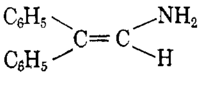
Nitrosation Reactions of Primary Vinylamines. 3-Amino-2-phenylindenone[1]

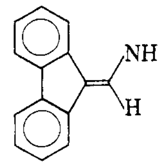
David Y. Curtin, J. A. Kampmeier,[2] and Melvin L. Farmer[3]

Contribution from the Noyes Chemical Laboratory, University of Illinois, Urbana, Illinois. *Received October 5, 1964*

3-Amino-2-phenylindenone (I) reacts with sodium nitrite or isoamyl nitrite in acetic acid to give a monoacetate IV and the diacetate V of cis-2,3-dihydroxy-2-phenyl-1-indanone (VI) in yields of 52–55 and 23–28%, respectively. The ratio of IV:V of 2.0–2.3 is not altered seriously by addition of acetic anhydride, water, or sodium acetate to the acetic acid. The reaction of amine I with nitrosyl chloride in methylene chloride gives 3-chloro-2-phenylindenone (XIV), 2,3-dichloro-2-phenylindanone (XV), and phthalimide (XVI) with a mole ratio of 1.7:1.4:1. With isoamyl nitrite in propionic acid a dipropionate of alcohol VI and 2-nitro-2-phenyl-1,3-indandione (10% yield) is isolated. The monoacetate IV, diacetate V, and hydroxy ketone VI are interconverted by acetylation and hydrolysis. That they have the same carbon skeleton as the amine I is shown by reduction with lithium aluminum hydride of IV or V to the triol VII and oxidation to phthalaldehyde, isolated as its dinitrophenylhydrazone, and benzoic acid. The cis orientation of the hydroxyl groups in the hydroxy ketone VI is demonstrated by the formation of a cyclic carbonate ester on treatment of VI with phosgene. The ester when reduced with lithium aluminum hydride gives the same triol VII obtained from reduction of IV or V. Reduction of ketodiacetate V with lithium aluminum deuteride gives a monodeuteriotriol VII-D with the position originally occupied by the carbonyl group labeled with a deuterium atom. Triol VII or VII-D with phosgene gives 1-chloroformyloxy-2-phenyl-2,3-indandiol carbonate (XI) or 1-chloroformyloxy-2-phenyl-2,3-indandiol carbonate-1-d (XI-D), the location of the deuterium showing that ring closure to the cyclic carbonate occurs only between the two oxygen atoms originally present as alcohol or ester oxygens in IV, V, and VI. The stereochemical configuration of the triol VII is deduced from the nonequivalence in the n.m.r. of the protons of the secondary alcohol functions. The stereochemical configuration of the dihydroxy ketone VI and its ester derivatives is deduced from the facts just given. Positions of the proton resonances of the protons on the five-membered ring of the chloroformate XI were assigned by comparing its spectrum with that of the methyl carbonate XII, obtained by treating the chloride with methanol. Examination of the infrared spectra suggests that 2-phenylindanones with a hydrogen atom at the 2-position show absorption at 1710–1715 cm.$^{-1}$, but that, with a chloro, nitro, hydroxy, acetoxy, propionoxy, or carbonate ester oxygen substituted at the 2-position, absorption falls in the region 1730–1740 cm.$^{-1}$. α-Carboxydibenzyl (XXI) demonstrates magnetically nonequivalent gem-methylene protons in the n.m.r. spectrum. Although neither α-cyanodibenzyl (XX) nor α,α-dibenzylphenylacetonitrile (XXIII) shows evidence of magnetic nonequivalence of the gem-protons in the n.m.r., the spectra of the o-chloro-substituted compounds XXII and XXIV reveal such nonequivalence.

An investigation of the reaction with diazotizing agents of primary amines whose diazonium salts should be intermediate in reactivity between aromatic and saturated aliphatic diazonium salts was initiated[4] with a study of 2,2-diphenylvinylamine (A) and 9-(aminomethylene)fluorene (B). The lack of success in isolation or interception of diazonium ions in the diphenylvinyl system could be attributed at least in part to ready rearrangement with phenyl migration, possibly with kinetic driving force; avoidance of rearrangement by employing the methylenefluorene system produced a new difficulty, a homolytic reaction leading to nitric oxide as a major reaction path. A possible factor contributing toward carbonium ion stability in the systems exemplified by A and B is the freedom of the vinylcarbonium ion to exist in a linear configuration C, with sp-bonds joining the carbonium carbon to its neighboring atoms and with the positive charge associated with the vacant p-orbital.


A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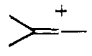
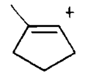
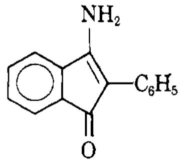
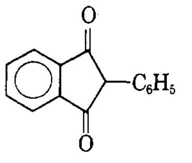
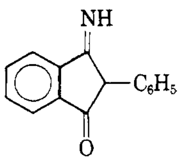

C


D

As an example of a vinylamine which it was hoped might be free from difficulties previously encountered and whose derived carbonium ion would be constrained to the bent configuration D, 3-amino-2-phenylindenone (I) was selected for investigation. At the time this work was initiated, compound I seemed attractive because of the availability of its precursor 2-phenyl-1,3-indandione (II) and of methods for conversion of β-diketones to the β-amino-α,β-unsaturated derivatives. Fusion of the diketone II with ammonium acetate, a method developed by Horton and Murdock[5] for


I


II


III

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[1] Taken from the Ph.D. Theses of J. A. Kampmeier, 1960, and M. Farmer, 1964, submitted to the University of Illinois.

[2] National Science Foundation Fellow, 1958–1960.

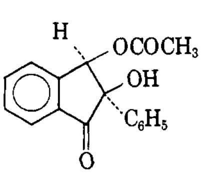
[3] Standard Oil Company of California Fellow, 1962–1963; U. S. Public Health Fellow, 1963–1964.

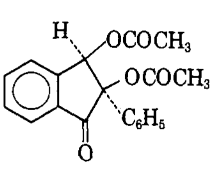
[4] D. Y. Curtin, J. A. Kampmeier, and B. R. O'Connor, *J. Am. Chem. Soc.*, **87**, 863 (1965).

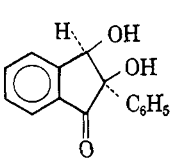
[5] R. L. Horton and K. C. Murdock, *J. Org. Chem.*, **25**, 938 (1960).

related compounds, gave the amine I in 97% yield. We were initially unaware of a reported[6a] synthesis of the imine III, tautomeric with I, in 85% yield by treatment of the diketone II with ammonium acetate in glacial acetic acid. The "imine III" was identical with our compound I and its structural assignment has recently been revised to I.[6b]

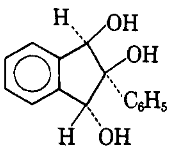
Reaction of amine I with sodium nitrite in glacial acetic acid at 17–18° gave two products identified as a monoacetate (IV) and the diacetate (V) of *cis*-2,3-dihydroxy-2-phenyl-1-indanone (VI) in yields of 55 and 28%, respectively, or a ratio of 2.0 for IV:V. Gas phase chromatography of the organic layer after extraction from water revealed no other major products and gave 2.1 for the ratio of IV:V. The use of isoamyl nitrite in acetic acid gave no significant change in the ratio of IV to V (2.2–2.3), but there was a somewhat cleaner reaction; gas phase chromatography indicated that IV and V accounted for up to 97% of the total organic phase remaining after extraction with water.

