

[CONTRIBUTION NO. 895 FROM THE CENTRAL RESEARCH DEPARTMENT, EXPERIMENTAL STATION, E. I. DU PONT DE NEMOURS AND CO., INC., WILMINGTON 98, DEL.]

Synthesis and Decomposition of 3-Diazo-6-dicyanomethylene-1,4-cyclohexadiene. Arylmalononitriles

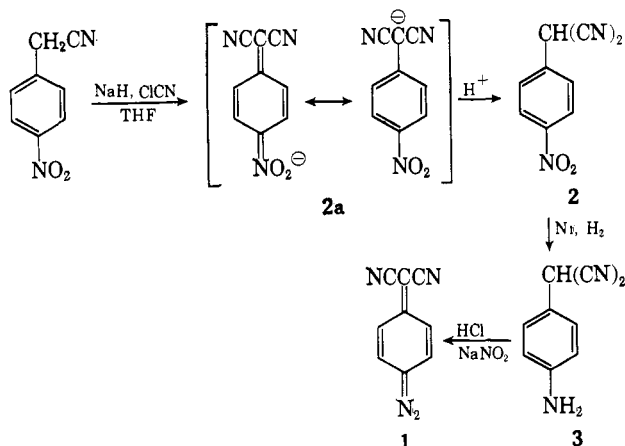
BY H. D. HARTZLER

RECEIVED DECEMBER 16, 1963

3-Diazo-6-dicyanomethylene-1,4-cyclohexadiene was obtained by diazotization of *p*-aminophenylmalononitrile prepared by reduction of *p*-nitrophenylmalononitrile. The diazo compound gave a phosphazene with triphenylphosphine and gave aryl-substituted phenylmalononitriles on thermal or photolytic decomposition in aromatic solvents. The intensely colored anion of *p*-nitrophenylmalononitrile gave only C-alkylated products. The effect of substituents on the acidity of arylmalononitriles was determined.

The recent synthesis of 7,7,8,8-tetracyanoquinodimethan¹ and its anion radical² suggested that other cyano-substituted quinodimethans and quinomethans would provide similarly interesting π -acid systems. The synthesis of 3-diazo-6-dicyanomethylene-1,4-cyclohexadiene (**1**) was pursued, for the diazo compound could serve as a useful intermediate in the synthesis of other π -acids. The electron-deficient species which could be obtained from **1** by loss of nitrogen also appeared interesting, both theoretically and synthetically. This paper describes the synthesis of **1**, its arylation with aromatic hydrocarbons, and some chemistry of the highly acidic, *p*-nitrophenylmalononitrile **2**.

The diazo compound **1** was obtained in three steps from *p*-nitrophenylacetone nitrile. Although phenylacetone nitrile reacted with sodium hydride and cyanogen



chloride to give benzotricyanide,³ *p*-nitrophenylacetone nitrile gave the anion **2a** under similar conditions. Stable sodium and potassium salts of **2a** have been prepared, and the free acid **2** was obtained in 79% yield upon acidification.

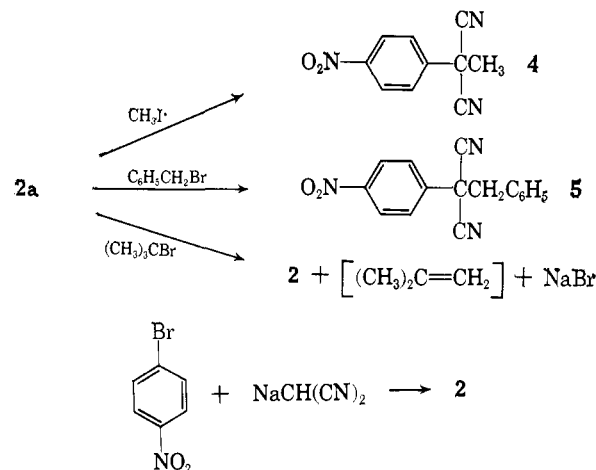
While **2a** resists reaction with cyanogen chloride, it can be alkylated with methyl iodide and with benzyl bromide to give the carbon-alkylated malononitriles **4** and **5**. In none of the three reactions were any products of O-alkylation found.

