTRIBUTIONS FROM THE DIVISION OF ANALYTICAL CHEMISTRY, NATIONAL PHYSICAL LABORATORY OF INDIA, NEW DELHI, AND CONVERSE MEMORIAL LABORATORIES, HARVARD UNIVERSITY]

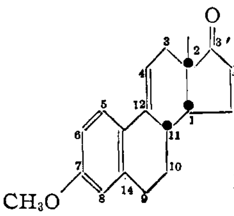
Condensation of 1-Vinyl-6-methoxy-3,4-dihydronaphthalene and 3-Methyl-3-cyclopentene-1,2-dione. Structure of Dane's Adduct

BY GURBAKHSH SINGH

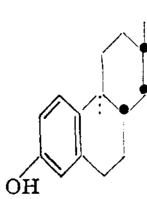
RECEIVED MAY 3, 1956

Dane and Schmitt's work on the condensation of 1-vinyl-6-methoxy-3,4-dihydronaphthalene and 3-methyl-3-cyclopentene-1,2-dione has been carefully repeated. The conclusions drawn by these authors as to the structure of the adduct thus obtained have been shown to be erroneous. This diene condensation has been found to give a mixture of two adducts, whose structures have been definitely established through degradative and synthetic experiments as 1-methyl-7-methoxy-1,2-cyclopenteno-1,2,3,4,9,10-hexahydrophenanthrene-4′,5′-dione (V) and 2-methyl-7-methoxy-1,2-cyclopenteno-1,2,3,4,9,-10-hexahydrophenanthrene-3′,4′-dione (VI). Their synthetic stereoisomer of estrone has been shown to be only a structural isomer of estrone.

One of the earliest attempts toward a total synthesis of estrone was that made by the German investigators Dane and Schmitt.[1] This consisted in the condensation of 1-vinyl-6-methoxy-3,4-dihydronaphthalene and 3-methyl-3-cyclopentene-1,2-dione. The adduct, which was assigned structure 2-methyl-7-methoxy-1,2-cyclopenteno-1,2,3,9,10,-11-hexahydrophenanthrene-3,4-dione (I), was converted through a series of steps (hydrogenation of the C_4–C_{12}-double bond and the $C_{4'}$-carbonyl group to the ketol, followed by the demethylation and dehydration to a $\Delta^{4'-5'}$-dehydroestrone by treatment with hydrogen bromide and acetic acid mixture and subsequent hydrogenation of the $C_{4'}$–$C_{5'}$-double bond) to what was claimed to be a stereoisomer of estrone, m.p. 210°. Dane and Schmitt's estrone appeared to be identical with the estrone "a" of Anner and Miescher[2] (m.p. 214–216°), to which the latter authors assigned the configuration II. It is easy to rationalise that Dane and Schmitt's estrone also had the same configuration (II). This follows from the considerations



I



II

that the adduct I is a Diels–Alder product from a *cis*-dienophile and, further, due to maximum accumulation of the unsaturation in the transition

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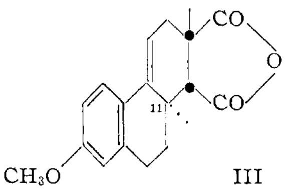
(1) E. Dane and J. Schmitt, *Ann.*, **537**, 246 (1939).

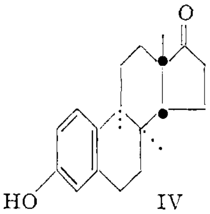
(2) G. Anner and K. Miescher, *Helv. Chim. Acta*, **32**, 1957 (1949); **33**, 1379 (1950).

state of the complex, the configurations of the three centers at C_2, C_1 and C_{11} could be considered as fixed, *i.e.*, they are all *cis*. Furthermore, during the hydrogenation of the C_4–C_{12}-double bond hydrogen would be expected to enter from the side opposite to that of the angular methyl group.

This situation became somewhat complicated when during their study of the Diels–Alder condensation of citraconic anhydride and 1-vinyl-6-methoxy-3,4-dihydronaphthalene, Heer and Miescher[3] made the observation that the adduct had the configuration III and that the rule of maximum accumulation of unsaturation in the transition state of the complex had been violated. Thus the C_{11}-configuration was found to be opposite to that expected. If a similar situation also operated in Dane and Schmitt's case, then their final estrone stereoisomer would most likely be represented by



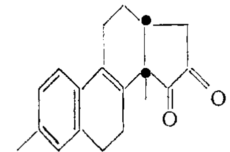
III



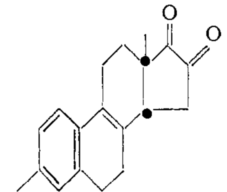
IV

the structure IV. This structure has, however, already been assigned[4] to estrone "d" of Anner and Miescher,[2] which had a different melting point (184–186°). It thus appeared important to find the correct situation regarding Dane and Schmitt's estrone.

As a result, it has now been shown conclusively that the adduct obtained by the German investigators from the reaction of 1-vinyl-6-methoxy-3,4-dihydronaphthalene with 3-methyl-3-cyclopentene-1,2-dione does not actually have the structure which they assigned to it, but that it has in fact, structure V, and is transformed to a structural isomer of estrone. A careful repetition of Dane and Schmitt's work further showed that in addition to the compound V isolated by these workers, a compound of structure VI is present.



V

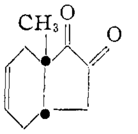


VI

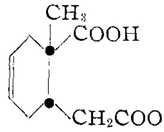
Structure of 1-Methyl-7-methoxy-1,2-cyclopenteno-1,2,3,4,9,10-hexahydrophenanthrene-4′,5′-dione (V).—The degradation of Diels–Alder adduct V was first studied in the model case of the adduct *cis*-Δ^5-hydrindene-1,2-dione (VII), m.p. 124–125°, obtained by the condensation of 3-methyl-3-cyclopentene-1,2-dione and butadiene. The diketone VII, on cleavage with alkaline hydrogen peroxide gave an almost quantitative yield of *cis*-2-methyl-2-carboxy-Δ^4-cyclohexene-1-acetic acid (VIII), m.p. 175–176°. This acid on catalytic hydrogenation in the presence of Adams catalyst, was converted to *cis*-2-methyl-2-carboxy-cyclohexane-1-acetic acid[5] (IX), m.p. 165–165.5°.

