2 molar equiv of hydrogen were absorbed. Work-up in the usual manner gave a product which was separated from a small amount of an oily polar impurity (R_f 0.12) by preparative tlc (silica, 1:1 benzene–ethyl acetate, R_f (major product) 0.90). Crystallization from petroleum ether gave nitrile XIII (0.067 g, 71%), mp 116°. Recrystallized XIII had mp 118–119°; $[\alpha]^{26}D$ +19.9° (*c* 1.00); λ_{max} 4.42, 6.81, 6.91, 7.20, and 7.25 μ.

Anal. Calcd for $C_{27}H_{44}N_2$: C, 81.75; H, 11.18; N, 7.06. Found: C, 81.87; H, 11.25; N, 6.94.

B. From 2-Oximinocholestan-3-one (XIV) by Beckmann Cleavage.—Oximino ketone XIV (0.200 g) was cleaved with thionyl chloride exactly as described for the synthesis of cyano ester XII. The resulting acid chloride XV was dissolved in methylene chloride (20 ml) and the solution was saturated with gaseous ammonia at 0°. Work-up in the usual manner, followed by crystallization from 1:1 chloroform–petroleum ether, gave brilliant colorless crystals of the cyano amide XVI (0.170 g, 86%): mp 261°; $[\alpha]^{26}D$ +33.6° (*c* 1.03); no uv maxima above 210 mμ.

Anal. Calcd for $C_{27}H_{46}ON_2$: C, 78.20; H, 11.18; N, 6.76. Found: C, 78.30; H, 11.02; N, 6.80.

A solution of amide XVI (0.100 g) in thionyl chloride (3 ml) was refluxed for 18 hr. Evaporation of the excess thionyl chloride, followed by crystallization of the residue from petroleum ether, afforded dinitrile XIII (0.060 g, 66%), mp 118–119°, identical with material obtained from dinitrile XI as described above (section A).

Registry No.—I, 13341-55-4; III, 16426-16-7; IV, 16426-17-8; V, 16426-18-9; VII, 16426-19-0; VIII, 16426-20-3; IX, 16426-21-4; X, 16426-22-5; XI, 16426-23-6; XII, 16426-24-7; XIII, 16426-25-8; XVI, 16426-26-9.

Acknowledgment.—This investigation was supported by Public Health Service Research Grants CY-4498 and CA-04498, National Institutes of Health.

The Alkaloids of *Cassytha americana* (*C. filiformis* L.)[1]

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Thirteen alkaloids have been isolated from Brazilian *Cassytha americana* (*C. filiformis* L., Lauraceae). The structures of 1,2,9,10-bismethylenedioxy-3-methoxydibenzo[*de,g*]quinolin-7-one and 1,2,9,10-bismethylenedioxydibenzo[*de,g*]quinolin-7-one are suggested for the new oxoaporphine bases cassamedine and cassameridine. The plant also yielded ten previously known aporphine bases.

Recent investigations have shown the parasitic genus *Cassytha* (Lauraceae) to be a rich source of aporphine alkaloids. Aporphines have been reported from the following species: *Cassytha filiformis*,[2] *C. melantha*,[3] *C. glabella*,[3] *C. pubescens*,[4] and *C. racemosa*.[5] The vine, *C. filiformis*, is a species which is widely distributed throughout the tropics. Plant material from Taiwan yielded the new aporphine cassyfiline (I),[1,6] whereas material from New Guinea and Australia gave cassythidine (III).[2] We now report the results of an investigation of the alkaloids of *Cassytha americana* of Brazilian origin. After the study was essentially complete, we learned that *C. americana* was apparently synonomous with *C. filiformis*.[7] Our work has resulted in the isolation of thirteen tertiary bases, two of which, cassamedine (IV) and cassameridine (V), are new oxoaporphines.

Separation of the Bases.—As described in detail in the Experimental Section, the bases were separated first into alkali-soluble and alkali-insoluble fractions. The latter were further fractionated by differential acid buffer extraction and chromatography. The yields of pure compounds were generally low, owing to experimental difficulties encountered in the separation steps. Thin layer chromatography indicated, however, the absence of significant quantities of alkaloids other than those identified.