The direct reaction of the sodium salt of malononitrile with 1-bromo-4-nitrobenzene in diglyme at 120° gave a 40% yield of **2**. This method is definitely inferior to that given above.

(1) (a) D. S. Acker and W. R. Hertler, *J. Am. Chem. Soc.*, **84**, 3370 (1962); (b) D. S. Acker, R. J. Harder, W. R. Hertler, W. Mahler, L. R. Melby, R. E. Benson, and W. E. Mochel, *ibid.*, **82**, 6408 (1960).

(2) L. R. Melby, R. J. Harder, W. R. Hertler, W. Mahler, R. E. Benson, and W. E. Mochel, *ibid.*, **84**, 3374 (1962).

(3) J. K. Williams, U. S. Patent 2,995,597 (1961).



The acidity of **2** was determined spectrophotometrically by the method of Bryson.⁴ The pK_a of **2** in water using acetate and chloroacetate buffers is 1.89. *p*-Nitrobenzoic acid in water has a pK_a of 3.44.⁵ Phenylmalononitrile itself is a weaker acid (pK_a = 5.80 in water using borax buffers) than is benzoic (pK_a = 4.21).⁵ The increased effect of the substituent on the acidity of arylmalononitriles is to be expected since the acidic hydrogen is on an atom adjacent to the aromatic ring. The effect, however, is still much larger than that found in phenols, thiophenols, or anilinium ions. Unlike the latter compounds, there is no resonance interaction between the aromatic ring and the acid group in arylmalononitriles. Delocalization occurs only in the ion. Consequently, substituent effects are even more pronounced.

The reduction **2** → **3** proved to be difficult, for most catalysts gave complex mixtures due to concomitant reduction of the nitrile groups. The amine was obtained in 52% yield when a Raney nickel catalyst was used and the reduction was halted when the theoretical amount of hydrogen had been absorbed.

The diazotization of **3** in 6 *N* hydrochloric acid (in which the amine is only slightly soluble) gave an 84% yield of crude **1**. The diazo compound **1** has not been successfully recrystallized, but it was nearly completely purified by dissolving it in tetrahydrofuran, drying the solution, and reisolating **1** as red-brown crystals by evaporation. The infrared and ultraviolet absorption spectra of **1** were in complete agreement with the assigned structure.

Upon standing at room temperature **1** slowly decomposed. After 16 hr. at room temperature, duplicate

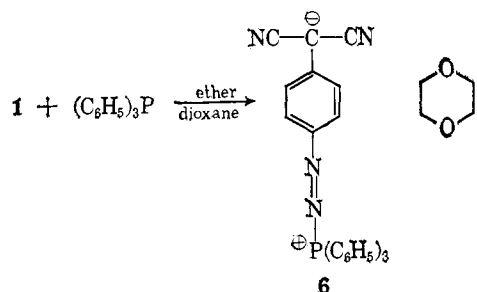
(4) A. Bryson, *J. Am. Chem. Soc.*, **82**, 4862 (1960).

(5) G. Briegleb and A. Breber, *Z. Elektrochem.*, **55**, 250 (1951).

nitrogen analyses showed a 1% loss of nitrogen. Upon slow heating, **1** does not melt, but an approximate decomposition temperature of 115° was obtained by immersion in a preheated bath.

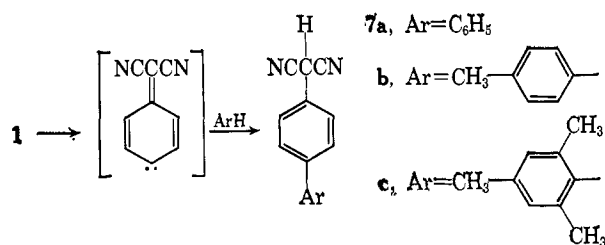
An attempted alternate synthesis of **1** by nitrosation of the acetamide of **3** failed.

