[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY OF THE STATE UNIVERSITY OF IOWA]

Nitroolefins. I. 2-Nitro-3-hydroxyindene[1]

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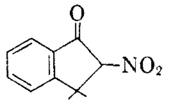
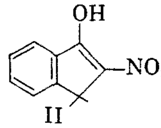
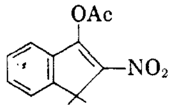
The condensation of nitromethane with *o*-phthalaldehyde has been studied. The product is shown to be a mixture of tautomers of 2-nitro-1-indanone. The tautomeric shift is not rapid. The enol form has been isolated in essentially pure form. The infrared and ultraviolet absorption spectra of this compound, its derivatives, and related compounds are reported and discussed.

In a study of condensation reactions of *o*-phthalaldehyde, Thiele and Weitz[2] reported that the condensation product with nitromethane was 2-nitro-1-indanone (I).

Derivatives of the enol form II were prepared, *viz.:* the acetyl derivatives III, its dibromide IV, and a methoxy compound V.


I


II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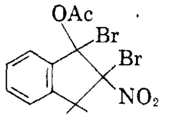
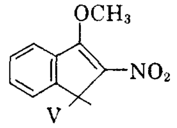
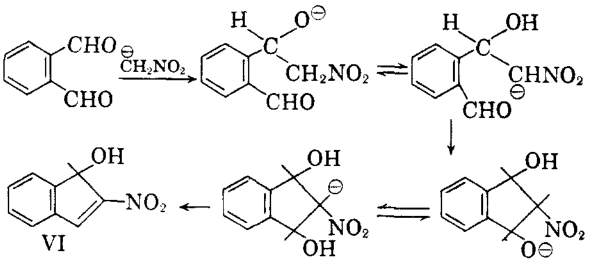
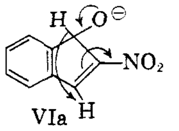

IV


V

That I is actually an anomalous product was not discussed or explained. One might expect rather that 1-hydroxy-2-nitroindene (VI) would be formed, as shown.



The formation of II (or I) involves a hydranion migration in structure VI A with an accompanying electron pair shift. Hydranion migration giving rise to a double bond shift in basic conditions is not unusual.[3]


VIa

Derivatives that Thiele prepared[2] could as well have been formed from compound VI. Theile reported that the condensation product had a m.p. 117°d. Subsequently the condensation was reported[4] to give a product with m.p. 148° and the correct percentage composition. No comment was made on the structure or the melting point discrepancy.

The possible tautomerism, spectral properties, and chemistry of 2-nitro-1-indanone (I) were of primary interest in this study. Essential to the study was either the establishment of the structures of the two condensation products and their derivatives or the development of an alternative synthesis of I.

Two alternate syntheses of I were attempted without success. The action of alkyl nitrates on indanone was studied, using acidic and basic conditions. Ethyl nitrate with sodium ethoxide in ethanol and with potassium *t*-butoxide in ether, and *iso*-amyl nitrate with potassium *t*-butoxide in ether, and *iso*-amyl nitrate or methyl nitrate in anhydrous ether with dry hydrogen chloride all failed to give the expected product, giving instead intractable tars or recovery of 40–85% of the indanone.

In the second method tried 2-isonitroso-1-indanone was treated with peroxytrifluoroacetic acid by the method of Emmons and Pagano,[5] with the recovery of 60% of the starting material.

The condensation of *o*-phthalaldehyde with nitromethane by the method of Thiele and Weitz was repeated. The product, melting from 117°, actually gave a melting range of 10–20°. Several recrystallizations from various solvents either did not change the melting behavior or raised the melting range without substantially narrowing it (e.g., m.p. 120–135°). Sublimation gave a product with a higher and sharper melting point reported by Schales and Graefe,[4] *viz.* 148°. Thus the former substance must be regarded as a mixture, and the latter, pure.

Derivatives corresponding to those reported by Thiele and Weitz were prepared from the 148°

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[1] Taken in part from the M.Sc. Thesis of C. L. Pitzer (1958). Presented before the Division of Organic Chemistry, A. C. S., 135th National Meeting, Boston, April, 1959.