The preparation of 3-methyl-3-cyclopentene-1,2-dione was carried out by treatment of 1-methylcyclopentene-5-one[6] with selenium dioxide according to Dane and Schmitt,[1] though in somewhat higher yields.

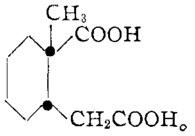
The Diels–Alder reaction between the enedione and 1-vinyl-6-methoxy-3,4-dihydronaphthalene[7] and the isolation of the product were carried out following exactly the directions of Dane and Schmitt.[1] This gave, in somewhat better yield than reported by these investigators, a crystalline adduct V, presumably identical with the one described by these authors. The formulation of the adduct with the double bond in the C_{11}–C_{12}-position is indicated by the observation that the compound is recovered unchanged after treatment with hydrogen chloride in chloroform solution.



VII, m.p. 124–125°



VIII, m.p. 175–176°



IX, m.p. 165–165.5

Oxidation of the adduct V with alkaline hydrogen peroxide gave mainly 1-methyl-1-carboxy-7-methoxy-1,2,3,4,9,10-hexahydrophenanthrene-2-acetic acid (X), m.p. 216–217°, along with a very small quantity of a product whose properties are best explained by the lactonic structure XI. The evidence for this formulation is discussed below. The diacid X on refluxing with acetic anhydride for a short time gave the corresponding anhydride XIV, m.p. 162–163°. The diacid X was decarboxylated and dehydrogenated with Pd–charcoal at 320° to the known 1,2-dimethyl-7-methoxyphenanthrene (XVII). The diester XII, m.p. 88.5–90°, prepared from the dicarboxylic acid X by the action of diazomethane, was recovered unchanged on attempted acid isomerization. This further confirms the assignment of the double bond in the adduct V to the C_{11}–C_{12}-position.

In contrast the diacid X on treatment with hydrogen chloride in warm acetic acid solution was converted to an isomer XV, m.p. 192–193°, which on treatment with diazomethane gave the corresponding methyl ester XVI, m.p. 125°. The lactonic ester structure follows from a consideration of the ultraviolet spectrum (λ_{max} 275 mμ, ϵ 1584). This shows the absence of a double bond conjugated with the benzene ring. In contrast to this, the intensity of absorption in the ultraviolet spec-

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(3) J. Heer and K. Miescher, *Helv. Chim. Acta*, **31**, 219 (1948); **32**, 1572 (1949).

(4) A. J. Birch, *Ann. Rep. Chem. Soc.*, 207 (1950).

(5) W. E. Bachmann and S. Kushner, THIS JOURNAL, **65**, 1963 (1943).

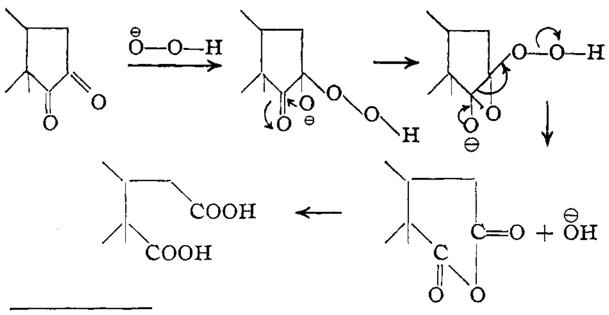
(6) A. M. Gaddis and L. W. Butz, *ibid.*, **69**, 1203 (1947).

(7) The preparation of this diene which has been perfected by R. B. Woodward, G. Stork, R. Wineman, A. Nelson and A. Bothner-By, (private communication) will be described by these authors.

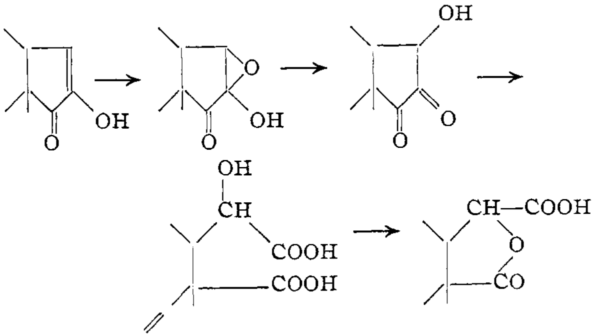
trum of the diester XII where the styrene system is retained, is much higher (λ_{max} 274 mμ, ε 18370). The infrared spectrum of the lactonic ester (XVI) (band at 5.63 and 5.74 μ) clearly indicates the presence of a five-membered lactone. The band at 5.74μ is due to the ester grouping present in the molecule. This may be compared to the simple diester XII, which has only one band at 5.76μ in the carbonyl region. The same lactonic ester XVI could be obtained directly from X by treatment with methanolic hydrogen chloride at room temperature.