Additional confirmation of the structure of **1** was obtained by its reaction with triphenylphosphine to give the phosphazene **6**.⁶



The phosphazene **6** was an intense purple in solution and had a golden metallic luster in the crystalline state. It has been obtained in the solid state only as a 1:1 solvate with dioxane. The infrared and ultraviolet absorption spectra of **6** are in complete agreement with the assigned structure. The charge-separated formula **6** is the best approximation of the structure of the phosphazene, for it has the huge dipole moment (obtained in dioxane) of 12.01 D. The phosphazene has an electrical resistivity of 1.9×10^{14} ohm cm. (powder compaction) and shows no photoconductivity. While **6** is stable in the solid state, it slowly decomposes in most solvents and is rapidly attacked by water and hydroxylic solvents.

When a suspension of **1** in an aromatic hydrocarbon is heated or illuminated with a sun lamp, partial nitrogen loss occurs (40–70%), and 4-arylphenylmalononitriles **7** are formed in low yields. Considerable amounts of noncrystalline, highly insoluble solids are

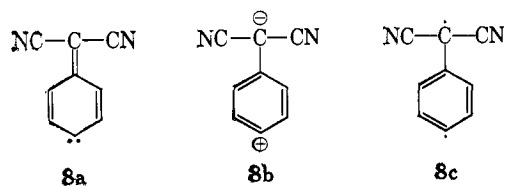


also formed. Irradiation with a sun lamp of a suspension of **1** in benzene gave a 33% yield of biphenylmalononitrile **7a**. The infrared and ultraviolet absorption spectra of **7a** were in complete agreement with the assigned structure.

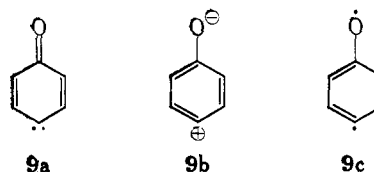
Similar reactions of **1** with toluene gave 4-(*p*-tolyl)phenylmalononitrile (**7b**) in 12% yield and with mesitylene gave 4-mesitylphenylmalononitrile (**7c**) in 21% yield. The ultraviolet and infrared spectra of **7b** and **7c** were quite similar to those of **7a**. The n.m.r. spectrum of **7c** showed the hydrogen adjacent to the nitriles at τ 4.94, the four aromatic hydrogens of the disubstituted ring as a weak, strong, strong, weak pattern centered at τ 2.65, the other two aromatic hydrogens at

τ 3.07, the two equivalent methyls at τ 8.05, and the other methyl at τ 7.70. The intensity ratios were the expected ones.

The data obtained thus far do not give much information concerning the nature of the intermediate formed by loss of nitrogen from **1**. It seems most reasonable that a transient such as **8a**, **8b**, or **8c** is involved rather than a direct reaction of **1** with the aromatic hydrocarbon because these reactions, as well as decompositions



of **1** in olefins, give essentially the same rates of nitrogen evolution. Any of these intermediates could conceivably give the arylation reactions. In the thermal reactions of **1**, however, one would expect the initial formation of **8a** or **8b** if spin is conserved. A subsequent conversion to a spin-unpaired intermediate **8c** might be energetically favorable, as has been suggested⁷ for the proposed intermediates (**9a**, **b**, **c**) derived from *p*-diazo oxides by loss of nitrogen. Most of the previous workers with diazo oxides^{7–10} have suggested that the spin-unpaired intermediate **9c** is the reactant in the



arylation reactions, although the zwitterion **9b** has been suggested¹⁰ as the intermediate in a copolymerization reaction with tetrahydrofuran. The photolysis of quinone monoazine also leads to this type of intermediate.¹¹