[2] J. Thiele and E. Weitz, *Ann.*, **377**, 1 (1910).

[3] R. C. Fuson, *Advanced Organic Reactions*, John Wiley and Sons, New York, N. Y., 1950, pp. 231-232.

[4] O. Schales and H. A. Graefe, *J. Am. Chem. Soc.*, **74**, 4486 (1952).

[5] W. D. Emmons and A. S. Pagano, *J. Am. Chem. Soc.*, **77**, 4557 (1955).

TABLE I

INFRARED ABSORPTION BANDS[a]

Substance	OH	C=O	C=C	NO_2[c]	NO_2[d]
II (m. 148°)	3584	—	1611	1577	1357, 1326
I + II (m. 120–134°)	3584	1712	1612	1577	1359, 1326
III	—	1742	1613	1582	1364, 1342, 1321
III[b]	—	1754	1618	1582	1372, 1348, 1323
IV[b]	—	1773	—	1575	1372
α-Nitroacetophenone	—[f]	1709	1605[g]	1565	1379, 1328
1-Indanone[h]	—	1705	1618[g]	—	—
β-Nitrostyrene[b]	—	—	1642	1530	1345
o-Nitrophenol[e]	3270	—	—	1540	1360
2-Nitroindene (VII)	—	—	1600	1570	1379, (1370), 1338

[a] Solvent was chloroform unless specified. Data in cm.$^{-1}$ [b] Solvent was carbon tetrachloride. [c] A symmetrical stretching mode. [d] Symmetrical stretching mode. [e] From R. J. Francel, *J. Am. Chem. Soc.*, **74**, 1265 (1952). [f] A band at 2940 cm.$^{-1}$ was observed using pure crystals. [g] Aromatic ring. [h] Band at 1466 (C—H), weak band at 1325.

melting substance. The acetyl derivative III gave m.p. 130–131°; its dibromide IV gave m.p. 93–94°. The derivatives prepared from the 117° melting substance gave melting points of 120 and 136° respectively.[1] It was supposed at first that the isomerism involved structures I and VI, but further examination, with spectral evidence discussed below, indicated that the isomerism involved structures I and II and that the acetyl derivatives were identical. On subsequent purification dibromide IV gave m.p. 136°, which agrees with Thiele.[1] His sample of the acetyl derivative III was apparently impure.

The substance, m.p. 148°, was found to be soluble in alkali, with decomposition. It gave no reaction with ferric chloride. The compound gave a correct value for percent nitro group. The 2,4-dinitrophenylhydrazine VII formed readily. The compound did not form a quinoxaline derivative with o-phenylene diamine.[6] Neither substance (m.p. 117°, 148°) decolorized bromine in chloroform or acetic acid except on long standing. Both decolorized potassium permanganate in acetone; the higher melting tautomer appeared to react more rapidly. No quantitative determination could be made and no oxidation products were isolated.

On standing for several weeks the pure enol, m.p. 148°, slowly reverted to a mixture of I and II, suggesting that the enol is somewhat less stable.

The infrared and ultraviolet spectra of the compounds studied are listed in Tables I and II respectively. The intense ultraviolet absorption at 3430 Å is expected for the enolic structure of II. The acetyl derivative III (3400 Å) and the unsubstituted nitroindene VIII (3370 Å) exhibit the typical β-nitrostyrene chromophore. The small shifts caused by substituents are in the expected order, if they are explained on the basis of resonance stabilization of the excited state. Such shifts have been[7] smaller in some cyclic systems than in the open chain analogs.

TABLE II

ULTRAVIOLET ABSORPTION SPECTRA

Compound	Absorption maxima[a]
3-Hydroxy-2-nitroindene (II)	2430 (7.1), 3430 (9.75)
3-Acetoxy-2-nitroindene (III)	2430 (7.1), 3400 (9.21)
2-Nitroindene (VIII)	2330, 2390 (6.3, 6.2), 3370 (11.0)
α-Nitroacetophenone	2460 (11.4), 3510 (9.3)
β-Nitrostyrene	2280 (7.8), 3110 (16.6)
1-Indanone	2450 (13.2), 2940 (2.8)
1-Acetoxy-1,2-dibromo-2-nitroindane (IV)	No max. $\epsilon = 3.5$ to 2500 Å.