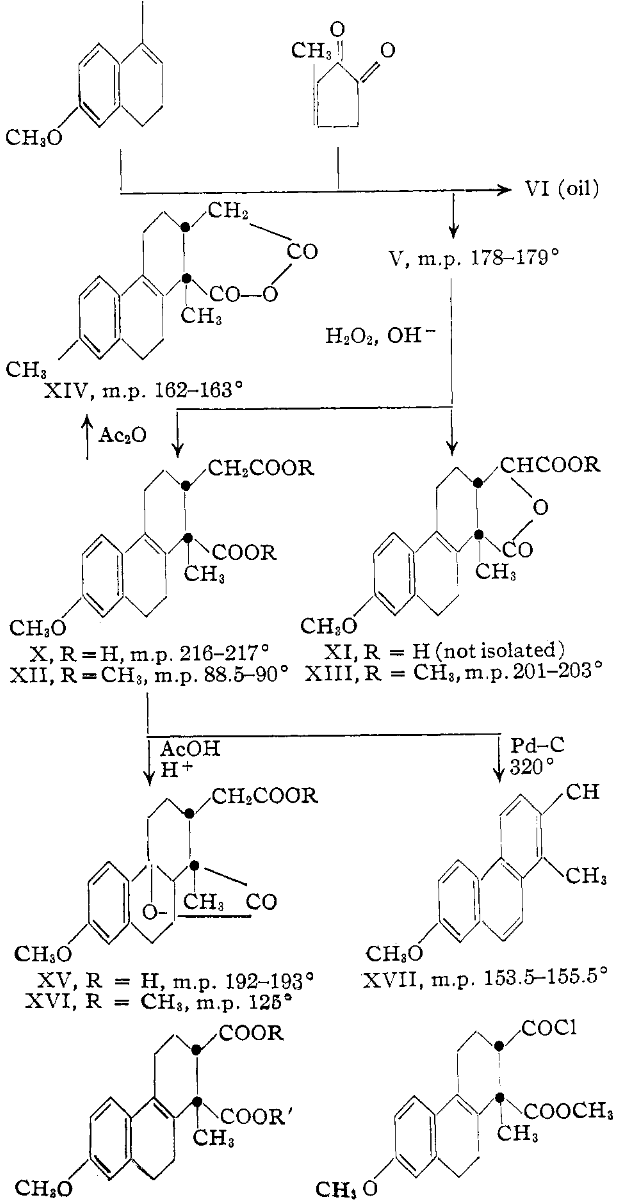
Final confirmation for the structure assigned to the diacid X was obtained by its synthesis from *cis*-dimethyl-1-methyl-7-methoxy-1,2,3,4,9,10-hexahydrophenanthrene-1,2-dicarboxylate[8] (XVIII) by the Arndt–Eistert homologation *via* the half-ester acid XX, m.p. 176–177°, and the half-ester-acid chloride XIX. That no isomerization had taken place at C_2 during the hydrolysis of XVIII or the acid chloride formation is evident from the fact that XIX and XX could both be reconverted to the dimethyl ester XVIII. The dicarboxylic acid XXI, m.p. 221–223°, also obtained during the hydrolysis of the diester XVIII, was also reconvertible to XVIII by treatment with excess diazomethane. These results make it clear that the crystalline adduct of Dane and Schmitt[1] is represented by V and that their final estrone isomer is only a structural isomer.

Structure of (XI).—The mixture of the two carboxylic acids X and XI as obtained directly by the oxidation of the adduct V without any purification was esterified by diazomethane. This mixture of the two esters on repeated recrystallizations from a mixture of ethyl acetate and cyclohexane gave in about 1% yield a compound $C_{19}H_{22}O_5$, m.p. 201–203°, which was assigned the structure XIII. A study of the ultraviolet spectrum indicated the presence of a double bond in conjugation with the benzene ring (λ_{max} 276 mμ, ε 17290). The infrared spectrum revealed the presence of two bands at 5.58 and 5.70μ. These two bands indicate the presence of a lactone ring and an ester grouping in the molecule. These values are somewhat low for a normal five-membered lactone or a normal ester. Such was also the experience of Jones and co-workers,[9] who showed that the introduction of an acetate group in the α-position to a ketone reduces the wave length of the bands due to the ketone and to the acetate to the extent of 0.03 to 0.06.



It is interesting to consider the mechanism of the formation of XI from the adduct V by alkaline hydrogen peroxide. The normal cleavage of an α-diketone to a dicarboxylic acid as shown above probably consists in the addition of $\overset{\ominus}{O}$–O–H to one





V, m.p. 178–179°

XIV, m.p. 162–163°

X, R = H, m.p. 216–217°
XII, R = CH_3, m.p. 88.5–90°

XI, R = H (not isolated)
XIII, R = CH_3, m.p. 201–203°

XV, R = H, m.p. 192–193°
XVI, R = CH_3, m.p. 125°

XVII, m.p. 153.5–155.5°

XVIII, R = R′ = CH_3, m.p. 86°
XX, R = H, R′ = CH_3, m.p 176–177°
XXI, R = H, m.p. 221–223°

XIX (oil)

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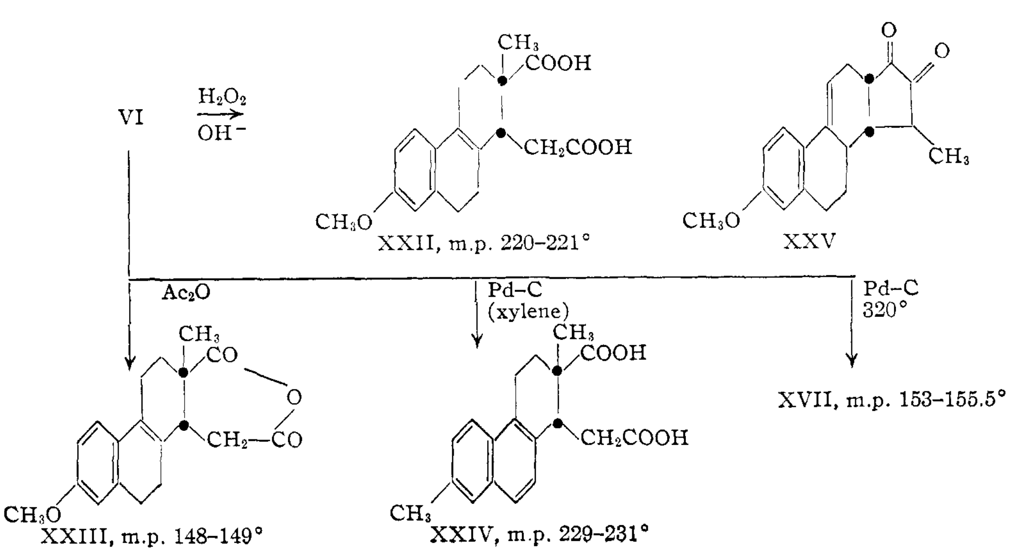
[8] J. Heer and K. Miescher, *Helv. Chim. Acta*, **31**, 219 (1948).