In the reactions of **1** with toluene and mesitylene we found no coupling products of benzyl radicals which might have arisen from hydrogen abstraction by **8c**. The absence of bibenzyls does not exclude the intermediacy of **8c**, because **8c** should be as reactive as a phenyl radical which would react primarily by addition to aromatics rather than by abstraction of α -hydrogen. While only **7b** was isolated in the reaction of **1** with toluene, the infrared spectrum of the crude reaction product suggested the presence of the *o*-substituted product; *o*- and *p*-substituted products have been isolated by Süss⁸ in the reaction of benzene-1,4-diazo-oxide with toluene and anisole. This, however, is the orientation to be expected of either a radical or electrophilic intermediate. A more careful examination of isomer distribution may offer a basis for choosing between **8c** and **8b** as the intermediate in the arylation reaction. We were unable to isolate arylation products from **1** and nitrobenzene.

(6) Phosphazenes from *p*-diazo oxides have recently been obtained: W. Ried and H. Appel, *Ann.*, **646**, 82 (1961); L. Horner and H. G. Schmelzer *Ber.*, **94**, 1326 (1961).

(7) M. J. S. Dewar and A. N. James, *J. Chem. Soc.*, 917 (1958).

(8) O. Süss, K. Möller, and H. Heiss, *Ann.*, **598**, 123 (1956).

(9) T. Kunitake and C. C. Price, *J. Am. Chem. Soc.*, **85**, 761 (1963).

(10) J. K. Stille, P. Cassidy, and L. Plummer, *ibid.*, **85**, 1318 (1963).

(11) C. Wang, *Proc. Chem. Soc.*, 309 (1961).

Thermal decomposition of **1** in aliphatic olefins did not give isolable products.

Experimental¹²

***p*-Nitrophenylmalononitrile (2).** **A.** From *p*-Nitrophenylacetonitrile.—A slurry of sodium hydride dispersion in mineral oil (92 g., 2.0 moles of hydride) in 1 l. of tetrahydrofuran was stirred under nitrogen and cooled in an ice bath. *p*-Nitrophenylacetonitrile (162 g., 1.0 mole) was added in portions. Hydrogen was evolved, and the mixture became dark red. Cyanogen chloride (70 g.) was passed into the mixture. The color deepened, and more hydrogen was evolved. The mixture was stirred overnight at room temperature under nitrogen. Most of the solvent was removed under reduced pressure. Cold, dilute hydrochloric acid was added to neutralize the base, and the crude product was filtered. Recrystallization from benzene–heptane (2:1) gave **2** as pale yellow plates (148 g., 79.4%), m.p. 109–110°.

Anal. Calcd. for C₉H₅N₃O₂: C, 57.75; H, 2.70; N, 22.45. Found: C, 58.09; H, 2.87; N, 22.34.

The potassium salt of **2** was prepared from **2** and aqueous potassium hydroxide. The salt may be recrystallized from acetonitrile. The ultraviolet spectrum of the anion **2a** was obtained in 50% aqueous ethanol *ca.* 0.05 *N* in KOH. There was absorption at 475 mμ (ε 20,000), 264 (7330), and 224 (12,200). The infrared spectrum of **2** showed very weak nitrile at 4.45 μ and nitro at 6.53 and 7.4 μ, as well as saturated and unsaturated CH absorptions.

Anal. Calcd. for C₉H₄O₂K: C, 48.0; H, 1.79; K, 17.4. Found: C, 48.4; H, 1.96; K, 16.8.

B. From 1,4-Bromonitrobenzene.—A mixture of 1,4-bromonitrobenzene (10.10 g.), sodiomalononitrile (4.40 g.), and diglyme (50 ml.) was stirred and heated at 120° for 4 hr. The mixture was cooled, poured into 400 ml. of water, and acidified with hydrochloric acid. Filtration yielded 9 g. of dark solid. Base extraction and reacidification yielded 3.65 g. (40%) of **2** as a pale yellow crystalline solid, m.p. 105–108°.