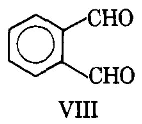

IV

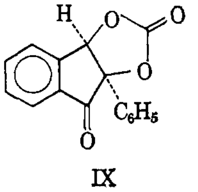

V

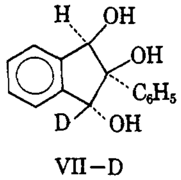

VI

The structure determination of IV and V warrants careful consideration. The fact that IV and V are a mono- and diacetyl derivative of a single dihydroxy compound was established by a series of acetylations and hydrolyses. Thus, the monoacetate IV could be acetylated in quantitative yield to diacetate V, and V hydrolyzed to IV with methanolic potassium hydroxide. Both IV and V were hydrolyzed with 20% sulfuric acid to the dihydroxy ketone VI which on reacetylation gave the diacetate V. Finally, both the mono- (IV) and diacetate (V) were converted by treatment with lithium aluminum hydride in methylene chloride–ether[7] (2:1) to the same triol VII whose stereochemical assignment will be discussed subsequently. The possibility that a rearrangement of the carbon skeleton had occurred in the deamination reaction of I (to IV and V) was excluded by the demonstration that the triol VII was oxidized with potassium periodate to phthalaldehyde, isolated as the dinitrophenylhydrazone, and benzoic acid. The *cis* stereochemistry of the dihydroxy ketone VI was shown by its reaction with phosgene in benzene containing pyridine to form the five-membered carbonate IX in 40% yield. That the reaction occurred without a change in configuration at the stereochemical centers was supported by the conversion with lithium aluminum hydride of the keto carbonate IX to the same triol VII which had been obtained by reduction of the esters IV and V. The n.m.r. spectrum of the triol VII provided evidence sufficient to deduce its stereochemistry. The spectrum showed two absorptions at τ 4.59 and 5.10 attributed to the protons attached to the carbon atoms of the secondary alcohol functions. The implied requirement that the two secondary alcohol functions must be nonequivalent leaves the stereochemistry shown for VII as the only possibility.[8] In order to complete the n.m.r. assignments the diacetate V was reduced with lithium aluminum deuteride to give the monodeuteriotriol VII-D which showed the absorption at τ 4.59 but not that at 5.10. It is concluded that the proton on the five-membered ring of triol VII and *cis* to the phenyl group on the adjacent carbon atom has its n.m.r. absorption at lower field than the corresponding proton *trans* to the phenyl group. This is contrary to the behavior of n.m.r. absorptions of protons in other simpler phenylcyclopentanes,[9] but the triols here are too complex to permit further analysis at this point.

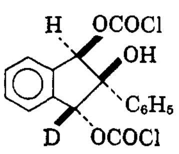

VII

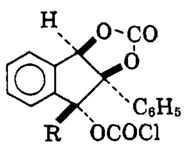

VIII

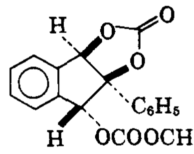

IX

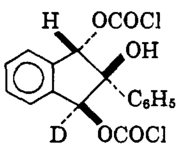

VII–D

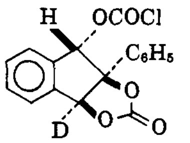
Since the stereochemical assignments of the esters IV and V just presented depend on the unproved assumption that the reaction of dihydroxy ketone VI with phosgene proceeds with retention of configuration at the two centers, it was deemed advisible to provide additional evidence.[10] A somewhat different approach makes use of the reaction of deuterated triol VII-D with excess phosgene. Bischloroformate X-D thus

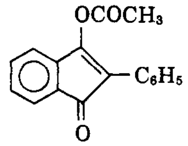

X-D


XI, R = H; τ 3.80, 3.50
XI-D, R = D; τ 3.80


XII, τ 3.79, 3.6


X-D′


XI-D′


XIII

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(6) (a) G. Ya. Vanag, Ya. F. Freimanis, and G. F. Zakis, *Zh. Obshch. Khim.*, **27**, 2509 (1957); (b) Ya. F. Freimanis and G. Ya. Vanag, *ibid.*, **34**, 445 (1964).

(7) The use of methylene chloride was dictated by the insolubility of the esters in ether and might be of value in other such cases.

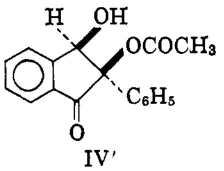
(8) It is understood, of course, that asymmetric molecules such as VII exist as pairs of mirror images. This work was carried out entirely with *dl* mixtures. The mirror images will not be shown, however.

(9) D. Y. Curtin, H. Gruen, and B. A. Shoulders, *Chem. Ind.* (London), 1205 (1958); D. Y. Curtin, Y. G. Hendrickson, and H. E. Knipmeyer, *J. Am. Chem. Soc.*, **83**, 4838 (1961).

(10) It may have been noted that the assignments of configuration to IV and V could be reversed to *trans* and be consistent with the data thus far presented if it is assumed that formation of the cyclic carbonate IX involves a change of configuration at the tertiary center *and* that the lithium aluminum hydride reduction of IX involves attack from the side of the molecule with respect to the adjacent phenyl group opposite to the side of attack in the reductions of esters IV and V.

formed would be expected to undergo ring closure preferentially between the two *cis*-hydroxyl groups. A deuterium label is necessary to distinguish between the hydroxylic center introduced during the diazotization reaction and that introduced by the reduction with lithium aluminum hydride. In order to use n.m.r. to interpret the results of the reaction, the undeuterated compound XI was prepared from the triol VII and phosgene. The two five-membered ring protons absorbed at τ 3.80 and 3.50. Chloroformate XI was converted to the methyl carbonate ester XII by treatment with methanol. The ester XII showed almost no shift of the absorption at τ 3.80 (to 3.79) but a shift of 0.13 p.p.m. to τ 3.63 of the absorption at 3.50 which is accordingly assigned to the proton adjacent to the carbonyl chloride function. Reaction of the deuterated triol VII-D with excess thionyl chloride and pyridine in chloroform, initially at $-70°$ and then warmed to room temperature, gave a reaction mixture showing absorption at τ 3.80 but not at 3.50. It follows that only XI-D was formed and no appreciable amount of XI-D′ from X-D′, the bischloroformate which would have been formed had the two hydroxyl groups in the keto diol VI and its esters been *trans*. The argument would, of course, be strengthened by a direct demonstration that the bischloroformate X-D had formed before ring closure to XI-D had taken place. Although no single line of reasoning is rigorous, the evidence taken as a whole appears to favor strongly assignment of the *cis* configuration to VI and all of its relatives considered here. A further conclusion arising incidently is that the lithium aluminum hydride (or deuteride) reductions of the keto acetates IV and V and the keto cyclic carbonate IX give very largely the isomer formed by attack of hydride ion from the side of the ring containing the two adjacent oxygen atoms.

As a final structural problem there remains the location of the acetyl group on one of the two oxygen atoms of the monoacetate IV. The n.m.r. spectra in deuteriochloroform and dimethyl sulfoxide show the hydroxyl proton as a sharp singlet which, assuming that there is slow proton exchange in these solvents, leads to the structure already assigned since the alternative structure IV′ in dimethyl sulfoxide should show its hydroxyl proton absorption as a doublet because of splitting by the proton on the adjacent (secondary) carbon atom.[11] Since 1,2-hydroxy esters with the correct geometry (which is present in IV) have been shown in other instances to undergo rapid migration of the acyl group from one oxygen atom to another,[12] the question of the location of the acyl group in IV may have little mechanistic significance.