[9] R. N. Jones, V. Z. Williams, M. J. Whalen and K. Dobriner, THIS JOURNAL, **70**, 2030 (1948).



XXII, m.p. 220–221°

XXV

XXIII, m.p. 148–149°

XXIV, m.p. 229–231°

XVII, m.p. 153–155.5°

of the carbonyl groups giving rise to the anhydride which opens up in the basic medium. If the α-diketone is, however, supposed to react in the corresponding enolic form, the reaction with hydrogen peroxide could also give rise to the epoxide, which on hydrolysis is converted to the hydroxy α-diketone. Subsequent cleavage followed by lactonization on acidification would result in the formation of XI.

Structure of 2-Methyl-7-methoxy-1,2-cyclopenteno-1,2,3,4,9,10-hexahydrophenanthrene-3′,4′-dione (VI).—The crystalline adduct V was the only product isolated by Dane and Schmitt[1] from the Diels–Alder reaction. Careful examination of the mother liquors demonstrated, however, the presence of a second adduct, which unfortunately resisted all attempts at crystallization. That the latter must be formulated as VI becomes clear from the following reasons. Direct hydrogen peroxide oxidation of the mother liquors from the separation of V gave 2-methyl-2-carboxy-7-methoxy-1,2,3,4,9,10-hexahydrophenanthrene-1-acetic acid (XXII), m.p. 220–221°, identical with that described by Heer and Miescher[10] (mixture melting point undepressed) and unchanged by treatment with hydrogen chloride in acetic acid. The anhydride XXIII, m.p. 149°, which also has been described by these authors, was obtained from XXII by refluxing with acetic anhydride. Drastic dehydrogenation of XXII with Pd–charcoal at 320° gave as expected 1,2-dimethyl-7-methoxyphenanthrene (XVII). Partial aromatization of XXII by the action of Pd–charcoal in refluxing xylene gave *cis*-2-methyl-2-carboxy-7-methoxy-1,2,-3,4-tetrahydrophenanthrene-1-acetic acid (XXIV), m.p. 229–231°, identical (mixture melting point undepressed) with that described by Bachmann, Cole and Wilds[11] and converted by them through homologation and ring closure into C_{14}-*epi*-equilenin. This evidence must also be considered as conclusive proof of the *cis*-C/D junction in C_{14}-*epi*-equilenin. The bearing of this evidence on the C/D junction in steroids already has been discussed in an earlier communication.[12]

Evidence that no further isomer[13] was formed in the Diels–Alder reaction was obtained from the following experiments. The mother liquor from the separation of the diacid XXII was esterified by treatment with diazomethane, the crude product was evaporatively distilled under high vacuum and the ester after hydrolysis gave a product which after recrystallization proved to be identical with the original diacid XXII.

Formation of V and VI.—One point needs further comment, namely, the direct formation of adducts V and VI with the double bond isomerized from the expected position at C_4–C_{12} to the stable C_{11}–C_{12} position. This isomerization becomes understandable when it is considered that the dienophile α-diketone may be expected to be strongly acidic (carboxyl type resonance in the anion), and could bring about the easy isomerization of the double bond during the course of the reaction.

It is of interest to examine the reasons for the formation of the two isomeric adducts V and VI in the Diels–Alder reaction between 1-vinyl-6-methoxy-3,4-dihydronaphthalene and 3-methyl-3-cyclopentene-1,2-dione. The diene would be expected to be polarized as shown in XXVI. This seems to be substantiated by the experiments of Dane and Hoss,[14] who obtained as the sole product of addition of acrylic acid to the diene, an adduct which was esterified and dehydrogenated to the known methyl 7-methoxyphenanthrene-2-carboxylate (XXVII).

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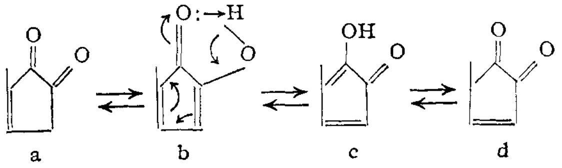
[10] J. Heer and K. Miescher, *Helv. Chim. Acta*, **31**, 1289 (1948).

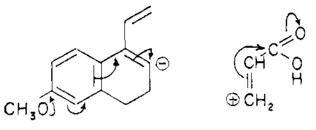
[11] W. E. Bachmann, W. Cole and A. L. Wilds, THIS JOURNAL, **62**, 24 (1940).

[12] G. Stork and G. Singh, *Nature*, **165**, 816 (1950).

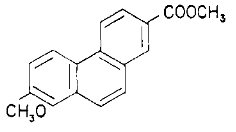
[13] It might have been expected that Diels–Alder reaction could give rise to a third isomer corresponding to XXV. This would arise from the consideration that the dienophile 3-methyl-3-cyclopentene-1,2-dione (a) might react in the less hindered tautomeric form (d) as



[14] E. Dane and O. Hoss, *Ann.*, **552**, 113 (1942).

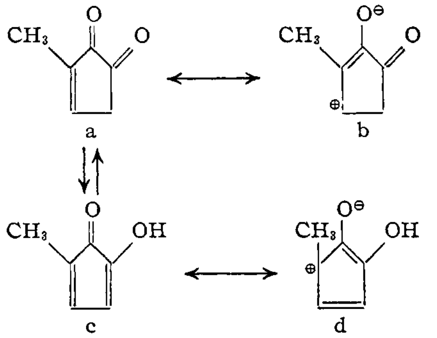


XXVI



XXVII

The formation of the two adducts V and VI corresponding to the two possible modes of addition of the cyclopentene-dione, and of the corresponding adducts from citraconic anhydride,[15] suggests that these two dienophiles are not very strongly polarized. This is not surprising in the case of citraconic anhydride and may be rationalised in the case of the enedione by taking into account the contribution of form d as well as that of b.