Methyl-*p*-nitrophenylmalononitrile (4).—A solution of 1.50 g. of **2** in 20 ml. of tetrahydrofuran was added to a slurry of 1.60 g. of potassium *t*-butoxide in 30 ml. of tetrahydrofuran under nitrogen. Methyl iodide (4.3 g.) was added, and the mixture was heated at reflux for 16 hr. The mixture was cooled and filtered to remove 1.26 g. of unreacted potassium salt of **2**. The product (0.43 g.), m.p. 120–122°, was recrystallized from cyclohexane to give pure **4**, m.p. 125–126°. The infrared spectrum showed absorptions due to nonconjugated nitrile at 4.45 μ (very weak) and nitro at 6.55 and 7.45 μ.

Anal. Calcd. for C₁₀H₇N₃O₂: C, 59.69; H, 3.51; N, 20.89. Found: C, 59.66; H, 3.57; N, 20.61.

Benzyl-*p*-nitrophenylmalononitrile (5).—To a slurry of 2.3 g. of sodium hydride–mineral oil dispersion in 50 ml. of glyme was added 9.37 g. of **2**. Benzyl bromide (17.1 g.) was added, and the mixture was heated at 80° under nitrogen for 6 hr. The mixture was filtered to remove sodium chloride and evaporated. The residue was stirred with pentane and filtered to give 11.54 g. (84%) of crude **5**, m.p. 128–130°. Recrystallization from methanol gave pale yellow crystals, m.p. 130.4–131°. The ultraviolet spectrum of **5** in acetonitrile showed absorption at 258 mμ (ε 11,000). The infrared spectrum of **5** showed nonconjugated nitrile at 4.43 μ and nitro absorptions at 6.55 and 7.40 μ. Both mono- and *p*-substituted benzene absorptions were present.

Anal. Calcd. for C₁₆H₁₁N₃O₂: C, 69.30; H, 4.00; N, 15.16. Found: C, 68.92; H, 4.00; N, 15.02.

Reaction of Sodium Salt of 2 with *t*-Butyl Bromide.—The sodium salt of **2** was prepared by adding a solution of 5.6 g. of **2** in 20 ml. of glyme to a stirred slurry of 1.38 g. of a 52% dispersion of sodium hydride in mineral oil in 20 ml. of glyme. A solution of 8.2 g. of *t*-butyl bromide in 10 ml. of glyme was added, and the mixture was heated at 90° for 16 hr. Filtration of the hot solution gave 3.03 g. (99%) of sodium bromide. The filtrate was evaporated, and the residue crystallized from benzene–heptane to give 3.69 g. (66%) of **2**, m.p. 102–106°.

***p*-Aminophenylmalononitrile (3).**—A solution of 14.0 g. of **2** in 90 ml. of acetone with *ca.* 5 g. of Raney nickel was hydrogenated

at room temperature in a Parr apparatus. Absorption ceased after approximately 0.2 mole (90%) of hydrogen has been absorbed. The catalyst was removed by filtration, and the crude amine (8.74 g.) was obtained by concentration of the filtrate. Recrystallization from 50% aqueous ethanol gave 6.11 g. (52%) of **3**, m.p. 135–136°. The infrared spectrum of **3** showed absorption due to NH at 2.8 and 2.9 μ and nonconjugated nitrile at 4.45 μ.

Anal. Calcd. for C₉H₇N₃: C, 68.77; H, 4.49; N, 26.74. Found: C, 68.82; H, 4.74; N, 26.42.

***p*-Acetamidophenylmalononitrile.**—A similar reduction of **2** with Raney nickel in acetic anhydride solution gave the acetamide in 49% yield, m.p. 181.5–182.5° after two recrystallizations from benzene–ethyl acetate (2:1). The infrared spectrum of the amide showed absorption due to nonconjugated nitrile (4.4 μ), amide carbonyl (6.0 μ), and *p*-substituted benzene (11.8 μ).