The Alkali-Soluble Aporphines.—The largest portion of the total alkaloids was alkali soluble and consisted of a mixture of cassyfiline (I), actinodaphnine (VI), and N-methylactinodaphnine (VII). Compound VI was the major component of the mixture, although an efficient procedure for its separation was not devised. Compound VII has been described as a transformation product of VI,[8] but it had not been encountered as a naturally occurring alkaloid prior to the completion of our investigation. Very recently, however, it has been reported to be the major alkaloid of both *Cassytha melantha* and *C. glabella* and has been given the name cassythicine.[3]

The Alkali-Insoluble Aporphines.—The alkali-insoluble alkaloids consisted mainly of a mixture of seven aporphines. These included the cryptophenolic bases launobine (VIII) and bulbocapnine (IX), as well as the closely related nonphenolic bases O-methylcassyfiline (II), cassythidine (III), dicentrine (X), neolitsine (XI), and (+)-nornuciferine (XII). Compound XII could be separated from the natural alkaloid mixture only in the form of (+)-nuciferine (XIII) after N-methylation with formaldehyde and sodium borohydride. Thin layer chromatography showed definitely that no XIII was present before N-methylation.

(1) The plant material used in this investigation was collected near Porto Seguro in the State of Bahia, Brazil, by Dr. Aparicio Duarte whose assistance is gratefully acknowledged. A reference specimen, R. B. 130345, has been filed in the Herbarium of the Botanical Garden at Rio de Janeiro.

(2) (a) M. Tomita, S. T. Lu, and S. J. Wang, *J. Pharm. Soc. Jap.*, **85**, 827 (1965); (b) S. R. Johns, J. A. Lamberton, and A. A. Sioumis, *Aust. J. Chem.*, **19**, 297 (1966).

(3) S. R. Johns, J. A. Lamberton, and A. S. Sioumis, *ibid.*, **19**, 2339 (1966).

(4) S. R. Johns, J. A. Lamberton, and A. A. Sioumis, *ibid.*, **19**, 2331 (1966).

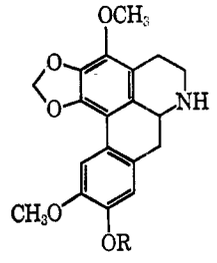
(5) S. R. Johns, J. A. Lamberton, and A. A. Sioumis, *ibid.*, in press.

(6) Alkaloid I is named cassyfiline in ref 1a and cassythine in ref 1b in which an independent isolation and structure determination are described. In view of the earlier publication of ref 1a, the name cassyfiline will henceforth be used in this paper.

(7) The preferred binomial is *Cassytha filiformis* L. with *C. americana* Nees. and *C. capillaris* F.-Vill. occasionally given as synonyms.

(8) M. Tomita, M. Kozuka, E. Nakagawa, and Y. Mitsunori, *J. Pharm. Soc. Jap.*, **83**, 763 (1963).

Compound XII has been isolated from natural sources previously only as (−)-nornuciferine.[9]



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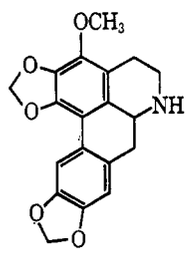
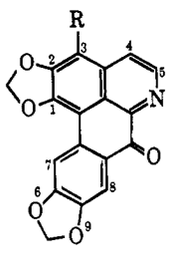
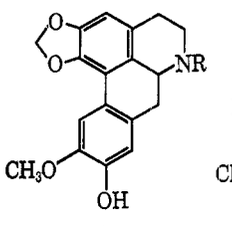
II, R = CH_3