Acknowledgment.—The author is obliged to Prof. Gilbert Stork, Columbia University, and Prof. R. B. Woodward, Harvard University, for many stimulating discussions and other help.

Experimental[16]

1-Methylcyclopentene-5-one was prepared by the method of Gaddis and Butz[6] with some modifications. The addition of concentrated hydrochloric acid to the mixture of 1-methylcyclopentene, ethyl nitrite and acetic acid was carried out in such a way that the temperature of the reaction mixture was maintained between −10 to −5° (Dry Ice-bath). When the reaction was run on 20 times the scale, the yield of the pure 1-methylcyclopentene nitrosochloride was 70% as compared to 51% obtained by Gaddis and Butz. It is desirable to filter the nitrosochloride in a cold room and to use the product immediately. In one of the experiments when the freshly filtered nitrosochloride was allowed to warm to room temperature, the entire product suddenly decomposed with evolution of white fumes and deposition of carbon. The dehydrohalogenation of the nitrosochloride could also be carried out on ten times larger quantities. The steam distillate obtained during the hydrolysis of the oxime or the pyridine salt was saturated with ammonium sulfate and extracted, etc. The yield of the pure 1-methylcyclopentene-5-one based on the amount of the nitrosochloride used was 75%, compared with 47.6% obtained by the workers cited.

3-Methyl-3-cyclopentene-1,2-dione was prepared by treatment of 1-methylcyclopentene-5-one with selenium dioxide according to the procedure described by Dane, Schmitt and Rautenstrauch.[17] Twenty grams of the eneone gave 9.5 g. (35.2%) of the pure enedione. Dane, *et al.*, reported a yield of 20–27% of the uncrystallized product.

***cis*-8-Methyl-Δ^5-hydrindene-1,2-dione** (VII).—Four and one-half grams of methylcyclopentenedione, 30 cc. of redistilled butadiene and 100 mg. of hydroquinone were sealed in a thick walled Pyrex tube and the mixture was heated at 100° for 40 hours. On cooling the reaction mixture the greater part of the product separated out. After removal of the unreacted butadiene, the residual product was treated with an excess of 4% cold sodium hydroxide solution which removed the adduct VII as its soluble sodium salt from the adhering butadiene polymer. The alkaline extract was washed with ether and then decomposed cautiously with cold dilute hydrochloric acid. The precipitated *cis*-8-methyl-Δ^5-hydrindene-1,2-dione was filtered off and dried; yield 5 g. or 74.6%. A portion was crystallized from ether into colorless needles, m.p. 123–125°. It gives a violet color on treatment with an alcoholic solution of ferric chloride. In the absence of hydroquinone, the formation of butadiene polymer considerably increases and the yield of the adduct is reduced to 25%. Dane, *et al.*,[17] who also made this compound, reported a melting point of 110°. No yields were given.

Oxidation of *cis*-8-Methyl-Δ^5-hydrindene-1,2-dione (VII) with Alkaline Hydrogen Peroxide.—One gram of the adduct was dissolved in about 25 cc. of 4% sodium hydroxide solution. With gentle warming and stirring of the solution, 5 cc. of 30% hydrogen peroxide was added to the solution during a period of about 10 minutes. The reaction mixture was warmed on a steam-bath for an additional 15 minutes. The solution was cooled in an ice-bath and treated with cold dilute hydrochloric acid. The precipitated dicarboxylic acid was redissolved in a dilute solution of potassium bicarbonate. Any insoluble impurities were filtered off and the potassium salt was decomposed with hydrochloric acid. The precipitated ***cis*-2-methyl-2-carboxy-Δ^5-cyclohexene-1-acetic acid (VIII)** was collected and dried; yield 0.96 g. or 80%. A portion was crystallized from water into colorless stout prisms, m.p. 175–176°.

Anal. Calcd. for $C_{10}H_{14}O_4$: C, 60.66; H, 7.07. Found: C, 60.44; H, 7.20.

***cis*-2-Methyl-2-carboxycyclohexane-1-acetic Acid (IX).**—One gram of the above unsaturated acid was dissolved in 20 cc. of purified glacial acetic acid. One hundred mg. of Adams platinum oxide was added and the mixture subjected to hydrogenation at atmospheric pressure. The hydrogenation was complete in about 30 minutes. Catalyst was filtered off and acetic acid was removed under vacuum. The residual solid (yield almost quantitative), after one crystallization from xylene–petroleum ether, had a m.p. 165–165.5°. A mixture melting point determination with an authentic sample provided by the late Professor Bachmann[5] did not show any depression.

Condensation of 1-Vinyl-6-methoxy-3,4-dihydronaphthalene with 3-Methyl-3-cyclopentene-1,2-dione and Isolation of 1-Methyl-7-methoxy-1,2-cyclopenteno-1,2,3,4,9,10-hexahydrophenanthrene-4',5'-dione (V).—Twenty grams of 1-vinyl-6-methoxy-3,4-dihydronaphthalene (a trial condensation with maleic anhydride and isolation of the adduct indicated that the diene was at least 80% pure) and 14 g. of the enedione were added to 250 cc. of purified dioxane and the reaction mixture was heated under a gentle reflux in an atmosphere of nitrogen for 50 hours. Dioxane was removed under suction and the residual oil was dissolved in excess 4% potassium hydroxide solution. The insoluble material was removed by several extractions with ether. The alkaline solution was cautiously decomposed with cold dilute hydrochloric acid. The brown oil thus obtained was extracted with benzene. Removal of the solvent yielded 25 g. (73%) of an oil which is a mixture of the two adducts V and VI. Dane and Schmitt[1] reported a 15.7% yield of the crude solid product. On trituration of the oil with about 100 cc. of methanol, the solid adduct V slowly crystallized. After standing overnight in a cold room, the crystals were separated and washed with cold methanol to give 7.5 g. (23.4%) of the adduct V. The mother liquors contain the adduct VI. After one crystallization from a mixture of benzene and methanol, V was obtained as almost colorless needles, m.p. 178–179°.