Anal. Calcd. for C₁₁H₉N₃O: C, 66.32; H, 4.56; N, 21.10. Found: C, 66.45; H, 4.59; N, 20.91.

3-Diazo-6-dicyanomethylene-1,4-cyclohexadiene (1).—A slurry of 12.3 g. of **3** in 50 ml. of 6 *N* hydrochloric acid was stirred at –5° while a cold solution of 8.0 g. of sodium nitrite in 60 ml. of water was added in 5 min. The mixture was stirred for another 10 min. and filtered to give 11.3 g. (84%) of crude **1**. Analysis indicated this product to be about 90% pure. It was purified by dissolving in tetrahydrofuran and drying over magnesium sulfate at 0° overnight. The drying agent and most of the solvent were removed to give **1** as red-brown crystals, m.p. 115° dec. After standing 16 hr. at room temperature the nitrogen analysis dropped to 32.04%. The infrared spectrum of **1** showed absorption due to unsaturated CH at 3.4, conjugated nitrile at 4.55, diazo at 4.70, and conjugated C=C at 6.3 μ. The ultraviolet absorption spectrum in tetrahydrofuran showed absorption at λ 482 mμ (ε 2.3 × 10⁴), 456 mμ (ε 2.7 × 10⁴), and 290 mμ (ε 0.35 × 10⁴).

Anal. Calcd. for C₉H₄N₄: C, 64.28; H, 2.40; N, 33.32. Found: C, 64.03; H, 3.22; N, 32.34.

Triphenylphosphine and 1(4-Dicyanomethylene-2,5-cyclohexadiene-1-ylidenehydrazono)triphenylphosphorane (6).—A solution of 2.6 g. of triphenylphosphine in 20 ml. of ether–dioxane (1:1) was added to a stirred slurry of 1.6 g. of **1** in 50 ml. of ether–dioxane. The mixture was stirred for 2 hr. and filtered. The filtrate was concentrated under nitrogen to half its original volume and filtered to give 2.87 g. (58%) of **6**, m.p. 133–134.6° dec. The infrared spectrum of **6** showed saturated CH at 3.50 and C–O at 8.75 μ, indicating the presence of dioxane. Absorptions of unsaturated CH (3.27 μ), conjugated nitrile (4.55 and 4.61 μ), and double bonds (6.23, 6.59, and 6.72 μ) were also present. The ultraviolet spectrum of **6** in acetonitrile showed λ_{max} 600 mμ (ε 3.12 × 10⁴), 563 (3.63 × 10⁴), 337 (0.435 × 10⁴), 318 (0.435 × 10⁴), and 262 (0.695 × 10⁴).

Anal. Calcd. for C₂₇H₁₉N₄P·C₄H₈O: N, 11.15; P, 6.17. Found: N, 10.85; P, 6.02.

Biphenylmalononitrile (7a).—A slurry of 6.50 g. of **1** in 100 ml. of benzene was stirred and illuminated with a G.E. sun lamp. After 2 hr. gas evolution ceased (70%). Cooling the reaction flask in an ice bath increased reaction time without changing the yield. The hot reaction mixture was filtered to remove dark solid. Evaporation of the filtrate left a gum from which **7a** could be separated by trituration with hot hexane. Recrystallization from hexane and then from aqueous ethanol gave 2.68 g. (33%) of **7a**, m.p. 110–111°. The infrared spectrum of **7a** shows absorption due to unsaturated CH at 3.3, saturated CH at 3.45, nonconjugated nitrile at 4.45, *p*-substituted benzene at 11.95, and monosubstituted benzene at 13.1 and 14.4 μ. The ultraviolet spectrum of **7a** in acetonitrile showed the biphenyl absorption at 253 mμ (ε 19,800).