[a] Numbers are wave lengths in angstroms. Numbers in parentheses are $\epsilon = 10^{-3}$.

The analogous α-nitroacetophenone absorbs at 3510Å. Structure I contains the benzoyl chromophore which absorbs at 2450 Å, with a much less intense band at 2940 Å as shown in indanone. Small amounts of I in the presence of II would be difficult to detect by the ultraviolet absorption. Structure VI would absorb below 3400 Å, because the hydroxyl group is not in a position to affect the nitrostyrene chromophore. The acetyl derivative has essentially the same chromophore as II and shows nearly identical ultraviolet absorption. In the dibromide IV the conjugated system is broken and no absorption maximum is observed.

The infrared spectra of the two substances m.p. 117° and m.p. 148° offer the best evidence for their identification as a mixture of I and II, and pure II respectively. Pure enol II gave no carbonyl absorption and showed characteristic bands with assignments indicated in Table I. The enolic O—H stretching frequency at 3584 cm.$^{-1}$ is normal for the unassociated enol group, indicating a lack of hydrogen bonding. Where hydrogen bonding is possible, as in o-nitrophenol, the band is shifted to lower wave number (3270 cm.$^{-1}$). The geometry of the five membered ring in II holds the enol and nitro groups too far apart for effective hydrogen bonding.

The splitting of the symmetrical stretching

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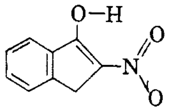
(6) A. Darnow and W. Sassenberg, *Ann.*, **594**, 185 (1955).

(7) R. D. Campbell and N. H. Cromwell, *J. Am. Chem. Soc.*, **79**, 3456 (1957).

frequency of the nitro group has been observed[8] in nitroketones, dinitro compounds, and nitro alcohols, and may well have been unobserved because of assignment difficulty and proximity of the weaker CH and CH_2 absorptions. We have tentatively assigned two intense bands in the 7.20–7.60 μ region to the symmetric nitro group stretching mode.



The mixture of I and II showed essentially the same bands, with the addition of a medium intensity band at 1710 cm.$^{-1}$. The inductive effect of the nitro group decreases the polar character of the carbonyl group relative to the carbonyl group (1705 cm.) in 1-indanone. The carbonyl adjacent to phenyl normally[9] absorbs at 1686 cm.$^{-1}$, but the effect of the phenyl conjugation is countered by the effect of the five membered ring (cyclopentanone: 1740 cm.$^{-1}$).

The acetyl derivative III has only the expected ester carbonyl band. Again the symmetric nitro band is split. The dibromide IV does not show the splitting seen in the other compounds.

The position of the nitro group bands has been[8] irregularly dependent on structural environment. The nitro group bands in this series do not afford a clear correlation, with the complication of splitting. More extensive studies of the effect of conjugation and of polar groups are planned. The β-nitrostyrene series is now being studied.

The chemistry and tautomerism of nitroketones also are being studied further.

EXPERIMENTAL[10]

2-Nitro-3-hydroxyindene (II). The condensation of *o*-phthalaldehyde with a large excess of nitromethane in methanolic potassium hydroxide was carried out as previously reported.[1] The powdery yellow product was obtained in 65–70% yield and was melted at 110–124°. Recrystallization from benzene several times gave m.p. 117–140°d. Several recrystallizations from isooctane-tetrahydrofuran gave yellow needles, m.p. 120–135°. This sample was identified by the infrared spectrum as a mixture of I and II.

The mixture (m.p. 120–134°) slowly decolorized potassium permanganate in anhydrous acetone. In a preparative run no oxidation product was isolated. The mixture also decolorized bromine in chloroform slowly. No crystalline bromination product was isolated.

The mixture of I and II was sublimed at 100°/3 mm. with a short path (1–1.5 cm.) between hot and cold surfaces. The sublimate, fine pale yellow needles, gave m.p. 148°, identified as II.

Anal. Calcd. for $C_9H_7NO_3$: C, 61.0; H, 3.95; N, 7.91; NO_2, 26.0. Found: C, 60.3; H, 3.91; N, 7.82; NO_2, 25.6.