Anal. Calcd. for $C_{19}H_{20}O_3$: C, 76.99; H, 6.82. Found: C, 76.79; H, 7.01.

Dane and Schmitt[1] reported a melting point of 172° with previous softening.

Attempted Acid Isomerization of 1-Methyl-7-methoxy-1,2-cyclopenteno-1,2,3,4,9,10-hexahydrophenanthrene-4',5'-dione (V).—One hundred mg. of the adduct V was dissolved in about 5 cc. of dry chloroform and the solution was saturated with dry hydrogen chloride. After one hour the sol-

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(15) (a) J. Heer and K. Miescher, *Helv. Chim. Acta*, **31**, 219 (1948); (b) W. E. Bachmann and J. M. Chemerda, This Journal, **70**, 1468 (1948).

(16) All melting points were taken on fully immersed thermometers. Analyses were performed by W. Manser, E. T. H. Laboratory, Zurich.

(17) E. Dane, J. Schmitt and C. Rautenstrauch, *Ann.*, **532**, 29 (1937).

vent was removed under suction and the residual solid after recrystallization from benzene–methanol proved to be unchanged adduct V through determination of melting point and mixture melting point.

Oxidation of 1-Methyl-7-methoxy-1,2-cyclopenteno-1,2,-3,4,9,10-hexahydrophenanthrene-4′,5′-dione (V) with Alkaline Hydrogen Peroxide.—One gram of the adduct V was dissolved in about 30 cc. of 2 *N* potassium hydroxide solution and treated with 8 cc. of 30% hydrogen peroxide. The reaction mixture was warmed on a steam-bath for about 20 minutes and then cooled in an ice-bath. The potassium salt was decomposed with cold hydrochloric acid. The solid thus obtained was further purified through another precipitation from a potassium bicarbonate solution. The white material thus obtained proved to be a mixture of the dicarboxylic acid X and the lactonic acid XI; total yield almost quantitative. After two recrystallizations from ethyl acetate–cyclohexane, about 0.7 g. of **1-methyl-2-carboxy-7-methoxy-1,2,3,4,9,10-hexahydrophenanthrene-1-acetic acid (X)**, m.p. 210–212° was obtained. For analytical purposes, this sample was repeatedly crystallized from ethyl acetate–cyclohexane mixture, until a constant melting point 214–215° was reached.

Anal. Calcd. for $C_{19}H_{22}O_3$; C, 69.09; H, 6.66. Found: C, 68.71; H, 6.86.

The corresponding **anhydride XIV** was obtained by refluxing 200 mg. of the dicarboxylic acid with about 3 cc. of acetic anhydride. Removal of the acetic anhydride under suction and crystallization of the residue from benzene–petroleum ether gave white needles, m.p. 162–163°.

The dimethyl ester (XII) was made by treatment of the dicarboxylic acid X with excess diazomethane in ether. It was crystallized from methanol to give white prisms, m.p. 88.5–89.5°.

Anal. Calcd. for $C_{21}H_{26}O_5$; C, 70.39; H, 7.26. Found: C, 70.08; H, 7.41.

The dimethyl ester was recovered unchanged after treatment with dry hydrogen chloride in chloroform. It was hydrolyzed to the parent dicarboxylic acid on refluxing with an excess of 20% aqueous alcoholic potassium hydroxide for about 8 hours.

The lactonic acid XI obtained as a by-product in the oxidation of the adduct V was characterized as its methyl ester XII as described below. The mixture of the crude acids directly obtained by the hydrogen peroxide cleavage of the adduct V was treated with excess of diazomethane. The neutral mixture (1 g.) thus obtained was crystallized from an ethyl acetate–cyclohexane mixture. About 50 mg. of a product melting at 190–195° was obtained. Two further recrystallizations from ethyl acetate gave 10–15 mg. of the **lactonic ester (XIII)** as white needles, m.p. 201–203°. This melting point could not be raised by further crystallization.

Anal. Calcd. for $C_{20}H_{22}O_5$; C, 70.17; H, 6.43. Found: C, 69.65; H, 6.53.

Conversion of 1-Methyl-2-carboxy-7-methoxy-1,2,3,4,9,-10-hexahydrophenanthrene-1-acetic Acid (X) to 1,2-Dimethyl-7-methoxyphenanthrene (XVII).—A mixture of 500 mg. of the dicarboxylic acid X, 500 mg. of 10% palladium–charcoal and 4 cc. of acetone was heated in a sealed tube at 320° for 10 hours. After cooling, the tube was opened and the catalyst was removed by filtration. After removal of the solvent the residue was dissolved in benzene and washed with a solution of sodium bicarbonate and then with water. After drying over anhydrous sodium sulfate, the solution was concentrated to a small volume and then passed through a short column of alumina. The clear benzene solution thus obtained after concentration was diluted with petroleum ether, and 1,2-dimethyl-7-methoxyphenanthrene crystallized as white needles, m.p. 153.5–155.5°. The literature[8] melting point is 154°.