IV′

Discussion of the Diazotization of Vinylamine I. The conversion of amine I to the *cis*-hydroxy ester IV and diester V with sodium nitrite or isoamyl nitrite in glacial acetic acid was further examined. It was found that the two products were stable in the reaction medium and were not readily interconverted. A suspected intermediate in their formation, the enol acetate XIII, was prepared by an independent synthesis and found to be stable under the reaction conditions; it is therefore not involved in the reaction.[13] Since the formation of hydroxy acetate IV requires that water be supplied either as a product of the diazotization or as an impurity in the acetic acid, the effect of added water on the ratio of hydroxy acetate IV to diacetate V was examined. The addition of 1.5 or 20% of water to the acetic acid solvent gave no significant change in the ratio of the two products. Addition of acetic anhydride as a scavenger of traces of water in the acetic acid also failed to change the relative amounts of the hydroxy acetate and diacetate. It is clear, then, that the hydroxyl group of the hydroxy acetate must be generated during reaction.[14] The addition of acetate ion or ethanol had no great effect on the product ratio.

In other nitrosations in acetic acid the active agent has been shown to be acetyl nitrite.[15] The equation for the reaction of a primary amine with acetyl nitrite disregarding timing of the individual steps is

$$RNH_2 + CH_3COONO = R\overset{+}{N}H_2NO + {}^{-}OCOCH_3 = RN_2^+ + {}^{-}OCOCH_3 + H_2O$$

An attractive postulate is that in the reaction of I in acetic acid, a solvent of intermediate ion-pair dissociating power,[16] the ion I-A remains complexed to the acetate ion and water; the complex must survive long enough to permit the addition of the nucleophile to the double bond to form the diazo compound I-B (where X = $OCOCH_3$ or OH_2^+). As a second limiting case there is, of course, the possibility that the diazonium ion is covalently bonded to acetate ion (or hydroxide ion) and that formation and breaking of bonds in going to I-B is concerted. There can also be an infinite sequence of intermediate mechanisms with varying amounts of covalent bonding to nitrogen and carbon in the transition state. Like other aliphatic diazo compounds, I-B in acid solution would be expected to be converted to the ester by protonation and replacement of the nitrogen by an acetoxyl group. If the carbonium ion I-D is an intermediate, the stereochemistry of the final product is explained by the preferential reaction of acetic acid at the side of the molecule opposite the phenyl ring. Alternatively, the stereochemistry of the products could be determined by the steric course of the protonation of I-B to I-C with a stereospecific replacement of nitrogen to give products IV and V. In any case the lack of sensitivity of the course of the reaction to the presence of water and

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(11) O. L. Chapman and R. W. King, *J. Am. Chem. Soc.*, **86**, 1256 (1964).

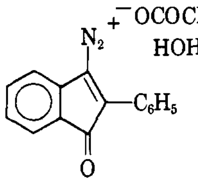
(12) See, for example, C. L. Stevens and S. J. Dykstra, *ibid.*, **75**, 5975 (1953); C. L. Stevens and B. T. Gillis, *ibid.*, **79**, 3448 (1957).

(13) As an aside it is of interest that the enol acetate XIII underwent decomposition on gas phase chromatography at 200° which led to an investigation of its behavior in decalin under reflux. After 8 hr. a small amount of the rearrangement product, 2-acetyl-2-phenyl-1,3-indandione, was formed. This is an example of a 1,3-acyl migration of which relatively few examples are known [see D. Y. Curtin and M. L. Poutsma, *J. Am. Chem. Soc.*, **84**, 4892 (1962)].

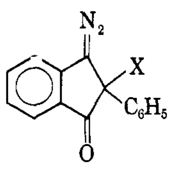
(14) S. Winstein and R. E. Buckles, *ibid.*, **64**, 2780, 2787 (1942).

(15) V. V. Kozlov and B. I. Belov, *Zh. Obshch. Khim.*, **33**, 1951 (1963).

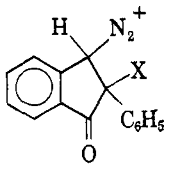
(16) P. Klinedinst, S. Smith, and L. Savedoff, unpublished work; see S. Winstein, P. E. Klinedinst, Jr., and G. C. Robinson, *J. Am. Chem. Soc.*, **83**, 885 (1961); S. Winstein, R. Baker, and S. Smith, *ibid.*, **86**, 2072 (1964).



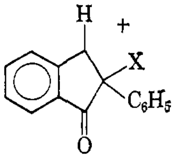
I–A



I–B



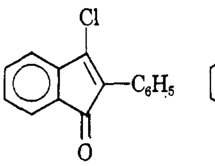
I–C



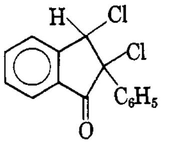
I–D

ethanol argues against the intervention of a bridged acetoxonium ion.[17] Attempts to intercept a diazonium intermediate with β-naphthol or N,N-dimethyl-β-naphthylamine have thus far been unsuccessful.

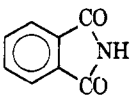
The reaction of the vinylamine I with nitrosyl chloride in methylene chloride[4] at 0° was hampered by the insolubility of I. The reaction mixture consisted of 3-chloro-2-phenylindenone (XIV) (27%), a dichloride (XV) (45%) analogous to the diacetate V, and phthalimide (XVI) (28%). Benzonitrile (XVII) was also isolated using gas phase chromatography. A test for nitric oxide which had been found[4] in reactions of other amines (A and B) with nitrosyl chloride was negative when I was treated with nitrosyl chloride in tetrahydrofuran (in which the amine was more soluble) at 0°. The reaction of I with nitrosyl chloride at −10° in dimethyl sulfoxide–tetrahydrofuran and other nonhydroxylic solvents showed the development of infrared absorption at 2090 cm.$^{-1}$ which then disappeared following a first-order rate law. Aromatic diazonium salts show infrared absorption at 2100–2350 cm.$^{-1}$, and aliphatic diazo compounds[18,19] have absorption at 2014–2173 cm.$^{-1}$. It has not been possible, thus far, to identify the species responsible for this absorption.[20] Attempts to intercept a diazonium ion by coupling with β-naphthol were unsuccessful. The formation of phthalimide XVI and nitrile XVII may well originate from initial attack of nitrosyl chloride at the doubly bound carbon atom to give E, whose conversion to XVI and XVII has several possible pathways.



XIV



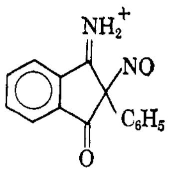
XV



XVI

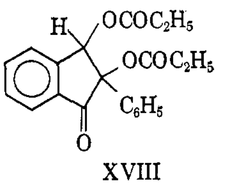
NCC_6H_5

XVII

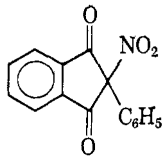


E

When the deamination of amine I was carried out with isoamyl nitrite in propionic acid at 0°, a dipropionate XVIII, analogous to diacetate V obtained in acetic acid, was isolated but, although there was infrared and n.m.r. spectral evidence that the hydroxy propionate analogous to IV was present, it could not be separated in pure form. An interesting by-product formed in about 10% yield was 2-nitro-2-phenyl-1,3-indandione (XIX), formed by attack of the nitrosating agent at a doubly bound carbon atom and subsequent oxidation of the nitroso group and hydrolysis of the imine group.



XVIII



XIX

Spectral Correlations. The infrared spectra in chloroform solution of the compounds discussed here have provided some worthwhile generalizations concerning the position of the carbonyl stretching absorption. 2-Phenylindanones with a hydrogen atom at the 2-position showed absorption at 1710–1715 cm.$^{-1}$, whereas those compounds with a chloro, nitro, hydroxy, acetoxy, propionoxy, or carbonate ester oxygen substituted at the 2-position had absorption in the region 1730–1740 cm.$^{-1}$. In a number of cases there was splitting of the carbonyl group suggestive of Fermi resonance of the carbonyl stretching vibration with an overtone of a low-lying vibration,[21] or in some cases an equilibrium between two species with different hydrogen bonding. Such complex carbonyl absorption has been observed in α- and β-indanones.[22] The 2-phenylindenones showed absorption in the region 1704–1711 cm.$^{-1}$ in agreement with previous compounds of this type.[23]

The n.m.r. spectra (in deuteriochloroform) of certain compounds prepared during the course of this work deserve comment. Although α-cyanobibenzyl (XX) showed as the aliphatic proton absorption, the first-order spectrum of a set of two equivalent protons and a single proton attached to adjacent carbon atoms of α-carboxybibenzyl (XXI) showed a complex multiplet which agreed with an ABC spectrum calculated[24a] using a coupling constant of 7.8 c.p.s. for J_{AB} and J_{AC} and

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(17) See C. B. Anderson, E. C. Friedrich, and S. Winstein, *Tetrahedron Letters*, 2037 (1963), and earlier references therein cited.