Anal. Calcd. for C₁₅H₁₀N₂: C, 82.54; H, 4.62; N, 12.83. Found: C, 82.66; H, 4.78; N, 12.61.

4-(*p*-Tolyl)phenylmalononitrile (7b).—A similar reaction of **1** with toluene gave a 12% yield of **7b**, m.p. 155–156° from hexane. The infrared spectrum of **7b** showed the weak absorption of the nonconjugated nitrile at 4.44 μ and was completely consistent with the assigned structure.

Anal. Calcd. for C₁₆H₁₂N₂: C, 82.73; H, 5.21; N, 12.06. Found: C, 82.59; H, 5.52; N, 11.91.

4-Mesitylphenylmalononitrile (7c).—A similar reaction of **1** with mesitylene gave a 21% yield of **7c**, m.p. 130–131° from methanol. The infrared spectrum of **7c** showed absorption of the nitrile at 4.45 μ and was completely consistent with the assigned structure. The n.m.r. spectrum of **7c** in deuteriochloroform with tetra-

(12) Melting points are uncorrected. Infrared spectra were determined on a Perkin–Elmer Model 21, ultraviolet and visible spectra on a Cary Model 14, and n. m. r. spectra on a Varian A60 spectrometer.

methylsilane as internal standard showed the two equivalent methyl groups at τ 8.05, the other methyl at τ 7.70, the malononitrile hydrogen at τ 4.94, the two equivalent aromatic hydrogens at τ 3.07, and the other four aromatic hydrogens as a weak, strong, strong, weak pattern centered at τ 2.65.

Anal. Calcd. for $C_{18}H_{16}N_2$: C, 83.04; H, 6.20; N, 10.76. Found: C, 82.90; H, 6.03; N, 10.50.

Acknowledgment.—The advice and encouragement of Dr. R. E. Benson is greatly appreciated.

[CONTRIBUTION FROM THE DEPARTMENT OF PHARMACEUTICAL CHEMISTRY, UNIVERSITY OF WISCONSIN, MADISON 6, WIS.]

Thalictrum Alkaloids. III.¹ The Structure, Configuration, and Total Synthesis of Thalicipine, a Novel Dimeric Aporphine-Benzylisoquinoline Alkaloid²

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Evidence is presented for assignment of structure and configuration (I) to thalicipine. Elementary analysis of the alkaloid and the Hofmann degradation products IV and V supported a $C_{41}H_{48}O_8N_2$ molecular formula for thalicipine. Sodium in liquid ammonia reduction of I afforded two nonphenolic bases (VI and VII) and a phenolic base (VIII). Base VI was characterized as the methiodide XVI and the Hofmann methine XIX. Positive identification as 3,6-dimethoxyaporphine was achieved by direct comparison with an authentic sample prepared from XIII. Phenol VIII was characterized as the hydriodide and the O-methyl methiodide (XXI). Hofmann degradation of XXI gave a methylmethine (XXIII). To locate the phenolic hydroxyl group, VIII was converted to the O-ethyl ethiodide (XX), which upon Hofmann degradation yielded the methine XXII. Methylation of XXII gave the methine methiodide XXIV, and Hofmann degradation gave the O-ethyl-des-N-methine (XXVI). Oxidation of XXVI with potassium permanganate gave 2-ethoxy-4,5-dimethoxybenzoic acid (XXV). Synthesis of thalicipine was accomplished by modified Ullmann condensation of (–)-6-bromo-laudanosine (XXVII) with isocorydine (XXVIII). Since practical total syntheses of laudanosine and of isocorydine had previously been accomplished, the condensation reaction constituted a total synthesis of thalicipine. Furthermore, since the absolute configurations of (–)-laudanosine and of isocorydine had been elucidated earlier, the synthesis served also to establish the absolute configuration of thalicipine.