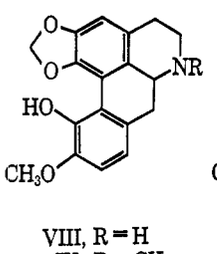
III



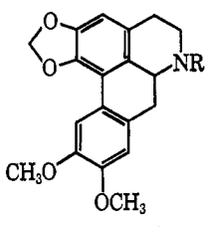
IV, R = OCH_3
V, R = H



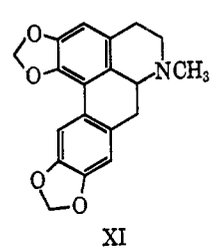
VI, R = H
VII, R = CH_3



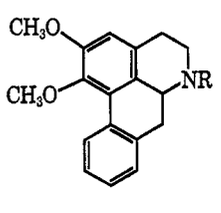
VIII, R = H
IX, R = CH_3



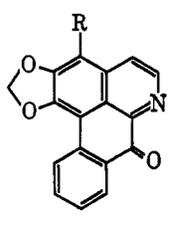
X, R = CH_3
XIX, R = H



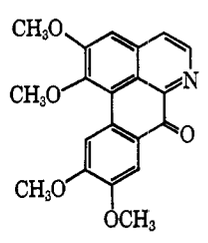
XI

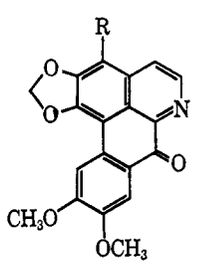


XII, R = H
XIII, R = CH_3



XIV, R = H
XV, R = OCH_3





XVI XVII, R = OCH_3
XVIII, R = H

The Oxoaporphine Bases.—The alkali-insoluble alkaloid mixture contained an orange compound, mp 278°, which was readily separable from the major bases because of its sparing solubility in benzene. This new compound, cassamedine, has been assigned the oxoaporphine structure IV on the basis of the following evidence. Elemental analysis was in fair agreement with the composition $C_{19}H_{11}O_6N$; the mass spectrum of IV confirmed the molecular weight (349) and indicated no ready skeletal fragmentation, in accord with a completely aromatic structure. Its infrared spectrum showed a highly conjugated carbonyl band at 1650 cm^{-1}, but no NH or OH absorption. The complex ultraviolet absorption spectrum of the compound in neutral and acidic ethanol solution was indicative of the oxoaporphine chromophore found in liriodenine (XIV);[10] the spectrum was unchanged by the addition of alkali, showing the absence of a cryptophenolic hydroxyl.

The nmr spectrum of cassamedine IV showed signals due to two unsplit methylenedioxy groups at δ 6.62 and 6.23[11] and a methoxyl at 4.48, as well as five aromatic protons at 7.83, 8.19, and 8.85 (two protons). The signals at δ 6.62 and 4.48 are analogous to those (6.72 and 4.55) observed in the spectrum of atherospermidine (XV);[12] consequently, they have been assigned to a 1,2-methylenedioxy group and a 3-methoxy group, respectively. The aromatic protons may be assigned by comparison with those of O-methylatheroline (XVI). In the latter compound, the signals at δ 7.08, 7.63, 8.76, 7.93, and 8.65 have been attributed to the protons at C-3, C-4, C-5, C-8, and C-11, respectively.[13] In IV the two lowest field protons at δ 8.85 are therefore those at C-5 and C-11; the 8.19 proton must be that at C-8; and the 7.83 proton must be that at C-4. The signal at δ 6.23 is assigned to the 9,10-methylenedioxy group.

Since IV is the aromatic oxoaporphine corresponding to III, it should be possible to prepare IV from III by oxidation. We were unable to carry out this reaction because of the small amount of III at our disposal and the poor yield of oxoaporphine to be expected in this reaction.[14] On the other hand, oxidation of II afforded, in 2% yield, the corresponding orange oxoaporphine (XVII). As expected, the ultraviolet spectra of IV and XVII were practically identical in both neutral and acid solution, thus providing further support for the assignment of structure IV to cassamedine.

Cassameridine (V) was first detected as an impurity in IV, the mass spectrum of which showed the presence of a small amount of a compound of mol wt 319, corresponding to a demethoxycassamedine. Careful chromatography of IV eliminated this extraneous 319 peak and afforded a small amount (*ca.* 1 mg) of V as a bright yellow solid. Oxidation of O-methylactinodaphnine (XIX) afforded, in 2% yield, an aromatic oxoaporphine (XVIII) having practically the same ultraviolet spectrum as V in both neutral and acid solution, thus suggesting structure V for cassameridine. We were unable to attempt the direct preparation of V by the oxidation of neolitsine (XI), owing to the small amount of XI at our disposal. The confirmation of structure IV and V for cassamedine and cassameridine by total synthesis is in progress.

Experimental Section

All melting points are uncorrected. Optical rotations were determined in chloroform at room temperature unless otherwise stated. Infrared spectra were measured in KBr disks. Ultraviolet absorption spectra were run in 95% ethanol. Nmr spectra were taken on a Varian A-60 spectrometer. Microanalyses were carried out by Midwest Microlab, Inc., Indianapolis, Ind. Comparison of isolated compounds with authentic samples where available was made by mixture melting point determination, tlc, and ir and uv spectroscopy.