(18) K. B. Wetsel, G. F. Hawkins, and F. E. Johnson, *J. Am. Chem. Soc.*, **78**, 3360 (1956).

(19) L. J. Bellamy, "The Infra-Red Spectra of Organic Molecules," 2nd Ed., John Wiley and Sons, Inc., New York, N. Y., 1958, p. 273.

(20) E. Müller and H. Haiss [*Chem. Ber.*, **96**, 570 (1963)] have detected a species believed to be ArNH–NO in the reaction at −78° of *p*-chloroaniline and nitrosyl chloride, but consideration of the infrared absorption of known compounds with the functional group N—N=O (ref. 19, p. 306) makes it appear unlikely that such a functional group absorbs at a frequency as high as 2090 cm.$^{-1}$.

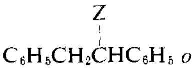
(21) See, for example, P. Yates and L. L. Williams, *J. Am. Chem. Soc.*, **80**, 5896 (1958).

(22) D. Biquard, *Bull. soc. chim. France*, **8**, 55 (1941).

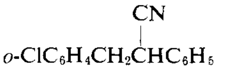
(23) E. D. Bergmann, A. Heller, and H. Weiler-Feilchenfeld, *ibid.*, 635 (1959).

(24) (a) K. B. Wiberg and B. J. Nist, "The Interpretation of NMR Spectra," W. A. Benjamin, Inc., New York, N. Y., 1962, p. 288; (b) P. M. Nair and J. D. Roberts, *J. Am. Chem. Soc.*, **79**, 319 (1957); J. S. Waugh and F. A. Cotton, *J. Phys. Chem.*, **65**, 562 (1961); H. S. Gutowsky, *J. Chem. Phys.*, **37**, 2196 (1962); G. M. Whitesides, F. Kaplan, K. Nagarajan, and J. D. Roberts, *Proc. Natl. Acad. Sci. U. S.* **47**, 49 (1961).

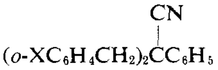
15.7 c.p.s. for J_{BC}. Such mutual coupling of geminal protons on a carbon atom attached to an asymmetric center has been frequently observed and its implications discussed.[24] In order to determine whether a change in temperature could alter the relative populations of the molecular conformations in such a way that a change in the magnetic nonequivalence of the methylene protons would produce a change in the n.m.r. spectrum, the spectrum of the nitrile XX was measured at temperatures down to −55° and the spectrum of the acid XXI up to 200°. In neither case was any significant change in the spectrum observed. One *o*-chlorine atom in the aromatic ring introduced sufficient nonequivalence of magnetic field of the *gem*-protons to make the methylene n.m.r. spectrum of XXII complex. Similarly, although α,α-dibenzylphenylacetonitrile (XXIII) showed a singlet *gem*-proton absorption (τ 6.72), the chlorine-substituted compound XXIV gave an AB quartet (doublets centered at τ 6.37 and 6.55, J = 14 c.p.s.).


$C_6H_5CH_2\overset{\overset{Z}{|}}{C}HC_6H_5$

XX, Z = CN
XXI, Z = COOH


$o\text{-}ClC_6H_4CH_2\overset{\overset{CN}{|}}{C}HC_6H_5$

XXII


$(o\text{-}XC_6H_4CH_2)_2\overset{\overset{CN}{|}}{C}C_6H_5$

XXIII, X = H
XXIV, X = Cl

Experimental[25]

2-Phenyl-1,3-indandione (*II*), prepared by the method of Nathanson,[26] had m.p. 149–150° and 150–152° (lit.[26] m.p. 145°) when recrystallized from ethanol. The infrared spectrum (10% chloroform) showed strong carbonyl absorption at 1715 cm.$^{-1}$ with a weaker sharp absorption at 1750 cm.$^{-1}$. The n.m.r. spectrum showed absorption at τ 5.75 (area 1.0), 2.75 (5.2), and 2.05 (4.0). Neither the infrared nor the n.m.r. spectra showed evidence of significant amounts of the enol form.

3-Amino-2-phenylindenone (*I*) was prepared by heating for 2.5 hr. at 120–240° a mixture of 35.5 g. (0.162 mole) of ketone II and 350.0 g. (9 moles) of ammonium acetate[6] in a nitrogen atmosphere. The dark red slurry was cooled to 80–90° and diluted with 600 ml. of water; the crystals so obtained were collected and washed with four 50-ml. portions of water to give 34.3 g. of crystalline I, m.p. 273–275° dec. (lit.[5] m.p. 272–274°). The amine I purified by crystallization from acetic acid (60 ml./g.) and sublimation had m.p. 274–275°. The infrared spectrum (*sym*-tetrachloroethane) showed absorption at 1705 (s) and at 3400, 3450, and 3650 cm.$^{-1}$ (m). The ultraviolet–visible spectrum (ethanol) showed λ_{max} 275 mμ (ε 36,800), 281 (sh), and 445 (1970). The n.m.r. spectrum in dimethyl sulfoxide-d_6 showed only aromatic proton absorption at τ 1.81 (area 2.0) and 2.1–2.7 (9.1). In dimethylformamide there was a somewhat broadened absorption at τ 6.33 attributable to the primary amine.

Anal. Calcd. for $C_{15}H_{11}NO$: C, 81.4; H, 5.0; N, 6.3. Found: C, 81.2; H, 5.1; N, 6.3.

The *N-acetyl derivative* of I (1.4 g., 0.0063 mole) was prepared by adding 20 ml. of acetyl chloride to 1.4 g. (0.0063 mole) of I in 100 ml. of boiling acetic acid and heating for 20 min., the time required for the dark red color of I to fade. More pyridine (5 ml.) and acetyl chloride (5 ml.) were added; boiling was continued for 5 min. after which the mixture was cooled and poured over ice and an orange product which precipitated was collected and washed with water to give 1.19 g. (0.0045 mole) of N-acetyl derivative, m.p. 237–238° dec. The infrared spectrum showed strong broad absorption at 1705 cm.$^{-1}$ and a singlet at 3400 cm.$^{-1}$. The n.m.r. spectrum (dimethyl sulfoxide-d_6) showed absorption at τ −0.54 (area 1), 2.50 (9), and 7.83 (3). The visible spectrum showed λ_{max} 430 mμ (ε 1900).

Anal. Calcd. for $C_{17}H_{13}NO_2$: C, 77.5; H, 5.0; N, 5.3. Found: C, 77.4; H, 4.9; N, 5.1.

Attempts to prepare the N-nitrosoacetamide of I by nitrosating the amide or its lithium salt failed.

The *N,N-diacetyl derivative* of I was prepared by adding 1.0 g. (0.0045 mole) of I to 150 ml. of acetic anhydride containing 5.0 ml. of pyridine. When no apparent reaction had occurred after 30 min. under reflux, 5.0 ml. of pyridine and then 10 ml. of acetyl chloride were added. After 15 min. under reflux, the mixture was poured over ice. Addition of water precipitated the yellow diacetyl derivative which when collected amounted to 0.78 g. (0.0025 mole) and melted at 162–163°. There was strong infrared absorption at 1715 cm.$^{-1}$ and a maximum in the visible at 415 mμ (ε 2450).