Acid Isomerization of 1-Methyl-2-carboxy-7-methoxy-1,2,3,4,9,10-hexahydrophenanthrene-1-acetic Acid (X) to the Lactonic Acid XV.—Five hundred mg. of the dicarboxylic acid X was dissolved in about 10 cc. of glacial acetic acid. A stream of dry hydrogen chloride was passed into the hot solution, until it was saturated. The reaction mixture was left overnight. Acetic acid was removed under suction and the residue was dissolved in a dilute solution of potassium bicarbonate. The solution was filtered from any insoluble impurities and then decomposed with hydrochloric acid. The white solid thus obtained was filtered, washed with water and dried in a vacuum desiccator. Three crystallizations from ethyl acetate–cyclohexane gave the lactonic acid XV as white micro-needles, m.p. 192–193°, yield 50–60%.

Anal. Calcd. for $C_{19}H_{22}O_5$: C, 69.09; H, 6.66. Found: C, 69.02; H, 6.79.

The corresponding **lactonic methyl ester (XVI)** was prepared by treatment of the lactonic acid XV with excess diazomethane. It was crystallized from a small volume of methanol as white needles, m.p. 125°.

Anal. Calcd. for $C_{20}H_{24}O_5$: C, 69.76; H, 6.98. Found: C, 69.28; H, 7.04.

The dicarbxylic acid X could also be converted directly to the **lactonic methyl ester** XVI according to the following procedure. Two hundred mg. of the dicarboxylic acid X was dissolved in about 10 cc. of anhydrous methanol and the warm solution was saturated with anhydrous hydrogen chloride. After 12 hours the solvent was removed under vacuum and the residual oil was taken up in ethyl acetate and washed with a dilute solution of sodium bicarbonate. The extract was dried over anhydrous sodium sulfate. Ethyl acetate was removed under vacuum and the residue was sublimed under high vacuum to give about 100 mg. of a white solid. After two crystallizations from methanol this gave white needles, m.p. 123–124°. A mixture melting point determination with the sample obtained from the lactonic acid as above showed no depression.

Conversion of Dimethyl 1-Methyl-7-methoxy-1,2,3,4,9,-10-hexahydrophenanthrene-1,2-dicarboxylate (XVIII) to 1-Methyl-2-carboxy-7-methoxy-1,2,3,4,9,10-hexahydrophenanthrene-1-acetic Acid (X).—1-Vinyl-6-methoxy-3,4-dihydronaphthalene was condensed with citraconic anhydride and 1-methyl-7-methoxy-1,2,3,9,10,11-hexahydrophenanthracene-1,2-dicarboxylic acid (m.p. 220° dec., literature[8] m.p. 216° dec.) was separated from the reaction mixture according to the elegant directions given by Heer and Miescher.[8] Treatment with excess of diazomethane gave the corresponding dimethyl ester, m.p. 163–164°. The isomerization of the double bond from C_4–C_{12} to C_{11}–C_{12} is best carried out by dissolving the dimethyl ester in dry chloroform and saturating with dry hydrogen chloride. After one hour chloroform was removed under suction and the residual oil was taken up in ethyl acetate and washed with a solution of sodium bicarbonate and then with water. After removal of the solvent and crystallization of the residue from methanol, XVIII was obtained as white stout prisms, m.p. 86°, literature[8] m.p. 84°. This method of isomerization is more convenient than that described by Heer and Miescher.[8]

The hydrolysis of the dimethyl ester XVIII to a mixture of the corresponding mono- and dicarboxylic acids XX and XXI was carried out by refluxing 5 g. of the ester with 15 g. of potassium carbonate dissolved in about 50 cc. of water for about 7 hours. After cooling, the clear solution was acidified with hydrochloric acid and the precipitate was dried in a vacuum desiccator. The product thus obtained was crystallized from ethyl acetate as white needles, m.p. 214–218°, yield 1.3 g. Two further recrystallizations from ethyl acetate raised the melting point to 221–223°. This proved to be **1-methyl-7-methoxy-1,2,3,4,9,10-hexahydrophenanthrene-1,2-dicarboxylic acid.**

Anal. Calcd. for $C_{18}H_{20}O_5$: C, 68.35; H, 6.33. Found: C, 68.39; H, 6.46.

Treatment of the dicarboxylic acid with excess diazomethane gave the original dimethyl ester XVIII. Melting point and mixture melting point with the authentic ester was 86°. Thus during the hydrolysis of the ester no inversion at C_2 had taken place. The mother liquors from the crystallization of the dicarboxylic acid were concentrated and a small quantity of cyclohexane was added, when **methyl-1-methyl-2-carboxy-7-methoxy-1,2,3,4,9,10-hexahydrophenanthrene-1-carboxylate (XX)** separated out as bold, stout prisms along with some dicarboxylic acid as needles. The separation is very easily effected by hand picking; yield about 1.6 g. Recrystallization from ethyl acetate–cyclohexane gave the half-acid-ester XX, m.p. 176–177°, which was not raised by further crystallizations.

Anal. Calcd. for $C_{19}H_{22}O_5$: C, 69.09; H, 6.66. Found: C, 68.56; H, 6.87.

Treatment with diazomethane gave the original diester XVIII.

Two grams of this half-acid ester XX was suspended in 10 cc. of anhydrous chloroform and about 3 cc. of freshly distilled oxalyl chloride was added. The reaction commenced immediately and the product had gone into solution after about 15 minutes. After another 20 minutes, the solvents were removed under vacuum and the last traces of oxalyl chloride were removed by adding more dry chloroform and distilling off under suction. A portion of the **ester acid chloride** (**XIX**) thus obtained on treatment with methanol and working up the reaction in the usual way gave the parent diester XVIII, as shown by melting point and mixture melting point determination. The oily acid chloride XIX was taken up in 50 cc. of anhydrous ether and treated with an excess of a dry ethereal solution of diazomethane. The evolution of nitrogen was instantaneous. After one hour the ether was removed under vacuum to give a solid diazoketone which was used without any purification. A solution of the diazoketone in 20 cc. of methanol was heated under gentle reflux and small portions of freshly precipitated silver oxide (1 g. in all) were added over a period of one hour. After the evolution of nitrogen had practically ceased, silver metal was removed by filtration. Methanol was removed under suction and the residual oil was dissolved in benzene. Colloidal silver was best removed by passing through a short column of alumina. Benzene was removed and the semi-solid mass left was crystallized twice from methanol as white prismatic crystals, m.p. 87–88.5°. Mixture melting determination with the diester obtained from X showed no depression. The diester thus obtained was also hydrolyzed to the dicarboxylic acid X according to the procedure already described; melting point and mixture m.p. 215–216°.