Thalicipine is a hypotensive alkaloid from *Thalictrum dasycarpum* Fisch. and Lall., and its isolation and preliminary characterization have recently been reported.⁴ It is the purpose of this paper to present, in detail, the elucidation of structure and absolute configuration (I) and the total synthesis of thalicipine. Thalicipine represents a novel type of alkaloid; it appears to be the first recognized dimeric alkaloid which contains an aporphine moiety.

The molecular formula $C_{41}H_{48}O_8N_2$ was assigned for thalicipine on the basis of elemental analysis and molecular weight determination by nonaqueous titration. Analysis showed the presence of seven O-methyl groups and two N-methyl groups. The n.m.r. spectrum in deuterated chloroform solution supports the formula, showing six N-methyl protons, twenty-one O-methyl protons, fourteen aliphatic protons, and seven aromatic protons. The infrared spectrum indicates the presence of aromatic rings and aromatic O-methyl groups, but absence of hydroxyl, carbonyl, and isolated double bonds.

A sequence of derivatives was prepared to seek confirmation of the empirical formula as well as to provide conversion products useful for structure elucidation.⁴ Treatment of thalicipine with methyl iodide afforded a product which resisted all attempts at crystallization. However, treatment of the amorphous methiodide II with alkali yielded a Hofmann methine (III) which was converted to a crystalline methiodide (IV). Analysis afforded results which support a $C_{46}H_{58}O_8N_2I_2$ formula for the Hofmann methine methiodide. A second Hof-

mann degradation yielded a des-N-methine (V), which afforded analytical results indicative of a $C_{39}H_{38}O_8$ empirical formula. The formulas of both methine derivatives support the $C_{41}H_{48}O_8N_2$ formula for thalicipine.

It is well known that diphenyl ethers can be reductively cleaved into phenolic and nonphenolic products by the action of metallic sodium in liquid ammonia.⁵ The latter reduction was carried out on thalicipine to cleave the suspected diphenyl ether linkage and split the molecule into two smaller moieties. Two nonphenolic bases (VI and VII) and a phenolic base (VIII) were obtained from the reaction. The yield of VIII was the same regardless of the reaction conditions, but the ratio of the yields of VI and VII varied according to the conditions used for the reaction. The stronger the conditions used, the more compound VII was obtained. This fact suggested that VI and VII were initially formed in the reaction and that VI was further transformed into VII.

For the preliminary characterization of VI, several crystalline derivatives were prepared. The hydriodide of VI afforded analytical results in agreement with the empirical formula $C_{19}H_{21}O_2N \cdot HI$, with two O-methyl functions. Compound VI was also treated with methyl iodide in methanol to give the methiodide XVI, $C_{20}H_{24}O_2NI$, with two O-methyl groups. Hofmann degradation of XVI in strong aqueous alkaline solution yielded a crystalline methine (XIX), $C_{20}H_{23}O_2N$, with two O-methyl groups. The ultraviolet spectrum of XIX shows characteristic peaks for a phenanthrene derivative. The n.m.r. spectrum of XIX in carbon tetrachloride solution shows only one peak for O-methyl protons (the area corresponds to six protons),

(1) Part II in the series: S. M. Kupchan and N. Yokoyama, *J. Am. Chem. Soc.*, **85**, 1361 (1963).

(2) This investigation was supported in part by research grants from the National Institutes of Health (H-2952 and CY-4500).

(3) Recipient of the 1962 Lunsford Richardson Pharmacy Award for a paper including part of this work.

(4) S. M. Kupchan, K. K. Chakravarti, and N. Yokoyama, *J. Pharm. Sci.*, **52**, 985 (1963).

(5) Cf. M. Tomita in "Progress in the Chemistry of Organic Natural Products," Vol. 9, L. Zechmeister, Ed., Springer Verlag, Vienna, 1952, p. 175; E. Fujita, *J. Pharm. Soc. Japan*, **72**, 213 (1952); F. G. Watt, *Chem. Rev.*, **46**, 331 (1949).