Anal. Calcd. for $C_{19}H_{15}NO_3$: C, 74.7; H, 5.0; N, 4.6. Found: C, 74.4; H, 5.1; N, 4.8.

3-(1′-Pyrrolidyl)-2-phenylindenone, prepared as a model compound from 2.0 g. (0.009 mole) of ketone II and 1.4 g. (0.02 mole) of pyrrolidine in 150 ml. of benzene heated under reflux for 45 hr. in a nitrogen atmosphere, was collected by distillation of the solvent and crystallization of the remaining oil by adding it to ethyl acetate. There was obtained 0.69 g. (28%) of product, m.p. 155–158°, which on recrystallization from ethyl acetate and sublimation had m.p. 157–158°. The ultraviolet spectrum showed λ_{max} 276 (ε 24,000).

Anal. Calcd. for $C_{19}H_{17}NO$: C, 82.9; H, 6.2; N, 5.1. Found: C, 83.3, 82.3; H, 6.4, 6.2; N, 5.3, 5.0.

Reaction of Amine I with Sodium Nitrite in Acetic Acid. (*a*) *Isolation of cis-3-Acetoxy-2-hydroxy-2-phenylindanone* (*IV*) *and cis-2,3-Diacetoxy-2-phenylindanone* (*V*). To 4.21 g. (0.019 mole) of amine I in 250 ml. of acetic acid at 16–18° was added 1.62 g. (0.024 mole) of sodium nitrite over a period of 1 hr. with rapid stirring. After 2 additional hr. of stirring, acetic acid was removed from the bright orange solution with a rotary evaporator at 25° and 5 mm. Addition of water, extraction with ether, washing of the ether layer with 5% sodium bicarbonate solution, drying over anhydrous sodium sulfate, and removal of the ether left a yellow oil which crystallized from methanol to give 1.72 g.

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(25) All melting points are corrected. Microanalyses were carried out by the microanalytical laboratory of the University of Illinois under the supervision of Mr. J. Nemeth, who also determined molecular weights with a Mechrolab vapor pressure osmometer Model 301A. Infrared spectra were obtained with a Perkin-Elmer Infracord Model 137 spectrometer, and by Mr. D. Johnson and his associates with Perkin-Elmer Models 21 and 521 spectrometers. Ultraviolet–visible spectra were obtained with a Bausch and Lomb Spectronic 505 spectrometer. N.m.r. spectra were determined by Mr. D. Johnson and his associates with a Varian Model A-60 spectrometer, and with a Model V-4300B spectrometer by Mr. B. Shoulders and Mr. O. Norton, and reported in p.p.m. from tetramethylsilane taken as 10 (τ-units). Spectra and other details are available in the Ph.D. theses of ref. 1.

(26) F. Nathanson, *Ber.*, **26**, 2576 (1893).

(0.0053 mole, 28%) of *diacetate V*, m.p. 171–173°, which when recrystallized from methanol amounted to 1.61 g. (0.0049 mole), m.p. 175–176°. The infrared spectrum (chloroform) showed strong absorption at 1740 and 1759 cm.$^{-1}$. The ultraviolet spectrum (ethanol) had λ_{max} 247 mμ (ϵ 13,200). The n.m.r. spectrum (deuteriochloroform) showed absorption at τ 7.89 (area 3.0), 7.77 (3.0), 3.20 (1.0), 2.60 (4.9), and 2.17 (4.5).

Anal. Calcd. for $C_{19}H_{16}O_5$: C, 70.4; H, 5.0. Found: C, 70.6; H, 5.3.

Removal of methanol from the filtrate left an oil which on addition of ether crystallized to yield 2.40 g. (0.0085 mole, 45%) of *hydroxyacetate-IV*, m.p. 105°. A sample recrystallized from methylene chloride–petroleum ether had m.p. 104–105°. The infrared spectrum (chloroform) had absorption at 1734 and 3650 cm.$^{-1}$. The n.m.r. (deuteriochloroform) had maxima at τ 2.28 (area 3.9), 2.73 (5.0), 3.60 (0.90), 6.36 (0.97), and 7.90 (3.0). *p*-Toluenesulfonic acid shifted the peak at τ 6.36. The n.m.r. spectrum in dimethyl sulfoxide had maxima at τ 2.20 (4.5), 2.72 (5.0), 3.37 (1.0) (singlet), and 3.67 (0.84) (singlet). The ultraviolet spectrum (ethanol) showed a maximum at 246 mμ (ϵ 17,200).

Anal. Calcd. for $C_{17}H_{14}O_4$: C, 72.3; H, 5.0. Found: C, 72.4; H, 5.1.

The products could be separated most conveniently by gas phase chromatography at 200° (injector 250°, detector 270°) through a 42-in. column packed with Dow Corning Silicone QF-1 and a helium flow rate of 75 ml./min. using a dual column programmed temperature Aerograph instrument, equipped with a Honeywell electronic integrator. When a sample of the product (10% in methanol) was injected, three peaks were recorded with the relative areas indicated: 2.28 (not identified), 13.38 (IV), and 7.40 (V). Identification was by comparison of retention times with those of authentic samples of IV and V. The mole ratio of IV:V was thus 2.1.

When 0.83 g. of IV in 80 ml. of acetic acid was stirred for 2.5 hr. with 0.8 g. of sodium nitrite, the product extracted and washed with sodium bicarbonate solution and water, and the solvent removed, there was obtained 0.61 g. of solid, m.p. 104–105°, whose infrared and n.m.r. spectra and gas phase chromatogram showed no evidence of contamination by V. Similarly V showed no evidence of contamination by IV when treated as above (56% recovery or extraction).

When solutions of amine I, sodium nitrite, and β-naphthol or N,N-dimethyl-β-naphthylamine in glacial acetic acid were mixed so as to give equimolar final concentrations (0.0000375 *M*) and the solutions were examined in the visible region (400–550 mμ) at various times after mixing, the amine I was seen to disappear rapidly (less than 20% remained after 9 min.), but there was no evidence of the formation of an azo compound absorbing strongly in the spectral region examined.

Reaction of Amine I with Isoamyl Nitrite. Isoamyl nitrite[27] was added to a solution of the amine I and the mixture stirred for the time indicated. The mixture was extracted between ether–methylene chloride and water. After the organic layer was washed with water and aqueous sodium bicarbonate, it was dried over sodium sulfate and the solvent removed on a rotary evaporator to leave an oil which was submitted to analysis by gas chromatography on a 2-ft. S.E.-30 silicon rubber column at 210°. In one experiment the oil was added to methanol and the products were crystallized to give 19% of diacetate V, m.p. 172–173°, and 42% of IV, m.p. 103–104°. The results are summarized in Table I.

Table I

Starting materials		Conditions		Products			
Amine I, g.	Acetic acid, ml.	Time, hr.	Temp., °C.	Yield, IV	% V	Oil IV and V, %	Molar ratio IV:V
2.5[a]	200	4	17	52	23	97	2.3
2.0[b]	200	4	17	42[c]	19[c]	. .	2.2
2.0[b]	200[d]	4	17	47	21	96	2.2
1.0[b]	50[e]	0.5	35	39	16	95	2.4
1.0[b]	50[f]	4	17	71	23	94	3.0
2.0[b]	150[g]	4.5	18	52	22	97	2.4
1.0[b]	60[h]	4.5	17	38	17	79	2.2
1.0[b]	50[i]	0.5	25	39	16	95	2.5
1.0[j]	75[k]	19	17	45	16	81	2.8

[a] The ratio of isoamyl nitrite to amine I was 1.0. [b] Ratio of isoamyl nitrite to amine I was 1.4. [c] Isolated as described in the text. [d] Freshly distilled. [e] Acetic anhydride (10 ml.) added to the acetic acid. [f] Acetic anhydride (50 ml.) added to the acetic acid. [g] Water (2 ml.) added to the acetic acid. [h] Aqueous acetic acid (80%). [i] Acetic anhydride (10 ml.) and sodium acetate (4.0 g.) added to the acetic acid. [j] The ratio of isoamyl nitrite to amine I was 1.9. [k] Ethanol (50 ml.) was added to the acetic acid.