(9) S. M. Kupchan, B. Dasgupta, E. Fujita, and M. L. King, *Tetrahedron*, **19**, 227 (1963).

(10) A. W. Sangster and K. L. Stuart, *Chem. Rev.*, **65**, 69 (1965).

(11) Nmr values are expressed as parts per million downfield from tetramethylsilane.

(12) I. R. C. Bick and G. K. Douglas, *Tetrahedron Lett.*, 1629 (1964).

(13) I. R. C. Bick and G. K. Douglas, *ibid.*, 4655 (1965).

(14) M. Tomita, T. H. Yang, H. Furukawa, and H. M. Yang, *J. Pharm. Soc. Jap.*, **82**, 1574 (1962).

Extraction of *Cassytha americana* and Isolation of Crude Bases.—The alcoholic extract from 41.8 kg of plant material was concentrated to a thick syrup and extracted, with stirring and gentle heating, with 12.1 of ammoniacal (10%) ethyl acetate. The ethyl acetate was decanted from the nonalkaloidal residue and extracted with fifteen 500-cc portions of 5% H_2SO_4. The combined acid extracts were washed twice with 1-l. portions of benzene and the benzene extracts were discarded. The aqueous extracts were adjusted to pH 10 with ammonia and extracted with chloroform until alkaloid negative. The chloroform was dried over Na_2SO_4 and concentrated to yield 80 g of total nonquaternary bases.

Alkali Separation of the Alkaloids.—The crude base mixture (80 g) was dissolved in 2 *N* H_2SO_4 and nonalkaloidal impurities were removed by chloroform extraction. The bases were then extracted with chloroform after basification with ammonia. Separation into alkali-insoluble (14.4 g) and alkali-soluble (30.2 g) fractions was accomplished by distributing the bases between chloroform and 2% aqueous NaOH; the bases were recovered from the latter by saturating it with solid NH_4Cl and then extracting with chloroform.

Alkali-Insoluble Bases.—The mixture of "nonphenolic" bases was triturated with benzene and the insoluble orange solid (100 mg) (*vide infra*) was filtered off. The benzene solution was then extracted successively with McIlvaine buffer solutions of pH 6.6, 6.0, 5.0, 4.0, 3.6, and 2.2. The base fractions were recovered from the buffer solutions by basification with aqueous NaOH followed by extraction with benzene. Screening of the extracts was done by thin layer chromatography on neutral alumina using chloroform as solvent; the spots were visualized with iodine vapor.

Neolitsine (XI).—The pH 2.2 (0.75 g) and pH 3.6 (1 g) fractions were chromatographed in benzene solution over neutral Gr II alumina. Elution with benzene gave in the earlier fractions neolitsine, crystallizing from acetone as colorless needles (36 mg): mp 145–146°; $[\alpha]_D$ +55°; λ_{max} 284 mμ (log ε 4.19) and 311 (4.33); identical with an authentic sample (lit.[15] mp 149–150°; $[\alpha]_D$ +56.5°).

Dicentrine (X).—The middle benzene eluates from the above fractions afforded dicentrine, crystallizing from ethanol as pale yellow needles (450 mg): mp 167–168°; $[\alpha]_D$ +55.3° (ethanol); λ_{max} 282 mμ (log ε 4.19) and 306 (4.23); identical with an authentic sample {lit.[16] mp 168–169°; $[\alpha]_D$ +56° (ethanol)}.

Cassythidine (III).—The later benzene eluates from the above fractions afforded, after crystallization from ethanol, cassythidine as a microcrystalline solid (22 mg): melting point and mixture melting point with an authentic sample, 206–208°; $[\alpha]_D$ +15.8°; λ_{max} 235 mμ (log ε 4.42), 286 (4.20), and 310 (4.26) (lit.[2] mp 206–207°; $[\alpha]_D$ +15°).

Launobine (VIII).—The pH 5.0 fraction (1.8 g) was chromatographed in benzene over neutral Gr IV alumina. Elution with benzene and crystallization of the residue from methylene chloride furnished a microcrystalline solid (12 mg): mp 197°; $[\alpha]_D$ +228.7°; λ_{max} 270 mμ (log ε 4.25) and 307 (3.88); identical with an authentic sample (lit.[16] mp 214–215°; $[\alpha]_D$ +192.7°).