Oxidation of the Adduct 2-Methyl-7-methoxy-1,2-cyclopentenophenanthrene-3′,4′-dione (VI) with Alkaline Hydrogen Peroxide.—The mother liquors from the separation of the adduct V were concentrated. All attempts at crystallization through chromatography or evaporative distillation under high vacuum were unsuccessful. Two grams of the crude adduct VI was oxidized by excess of alkaline hydrogen peroxide in a manner similar to that used for the adduct V. The original brown color of the alkaline solution was changed to light yellow after the oxidation was complete. The cooled solution on treatment with hydrochloric acid gave an oily product which was redissolved in a dilute solution of potassium bicarbonate. This solution was extracted with ether to remove the insoluble material and then treated with hydrochloric acid to give a semi-solid mass. This was filtered, washed and dried; yield 0.8–0.9 g. The dry product after two crystallizations from ethyl acetate as a white powder had a m.p. 220–221°, yield 0.3–0.4 g. This proved to be **2-methyl-2-carboxy-7-methoxy-1,2,3,4,9,10-hexahydrophenanthrene-1-acetic acid** (**XXII**). Heer and Miescher,[8] who prepared this dicarboxylic acid in a different manner, reported a m.p. 210–212°. A mixture of a sample provided by Dr. Miescher and our sample had a m.p. 216–218°. The dicarboxylic acid on treatment with hydrogen chloride in acetic acid was recovered unchanged. The dicarboxylic acid on treatment with acetic anhydride was converted to the corresponding **anhydride XXIII** which after crystallization from benzene–petroleum ether as white needles had m.p. 148–149°; literature[8] m.p. 147–148°.

The mother liquors from the crystallization of the dicarboxylic acid XXII were evaporated to dryness. The oily residue was treated with diazomethane and the diester thus obtained was distilled under high vacuum to yield a brown viscous oil. This was saponified with excess 20% potassium hydroxide solution. The semi-solid acid thus obtained was reconverted to the dimethyl ester and evaporatively distilled under high vacuum. Hydrolysis of the ester thus obtained gave the dicarboxylic acid XXII as a semi-solid mass, which after drying and crystallization from ethyl acetate had a m.p. 218–220°, and showed no depression in m.p. when mixed with an authentic sample of XXII obtained as above; yield 90–100 mg.

Partial Dehydrogenation of 2-Methyl-2-carboxy-7-methoxy-1,2,3,4,9,10-hexahydrophenanthrene-1-acetic Acid (XXII) to 2-Methyl-2-carboxy-7-methoxy-1,2,3,4-tetrahydrophenanthrene-1-acetic Acid (XXIV).—Two hundred mg. of the hexahydrodicarboxylic acid XXII was dissolved in about 20 cc. of purified xylene, 200 mg. of 10% palladium–charcoal was added and the mixture heated under a gentle reflux for about 30 to 40 minutes. The catalyst was filtered off and xylene removed under vacuum. The residue on trituration solidified. It was recrystallized from a mixture of xylene–acetic acid into glistening prismatic crystals, m.p. 229–231°. Bachmann, Cole and Wilds,[11] who prepared this acid by a different route, reported a m.p. 230–231°. A mixture melting point determination of our sample with that provided by Professor Bachmann showed no depression.

Conversion of 2-Methyl-2-carboxy-7-methoxy-1,2,3,4,9,-10-hexahydrophenanthrene-1-acetic Acid (XXII) to 1,2-dimethyl-7-methoxy-phenanthrene (XVII) was carried out in a manner similar to that described for the isomeric dicarboxylic acid X. The identity of 1,2-dimethyl-7-methoxyphenanthrene from the two sources was checked through determination of mixed melting point, which showed no depression, and comparisons of their infrared spectra which were identical.

NEW DELHI, INDIA

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

Arylation of Unsaturated Systems by Free Radicals. VII. The Meerwein Reaction. V.[1] Further Arylations of Maleimides. Ultraviolet Spectra of Arylmaleimides, Arylmaleic Anhydrides and Arylmaleo- and Fumaronitriles

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Arylation of maleimide and N-isopropylmaleimide by diazonium salts in the presence of cupric ion produces α-arylmaleimides and α-aryl-N-isopropylmaleimides. The yields are generally higher in arylations of the N-isopropyl derivative, chiefly because of the more favorable physical properties of aryl-N-isopropylmaleimides. Their ultraviolet spectra and those of related compounds are reported and discussed.

α-Arylmaleimides can be formed in a single operation by the arylation of maleimide with diazonium salts in the presence of cupric ion.[2] It appeared from two experiments that N-substituted (especially N-isopropyl) maleimides might generally give higher yields of arylated product than unsubstituted maleimide. Because of our interest in arylmaleic anhydrides,[3] which can be prepared in high yield by hydrolysis of arylmaleimides followed by cyclization,[2] we have tested this tentative conclusion by arylating N-isopropylmaleimide with a series of diazonium salts. Further information was sought concerning the effects of nuclear substitution on the yields in the Meerwein reaction.

The reactions were conducted by the methods de-

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[1] Paper IV, O. Vogl and C. S. Rondestvedt, Jr., THIS JOURNAL, **78**, 3799 (1956).

[2] C. S. Rondestvedt, Jr., and O. Vogl, *ibid.*, **77**, 2313 (1955).

[3] C. S. Rondestvedt, Jr., and A. H. Filbey, *J. Org. Chem.*, **19**, 119 (1954).