When an equimolar amount of β-naphthol was added to an acetic acid solution of the amine I 60 sec. after addition of isoamyl nitrite, the solution allowed to stand for 1 hr., and the acetic acid removed at 80°, the addition of ether precipitated 20% of the amine I. The only colored fraction (separated by chromatography) had very weak absorption at 1725 cm.$^{-1}$ and cannot have been a coupling product.

Acetylation of cis-3-Acetoxy-2-hydroxy-2-phenyl-1-indanone (IV). The hydroxy ester IV (1 g., 0.0035 mole) was treated with 10 ml. of acetic anhydride and 3 ml. of dry pyridine for 2 hr. on a steam bath and the solvent removed with a rotary evaporator to leave the diacetate V (1.13 g., 0.0035 mole), m.p. 175°. Identity with V obtained above was confirmed by infrared and n.m.r. spectra.

Hydrolysis of the Diacetate V to Hydroxyacetate IV. Treatment of 1.5 g. of V with 10% potassium hydroxide in methanol for 10 min. gave, on partitioning the mixture between methylene chloride and water, drying, and removal of the solvent, a residue which crystallized from hot methanol to yield 1.2 g. of hydroxyacetate IV, m.p. 104–105°, whose identity was confirmed by comparison of the infrared, ultraviolet, and n.m.r. spectra with a sample prepared above.

Reduction of Hydroxyacetate IV and Diacetate V. 2-Phenyl-1,2,3-indantriol (VII) and 2-Phenyl-1,2,3-indantriol-1-d (VII-D). To a solution of 3.2 g. (0.0099 mole) of diacetate V in 100 ml. of methylene chloride was added 50 ml. of ether and, at 5°, 3.0 g. (0.079 mole) of lithium aluminum hydride. After 2

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[27] W. A. Noyes, "Organic Syntheses," Coll. Vol. II, John Wiley and Sons, Inc., New York, N. Y., 1943, p. 108.

hr. of stirring, ice was added and then 10% sulfuric acid. Extraction with 5% sodium bicarbonate and water followed by drying over anhydrous sodium sulfate and removal of the solvent by a rotary evaporator left 2.19 g. (0.0099 mole) of light gray triol VII. The infrared spectrum in chloroform showed strong absorption at 3400 and 3540 cm.$^{-1}$ with no absorption maxima from 1600 to 1800 cm.$^{-1}$. The n.m.r. spectrum in deuteriochloroform showed singlets at τ 2.62 (area 9.2), 4.59 (1.0), 5.10 (1.0), and 7.35 (2.8). *p*-Toluenesulfonic acid shifted the peak at τ 7.35. Reduction of 2.1 g. of the hydroxyacetate IV in 50 ml. of methylene chloride and 50 ml. of ether by the same procedure gave 1.67 g. of triol VII with the same infrared and n.m.r. spectra.

Anal. Calcd. for $C_{15}H_{14}O_3$: C, 74.4; H, 5.8. Found: C, 74.1; H, 6.0.

Reduction of 0.5414 g. (0.0016 mole) of diacetate V with lithium aluminum deuteride (0.35 g., 0.00167 mole, 97%) gave 0.3309 g. (0.0014 mole) of triol VII-D. The n.m.r. spectrum showed absorption at τ 2.66, (area 9.8), 4.66 (1.0), and 7.17 (3.1).

Anal. Calcd. for $C_{15}H_{13}DO_3$: C, 74.1; H, 5.8; D, 7.1 atom %. Found: C, 73.8; H, 6.0; D, 6.6 atom %.

Acid Hydrolysis of the Hydroxyacetate IV and Diacetate V. cis-2,3-Dihydroxy-2-phenylindanone (VI). To 1 g. (0.0035 mole) of hydroxyacetate IV in 20 ml. of absolute ethanol was added 5 ml. of 20% sulfuric acid solution, and the mixture was heated on a steam bath for 1.5 hr. Extraction with ether and washing of the ether extract with sodium bicarbonate and water gave, after drying over anhydrous sodium sulfate and removal of the solvent at room temperature, 0.564 g. (0.0023 mole) of diol VI, m.p. 122–123°. The infrared spectrum showed strong carbonyl absorption at 1740 cm.$^{-1}$ and broad absorption from 3200 to 3550 cm.$^{-1}$ (max.). The n.m.r. in deuteriochloroform showed absorption at τ 2.29 (area 3.8), 2.74 (5.1), 4.85 (1.0), and 5.97 (1.8). Recrystallization from methylene chloride gave m.p. 122–123°.

Anal. Calcd. for $C_{15}H_{12}O_3$: C, 75.0; H, 5.0. Found: C, 74.7; H, 5.0.

Similar treatment of 500 mg. of diacetate V gave 0.324 g. of diol VI, m.p. 122–123°, identified by its n.m.r. and infrared spectra.

Acetylation of the Dihydroxyketone VI. When 300 mg. of VI in 10 ml. of acetic anhydride and 3 ml. of pyridine was heated on a steam bath for 12 hr. and the solvent removed with a rotary evaporator at 80°, there crystallized from ether 0.214 g. of diacetate V, m.p. 175.5°, identified by the infrared, ultraviolet, and n.m.r. spectra.

Oxidation with Potassium Periodate of 2-Phenyl-1,2,3-indantriol. When 2.10 g. (0.0087 mole) of triol VII in 75 ml. of absolute ethanol was warmed at 75° for 3 hr. with 3.95 g. (0.172 mole) of potassium metaperiodate in 75 ml. of 5% sulfuric acid, the bright orange solution formed was washed with water and 10% sodium bicarbonate, and after drying over sodium sulfate and removal of the solvent there was obtained 1.12 g. of brown-orange oil with strong infrared absorption at 1695 cm.$^{-1}$ and n.m.r. absorption at τ 0.22. Addition of 4.0 g. (0.20 mole) of 2,4-dinitrophenylhydrazine to 1.0 g. of the oil in 50 ml. of carbon tetrachloride gave brown-orange crystals which after 1 hr. were filtered and washed with pyridine to give 1.15 g. (0.0023 mole) of orange phthalaldehyde bis-2,4-dinitrophenylhydrazone, m.p. 265° dec. Recrystallization from hot pyridine gave 0.5 g. of product, m.p. 270° dec. (lit.[28] m.p. 275°) (sample placed in the oil bath at 255° and heated at 2°/min.). The ultraviolet spectrum in chloroform had λ_{max} 370 mμ (ϵ 30,500).

Anal. Calcd. for $C_{20}H_{14}N_8O_8$: C, 48.6; H, 2.9; N, 22.7. Found: C, 48.2; H, 2.7; N, 22.7.

Acidification of the alkaline extracts remaining after isolation of the phthalaldehyde and extraction with ether gave 0.725 g. (0.0059 mole) of benzoic acid, m.p. 115–116°, which on recrystallization from water gave 0.615 g., m.p. 120.5–121.5°, and which mixed with an authentic sample showed no depression.