Anal. Calcd for $C_{18}H_{17}O_4N$: C, 69.44; H, 5.50; N, 4.50. Found: C, 69.47; H, 5.60; N, 4.24.

Bulbocapnine (IX).—Preparative thin layer chromatography of pH 4.0 fraction (2.1 g) on neutral alumina with chloroform as developing solvent gave only partial resolution of the constituents. Elution of a fast-moving band afforded, after crystallization from ethanol, colorless needles (2 mg) of bulbocapnine, mp 202°, identical with an authentic sample.

O-Methylcassyfiline (II).—A slow moving compound from the above preparative tlc was obtained as a gum which was found to be highly soluble in the common organic solvents, but a few crystals, mp 150–152° (lit.[1,2] 150–151°, amorphous), could be obtained from ether: λ_{max} 236 mμ (log ε 4.43), 283 (4.31), 302 (4.30), and 312 (4.27). The compound was identical with an authentic sample of O-methylcassyfiline prepared from cassyfiline.

(+)-Nuciferine (XIII).—The pH 5.0 material remaining after the separation of VIII launobine was dissolved in methanol (10 ml) and stirred for 30 min with 37% formalin (0.5 ml), then for a further 30 min after adding sodium borohydride (50 mg). Buffer separation of the product and chromatography of the pH 2.2 fraction yielded (+)-nuciferine as colorless prisms from acetone (15 mg): mp 164°; $[\alpha]_D$ +159.3°; λ_{max} 230 mμ (log ε 4.36), 272 (4.27) and 310 (3.46). It was identical in all respects with an authentic sample of synthetic (+)-nuciferine.

Cassameridine (V).—The benzene-insoluble orange solid (100 mg) (*vide supra*) was dissolved in chloroform and adsorbed on neutral Gr III alumina (5 g) and dried. This material was added to fresh alumina (10 g) and the mixture was eluted with chloroform–benzene (1:3; 200 ml). Evaporation of the eluent gave, after crystallization from ethanol, a yellow microcrystalline solid (1 mg), mp 300°. It formed a red solution in mineral acid and exhibited a green fluorescence in $CHCl_3$ solution: λ_{max} 251 mμ (log ε 4.46), 274 (4.40), 323 (4.08), 353 (3.91), 388 (3.85), and 440 (3.73); $\lambda_{max}^{ethanol-HCl}$ 261 mμ (log ε 4.62), 290 (4.59), 385 (4.31), and 500 (3.62).

Cassamedine (IV).—Elution of the above column with chloroform–benzene (1:1; 200 ml) afforded after crystallization from chloroform–ethanol, an orange microcrystalline solid: mp 278°; λ_{max} 252 mμ (log ε 4.47), 281 (4.53), 324 (4.12), 364 (3.97) and 460 (3.76); $\lambda_{max}^{ethanol-HCl}$ 272 mμ (log ε 4.49), 286 (4.50), 408 (4.10), and 534 (3.40); nmr (in CF_3COOH), δ 7.83, 8.85 (2 H), 8.19, 4.48 (3 H), 6.62 (2 H), and 6.23 (2 H); ν_{max} 1650 cm^{-1}.

Anal. Calcd for $C_{19}H_{11}O_6N$: C, 65.33; H, 3.17; N, 4.01; mol wt., 349. Found: C, 64.61; H, 3.25; N, 4.29; mol wt (mass spectroscopy), 349.

Chromium Trioxide–Pyridine Oxidation of O-Methylcassyfiline (II).—O-Methylcassyfiline was prepared by methylation of cassyfiline (100 mg) in methanol (5 ml) with an excess of ethereal diazomethane for 2 days at 0°. A solution of the product in pyridine (2 ml) was treated with chromium trioxide (200 mg) in pyridine (3 ml) in the cold for 1 hr. Ethanol (2 ml) followed by water (10 ml) was added and the solution was extracted thoroughly with chloroform. The chloroform extract was extracted repeatedly with 5% aqueous HCl, basified, extracted with chloroform, and dried (K_2CO_3) and the solvent was removed. The orange residue was adsorbed on neutral Gr III alumina (5 g) and eluted with chloroform–benzene (1:1, 100 ml). The residue from the eluate was crystallized from chloroform–ethanol to give the orange microcrystalline XVII (2 mg), mp 274–275°. The mixture melting point with cassamedine IV was depressed and ir comparison showed that the compounds were different: λ_{max} 252 mμ (log ε 4.38), 282 (4.44), 281 (4.41), 406 (3.99), and 539 (3.39). The compound gave a red solution in mineral acid and its chloroform solution exhibited a green fluorescence.