Reaction of Triols VII and VII-D with Phosgene. Chloroformates XI and XI-D. To a solution of 1.0 g. (0.0042 mole) of VII in 35 ml. of chloroform was added 10 ml. of pyridine and, at −70°, 50 ml. of a 12% solution of phosgene in toluene (sealed tube). After 18 hr., addition of water and extraction with ether gave a solution which was washed with 5% hydrochloric acid and water and dried over sodium sulfate; the solvent was evaporated at room temperature. The chloroformate XI (0.558 g., 0.0017 mole, m.p. 152–152.5° with gas evolution) so obtained showed strong carbonyl absorption in the infrared (chloroform) at 1775 and 1805 cm.$^{-1}$ and n.m.r. absorption (deuteriochloroform) at τ 2.35 (area 4.1), 2.50 (5.0), 3.50 (0.95), and 3.78 (1.0).

Anal. Calcd. for $C_{17}H_{11}O_5Cl$: C, 61.7; H, 3.3; Cl, 10.7. Found: C, 59.9; H, 3.3; Cl, 12.7.

The same procedure was applied to 1.0 g. of XI-D to give 0.56 g. of oil which showed strong carbonyl absorption at 1800 cm.$^{-1}$ and crystallized when added to 5.0 ml. of ether to give gray crystals, m.p. 148–156°, which showed n.m.r. peaks of equal height at τ 3.80 and 3.88 as well as complex absorption at τ 2.3–2.8. The chloroformate XI-D could not be isolated in pure form, however.

Reaction of the Chloroformate XI with Methanol. Dicarbonate XII. When the chloroformate XI above was heated in methanol, there was formed 0.412 g. (0.00127 mole) of dicarbonate XII, m.p. 75–77°. The infrared (chloroform) showed strong absorption at 1807 and 1757 cm.$^{-1}$. Proton resonance absorption occurred in deuteriochloroform at τ 2.40 (area 3.9), 2.54 (5.2), 3.63 (1.0), 3.79 (1.0), and 6.50 (3.2).

Anal. Calcd. for $C_{18}H_{14}O_6$: C, 66.2; H, 4.3. Found: C, 66.0; H, 4.3.

Reaction of Dihydroxy Ketone VI with Phosgene. Keto Carbonate IX. When phosgene gas was bubbled over a period of 5 min. through a hot solution of 200 mg. (0.00083 mole) of diol VI in 30 ml. of benzene containing 3 ml. of pyridine, a precipitate formed. After 5 min. longer, 100 ml. of water was added (precipitate dissolved), the solution extracted with ether, the ether solution dried over sodium sulfate, and the ether removed with a rotary evaporator at room temperature. The yellow residue was added to 10 ml. of ethyl ether to give a precipitate of 185 mg. (0.00069 mole) of carbonate IX, m.p. 115–116°. The

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(28) M. R. Powell and D. R. Rexford, *J. Org. Chem.*, **18**, 810 (1953).

infrared spectrum (chloroform) showed strong absorption at 1810 and 1735 cm.$^{-1}$. The n.m.r. spectrum (deuteriochloroform) showed a sharp peak at τ 3.98 (area 1.0) and at τ 2.59 (4.0) and 2.12 (5.5).

Anal. Calcd. for $C_{16}H_{19}O_4$: C, 72.2; H, 3.8. Found: C, 72.1; H, 3.9.

Reduction of Keto Carbonate IX with Lithium Aluminum Hydride. Reduction of 48 mg. (0.0018 mole) of carbonate IX in 5 ml. of methylene chloride and 10 ml. of ether with 50 mg. of lithium aluminum hydride at 25° for 1 hr. gave after the addition of ice, acidification with dilute sulfuric acid, extraction with ether, extraction of the ether layer with dilute sodium carbonate, drying, and removal of the ether with a rotary evaporator, 22 mg. of triol VII with n.m.r. absorption at τ 7.05 (area 3.2), 5.17 (1.1), 4.69 (0.95), and 2.64 (10.5).

3-Acetoxy-2-phenylindenone (XIII). 2-Phenyl-1,3-indandione (1.0 g., 0.0038 mole) was stirred for 3 hr. with 50 ml. of acetic anhydride containing 1 drop of pyridine. Removal of the acetic anhydride at 80° (0.5 mm.) gave a residue which, purified by crystallization from carbon tetrachloride at 5°, gave 1.17 g. (98%) of XIII, m.p. 114.5–115°. The infrared spectrum in chloroform showed strong absorption at 1785 and 1717 cm.$^{-1}$. The n.m.r. in carbon tetrachloride showed peaks at τ 7.66 (area 3.0) and 2.73 (9.3). When 0.755 g. of XIII was subjected to treatment with 0.3 g. of sodium nitrite in 50 ml. of acetic acid at 16–18° for 3.5 hr. and the solvent removed, the recovered enol acetate, recrystallized from carbon tetrachloride, had m.p. 114–115°. Its identity was confirmed by its infrared, ultraviolet, and n.m.r. spectra.

Anal. Calcd. for $C_{17}H_{12}O_3$: C, 77.3; H, 4.58. Found: C, 77.3; H, 4.6.

Thermal Decomposition of the Enol Acetate XIII. 2-Acetyl-2-phenyl-1,3-indandione. The enol acetate (0.7383 g., 0.0028 mole) was heated in 60 ml. of decalin for 12 hr. under reflux. Extraction with methanol and concentration of the solution gave 26 mg. of 2-acetyl-2-phenyl-1,3-indandione, m.p. 244–248°. The infrared spectrum (chloroform) showed strong absorption at 1700 cm.$^{-1}$. The ultraviolet spectrum (ethanol) had $\lambda_{\max}$ 227 mμ (ϵ 34,700).

Anal. Calcd. for $C_{17}H_{12}O_3$: C, 77.3; H, 4.6. Found: C, 77.5; H, 4.3.

Deamination of Amine I with Isoamyl Nitrite in Propionic Acid. Amine I (1.0 g., 0.0045 mole) in 75 ml. of propionic acid at 0° was treated with 0.8 ml. (0.006 mole) of isoamyl nitrite for 16 hr. Partition between ether and water followed by washing of the ether layer with aqueous sodium carbonate and water and drying gave after removal of the ether 1.1 g. of orange oil which crystallized when added to methanol to give 100 mg. of XIX, m.p. 115–117° (lit.[29] m.p. 118–120°). The infrared spectrum in chloroform showed absorption at 1360 and 1560 cm.$^{-1}$ and at 1760 and 1730 cm.$^{-1}$.

On standing at 5° the mother liquors above deposited 66 mg. of crystals not fully characterized. Addition of 5 ml. of methanol to the filtrate and standing at 5° gave 0.13 g. of dipropionate XVIII, m.p. 155–156°. The infrared spectrum in chloroform showed strong absorption at 1760 cm.$^{-1}$, and the n.m.r. (deuteriochloroform) spectrum showed a singlet at τ 3.28 (area 0.9) with multiplets at 2.1–2.4 (3.9) and 2.69–2.72 (5.0) and with the propionyl group protons as slightly off-set quartets at τ 7.51 (4.2) and slightly off-set triplets at τ 7.83 (6.0).

Anal. Calcd. for $C_{21}H_{20}O_5$: C, 71.6; H, 5.7. Found: C, 71.4; H, 5.7.

Deamination of Amine I with Nitrosyl Chloride. Nitrosyl chloride (20.0 ml. of 0.5 *M* solution) was added to 2.0 g. (0.0090 mole) of amine I in 100 ml. of methylene chloride at 0° and the mixture stirred for 3 hr. Removal of the methylene chloride and addition of 100 ml. of ether precipitated 36 mg. of ammonium chloride which was filtered. Removal of the ether gave 1.6 g. of orange oil which was dissolved in methylene chloride and subjected to thin layer chromatography on silica gel G (carbon tetrachloride eluent). Four colored fractions were collected. The dichloride XV (0.16 g.), m.p. 120–122°, had in addition to the complex aromatic spectrum a signal at τ 4.13 (area 1).