Chromium Trioxide–Pyridine Oxidation of O-Methylactinodaphnine (XIX).—Actinodaphnine (*vide infra*) (100 mg) was methylated with excess diazomethane and the resulting O-methylactinodaphnine was oxidized with chromium trioxide–pyridine reagent as described for the oxidation of II. Crystallization from ethanol gave XVIII as a yellow microcrystalline solid (2 mg): mp 300°; λ_{max} 250 mμ (log ε 4.69), 272 (4.62), 313 sh (4.17), 351 (4.22), 392 (4.39), and 438 (4.29); $\lambda_{max}^{ethanol-HCl}$ 260 mμ (log ε 4.69), 292 (4.62), 382 (4.30), and 506 (3.64).

Alkali-Soluble Bases.—The alkali-soluble bases were dissolved in chloroform and the buffer separation was carried out as in the case of the alkali-insoluble bases. Tlc screening of the extracts was carried out on silica gel plates with 5% methanol in chloroform as solvent.

Cassyfiline (Cassythine) (I).—The pH 4.0 fraction (1.9 g) was crystallized directly from chloroform–ethanol to yield cassyfiline (430 mg): mp 211–213°; $[\alpha]_D$ +28.3°; λ_{max} 283 mμ (log ε 4.28) and 303 (4.27); identical with an authentic sample (lit.[2] mp 217–219°; $[\alpha]_D$ +24°).

The pH 5.0 fraction (2.1 g) was dissolved in chloroform and adsorbed on neutral Gr IV alumina. Elution of the column with benzene gave cassyfiline (230 mg).

Actinodaphnine (VI).—Further elution of the above column with chloroform–benzene (1:4) yielded actinodaphnine, crystallizing from ethanol as colorless prisms (112 mg): mp 202–203°; $[\alpha]_D$ +37.9° (ethanol); λ_{max} 284 mμ (log ε 4.12) and 307 (4.17); identical with an authentic sample {lit.[16] mp 210–211°; $[\alpha]_D$ +33° (ethanol)}.

The pH 6.6 fraction was found to be mostly actinodaphnine containing a small amount of I.

Cassythicine (N-Methylactinodaphnine) (VII).—The pH 2.2 (0.7 g) and pH 3.6 (1.4 g) fractions were chromatographed in chloroform–benzene (1:1) solution on neutral Gr IV alumina. Elution of the column with benzene and crystallization of the residue from ethyl acetate furnished colorless prisms of cassythicine (395 mg): mp 204–205°; $[\alpha]_D$ +53.1 (ethanol); λ_{max} 283 mμ (log ε 4.23) and 307 (4.27) {lit.[8] mp 210–211°; $[\alpha]_D$

(15) W. A. Hui, S. N. Loo, and H. R. Arthur, *J. Chem. Soc.*, 2285 (1965).
(16) M. Shamma and W. A. Slusarchyk, *Chem. Rev.*, **64**, 59 (1964).

57.0° (ethanol)}. The compound was identical with an authentic sample prepared by the N-methylation of actinodaphnine VI with 37% formalin and $NaBH_4$ in methanol solution. With excess of ethereal diazomethane it afforded dicentrine, mp and mmp 166–167°.

Registry No.—IV, 16408-75-6; V, 16408-76-7; XVII, 16408-77-8; XVIII, 16408-78-9.

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Coumarins. V. The Acid-Catalyzed Reaction of Phenols with β-Oxonitriles[1]

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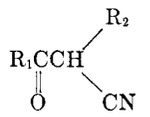
Benzoylacetonitrile (Ia) and acetoacetonitrile (Ib) were found to undergo carbon–carbon condensation with phenols providing a new route to coumarins, whereas carbon–oxygen condensation occurred with α-ethylacetoacetonitrile (Ic). The aluminum chloride catalyzed reaction of *meta*- and *para*-substituted phenols with Ia in the presence of dry hydrogen chloride yielded the corresponding iminocoumarins II and/or coumarins IV. Phenol as well as *o*-cresol gave predominantly β-(*p*-hydroxyphenyl)cinnamonitriles V. In contrast, Ib reacts with phenols in polyphosphoric acid or its ethyl ester to furnish 4-methylcoumarins in appreciable yields. The oxonitrile Ic on treatment with phenols in the presence of aluminum chloride and hydrogen chloride gave rise to both *cis*- and *trans*-β-aryloxy-α-ethylcrotononitriles VIIa and b in good yields. Mechanisms to account for the results are proposed.

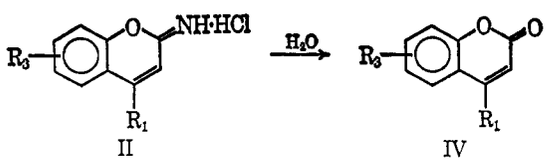
Previous papers in this series have demonstrated that anhydrous aluminum chloride, accompanied by dry hydrogen chloride, is an efficient reagent for nuclear addition reactions of phenols to α,β-unsaturated nitriles[3] and to 3-butenenitrile.[4] These studies have now been extended to β-oxonitriles. Whereas coumarins may be obtained by the acid-promoted condensation of phenols with β-keto esters (the von Pechmann reaction), little is known of a similar reaction with β-oxonitriles. It has been shown that benzoylacetonitriles condense with polyhydric phenols, such as resorcinol, in the presence of concentrated sulfuric acid to give the corresponding coumarins.[5,6] Mentzer and coworkers[7] have reported that the same acid-catalyzed reaction of resorcinol with α-aryl-β-ketonitriles yields 3-aryl-4-alkyl-7-hydroxycoumarins; no yields are given. While the reaction of the more active phenols, such as phloroglucinol, with 2-phenylacetoacetonitrile in trifluoroacetic acid is claimed[8] to give isoflavone in excellent yields, Cook and coworkers,[9] more recently, have noted that under identical conditions resorcinol reacts with α-(*p*-methoxyphenyl)acetoacetonitrile to provide the corresponding coumarin, which may be also secured by use of hydrogen fluoride as the condensation catalyst. No method of preparing coumarins by the acid-catalyzed reaction of phenols with aliphatic β-oxonitriles, such as acetoacetonitrile and its ethyl derivative, has yet appeared in the literature.

We have examined the condensation of phenols with β-oxonitriles Ia–c using anhydrous aluminum chloride, polyphosphoric acid (PPA), or its ethyl ester (PPE).[10]



Ia, R_1 = Ph; R_2 = H
b, R_1 = CH_3; R_2 = H
c, R_1 = CH_3; R_2 = C_2H_5

When equimolar amounts of resorcinol and benzoylacetonitrile (Ia) were treated with 2 equiv of anhydrous aluminum chloride in isopropyl ether saturated with dry hydrogen chloride, a nitrogenous product was obtained in nearly quantitative yield. The analytical data agreed with the formula $C_{15}H_{12}ClNO_2$, which is in accord with the structure of the coumarin derivative IIa



II IV

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(3) Part I: K. Sato, T. Amakasu, and S. Abe, *J. Org. Chem.*, **29**, 2971 (1964).

(4) Part IV: T. Amakasu, *Bull. Chem. Soc. Jap.*, **41**, 451 (1968).

(5) (a) B. N. Ghosh, *J. Chem. Soc.*, **109**, 105 (1916); (b) G. Bargellini and G. Forti-Forli, *Gazz. Chim. Ital.*, **41**, 747 (1911); (c) A. Sonn, *Chem. Ber.*, **51**, 821, 1829 (1918).

(6) W. Baker, *J. Chem. Soc.*, **127**, 2349 (1925).

(7) C. Mentzer, P. Gley, D. Molho, and D. Billet, *Bull. Soc. Chim. Fr.*, **5**, 13, 271 (1946).

(8) L. L. Wood and J. Sapp, *Texas J. Sci.*, **16**, 383 (1964); *Chem. Abstr.*, **62**, 6454 (1965).

(9) C. E. Cook, R. C. Corley, and M. E. Wall, *J. Org. Chem.*, **30**, 4114 (1965).

(10) T. Amakasu and K. Sato, *ibid.*, **31**, 1433 (1966).