Anal. Calcd. for $C_{15}H_{10}Cl_2O$: C, 65.0; H, 3.7; Cl, 25.6. Found: C, 64.9; H, 3.6; Cl, 25.4.

Removal of the methanol from the filtrate above and addition of cyclohexane gave 22 mg. of dichloride XV which was filtered. Evaporation of the cyclohexane and recrystallization of the resulting oil from methanol gave 34 mg. of 3-chloro-2-phenylindenone, m.p. 91–93° (lit.[30] 93–94°). No product was isolated from the second and third fractions, but the last when recrystallized from methanol yielded 147 mg. of phthalimide identified by its retention time on gas phase chromatography. Another similar reaction gave an organic layer (1.14 g. from 1.0 g. of amine I) which, submitted to gas phase chromatography on a 2-ft. S.E.-30 silicon rubber column at 207°, gave three major peaks with retention times and areas corresponding to phthalimide (48% yield), dichloride XV (41% yield), and chloride XIV (28% yield). Crystallization of the oil from methanol gave 0.10 g. (15% yield) of phthalimide, m.p. 230–233°. In another similar run, gas phase chromatography on an 8-ft. Carbowax 20M column at 200° showed a peak corresponding in retention time to benzonitrile. Collection of this fraction from several injections gave benzonitrile as shown by comparison of its infrared spectrum (carbon tetrachloride) with an authentic sample (maximum at 2240 cm.$^{-1}$).

An attempt to intercept a diazonium ion with β-naphthol was carried out by adding 3.8 ml. of 1.2 *M* nitrosyl chloride to 1 g. of amine I in 250 ml. of tetrahydrofuran at −68°, and after 5 min. 0.654 g. of β-naphthol in tetrahydrofuran at −68° was added. After 2 hr. the solution was allowed to warm to room temperature. At about 0° there was rapid gas evolution and 0.659 g. of amine I was recovered by removal of the solvent and crystallization from ether. No colored products showing carbonyl absorption in the infrared were obtained. Similar results were obtained with nitrosyl chloride and β-naphthol in dimethylformamide at −46°. A test for nitric oxide[4] in a reaction of amine I (1 g.) with nitrosyl chloride in tetrahydrofuran at −68° and allowed to warm to room temperature was negative.

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When the reaction of an equivalent amount of nitrosyl chloride with a 5% solution of amine I in dimethylformamide was carried out in a 0.1-mm. sodium chloride cell of a Perkin-Elmer Model 21 spectrophotometer at −46°, a new absorption at 2090 cm.$^{-1}$ developed quickly and its decay at −10 ± 1° was followed over a period of 2–6 hr. A plot of log A_0/A *vs.* time gave a reasonably straight line with k_1 (average of 7 points) = 6.25 × 10^{-4} sec.$^{-1}$ and in another reaction 5.35 × 10^{-4} (average of 5 points). In dimethyl sulfoxide at −11 ± 1°, k_1 (average of 8 points) was 5.00 × 10^{-4}. Details of the calculations are presented in the thesis of M. L. F.[1]

Dehydrohalogenation of the Dichloride XV. Reaction of 20 mg. of dichloride XV with 5 ml. of alcoholic potassium hydroxide on a steam bath gave an immediate orange color and after 10 min. the solution was neutralized and the products were partitioned between ether and water. Chromatography of the ether layer on neutralized alumina (elution with cyclohexane) gave 6 mg. of chlorindenone XIV, m.p. 93–94° (lit.[30] m.p. 93–94°). An authentic sample, m.p. 92–93°, was prepared from 2-phenyl-1,3-indandione and phosphorus pentachloride in carbon tetrachloride.[30]

α-Cyanobibenzyl (*XX*), b.p. 138–145° at 0.4–0.5 mm., m.p. 50–51° (lit.[31] m.p. 57–58°), had absorption at 2250 cm.$^{-1}$ in the infrared (chloroform) and a triplet centered at τ 6.02 (J = 14.5 c.p.s.) and a doublet centered at τ 6.87 (relative areas 1.0 and 2.1) in the n.m.r. in deuteriochloroform.

α,α-Dibenzylphenylacetonitrile (*XXIII*), m.p. 83–84° (lit.[31] 92–92.5°), showed weak absorption at 2250 cm.$^{-1}$ in the infrared (chloroform) and a singlet at τ 6.72 in the n.m.r. (deuteriochloroform).

α-Carboxybibenzyl (*XXI*), m.p. 94–94.5° (lit.[31] m.p. 88–89°), prepared from the nitrile XX by hydrolysis with sodium hydroxide in aqueous trimethylene glycol, showed in the n.m.r. in deuteriochloroform an ABC pattern[24a] with chemical shifts of H_A, H_B, and H_C at τ 6.00, 6.57, and 6.97; $J_{AB} = J_{AC} = 7.8$, $J_{BC} = 15.7$ c.p.s.

α-Cyano-o-chlorobibenzyl (*XXII*) was prepared from *o*-chlorobenzyl chloride by the same procedure employed with the parent nitrile XX. After distillation and crystallization there was obtained in 68% yield the chloronitrile XXII, m.p. 62–63°. The infrared absorption in chloroform showed absorption typical of the nitrile group at 2240 cm.$^{-1}$. The n.m.r. in deuteriochloroform showed a quartet centered at about τ 5.9 and another absorption at τ 7.8. Each of these showed evidence of further coupling between H_A and the *gem*-protons H_B and H_C.

Anal. Calcd. for $C_{15}H_{12}NCl$: C, 74.5; H, 5.8; N, 5.8; Cl, 14.7. Found: C, 74.8; H, 5.2; N, 5.7; Cl, 14.7.

α,α-Di(o-chlorobenzyl)phenylacetonitrile (*XXIV*) was obtained from the distillation residue in the preparation of XXII and recrystallized from ethanol, m.p. 92–93°. The infrared spectrum in chloroform showed absorption at 2240 cm.$^{-1}$. The n.m.r. in deuteriochloroform showed an AB quartet with centers of the two pairs of peaks at τ 6.37 and 6.55 (J = 14 c.p.s.).

Anal. Calcd. for $C_{22}H_{17}NCl_2$: C, 72.1; H, 4.7; N, 3.8. Found: C, 71.8; H, 4.6; N, 3.5.

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The Structures of Aflatoxins B and G_1

**Toyonobu Asao, G. Büchi, M. M. Abdel-Kader, S. B. Chang,
Emily L. Wick, and G. N. Wogan**

*Contribution from the Department of Chemistry and the Department of
Nutrition and Food Science, Massachusetts Institute of Technology,
Cambridge, Massachusetts. Received November 16, 1964*

The structures of the two mold metabolites aflatoxin B_1 and aflatoxin G_1 were elucidated. Acute toxicities in White Pekin ducklings are presented.

Aflatoxins are metabolites of *Aspergillus flavus* Link *ex* Fries, a fungus which under certain conditions grows prolifically on peanuts and on cereals.[1,2] The two compounds are of considerable interest because of their toxicity and carcinogenic potency in many animal species. Preliminary reports from other laboratories dealt with the isolation and characterization of two toxins,[3-5] and the present paper is concerned with the chemical structures of the two major metabolites.

Early attempts to produce the toxins in these laboratories led to concentrates with low activities, and isolation of the toxins became possible only when we received 200 mg. of a crude extract prepared by investigators of the U. S. Food and Drug Administration utilizing a different mold variant.[6] Cultures of *Aspergillus flavus* Link *ex* Fries were grown on sterilized crushed wheat and extracted with chloroform and the toxins precipitated by adding petroleum ether. Individual components were isolated from this concentrate by preparative thin layer chromatography, and the two

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(6) We are much indebted to Drs. H. R. Smith, F. A. Hodges, B. H. Armbrecht, and W. Horwitz for their contribution.