This product (II) dissolved in 5% sodium hydroxide to give a yellow-orange solution. The ferric chloride test was negative. The pure enol, on standing for several weeks, gave m.p. 120–130°.

The pure enol II decolorized permanganate in acetone rapidly at first, then slowly continued to react. Several attempts were made to titrate II and the mixture with permanganate. The reaction proved to be too slow and ill-defined for titration. No oxidation products were isolated. Bromine in chloroform was decolorized slowly by II.

The reaction reported[6] between *o*-phenylene diamine and α-nitroacetophenone was successfully repeated. When attempted with II, the reaction failed to yield the desired product.

The 2,4-dinitrophenylhydrazone VII was prepared in the usual manner.[11] It formed as red-orange crystals, m.p. 204–205°.

Attempted syntheses of (I). 1-Indanone was treated in anhydrous ether with potassium *t*-butoxide and *iso*-amyl nitrate at −30°. Some tar formation occurred with 40% recovery of 1-indanone. Using the same catalyst, 1-indanone was treated with ethyl nitrate in tetrahydrofuran at −30°. Only a small amount of starting material was obtained by distillation. The same procedure was followed using ether as solvent. Only tars were formed. Treatment of 1-indanone with sodium ethoxide and ethyl nitrate in ethanol gave the same result. The use of methyl nitrate or *iso*-amyl nitrate in ether with dry hydrogen chloride resulted in 80–85% recovery of indanone.

2-Oximino-1-indanone[12] was treated with peroxytrifluoroacetic acid in acetonitrile by the method of Emmons and Pagano.[5] The starting material was recovered in 60% yield.

3-Acetoxy-2-nitroindene (III). The mixture of I and II (m.p. 120–134°) (1.00 gm.) was dissolved in 10 ml. of acetic anhydride. Introduction of a trace of conc. sulfuric acid gave an exothermic reaction. The solution was poured onto crushed ice and water. A yellow solid, m.p. 112–119°, was isolated in 1.2 gm. yield. Recrystallization from petroleum ether (b.p. 60–100°) and from isooctane-tetrahydrofuran (10:1) gave yellow rods, m.p. 133°. Sublimation failed to raise the melting point.

Anal. Calcd. for $C_{11}H_9NO_4$: C, 60.3; H, 4.11; N, 6.39. Found: C, 60.1; H, 3.88; N, 6.58.

Bromination of III. A solution of 1.5 gm. of the acetate III in glacial acetic acid was treated with 2 gm. of bromine. The solution stood for two days exposed to sunlight. The yellow product isolated was recrystallized from petroleum ether to give a white solid, m.p. 93–94°. Several attempts to recrystallize the product gave oils. Recrystallization from *n*-pentane gave hard white crystals m.p. 136°.

Anal. Calcd. for $C_{11}H_9Br_2NO_4$: C, 34.85; H, 2.39. Found: C, 34.93; H, 2.49.

2-Nitroindene (VIII). The method of Wallach and Beschke[13] was used. The product of the steam distillation was recrystallized from ethyl acetate and petroleum ether. The fine yellow needles melted at 140–141°. (Reported[13] 141°.)

Infrared Spectra. The infrared spectra were determined using a Perkin-Elmer Model 21 double beam recording spectrophotometer over the range from 700 cm.$^{-1}$ to 4000 cm.$^{-1}$ The samples were studied in chloroform or carbon tetrachloride (Brothers Chemical Company) solution freshly prepared at a concentration of 6 mg. per ml., using

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[8] J. F. Brown, Jr., *J. Am. Chem. Soc.*, **77**, 6341 (1955).

[9] L. J. Bellamy, *The Infrared Spectra of Complex Molecules*, John Wiley and Sons, New York, N. Y., 1954, Chapters 9, 17.

[10] Melting points were determined on a Kofler hot stage equipped microscope, and are corrected.

[11] R. L. Shriner, R. C. Fuson, and D. Y. Curtin, *Identification of Organic Compounds*, John Wiley and Sons, New York, N. Y., 4th Ed., 1956, p. 219.

[12] N. Levin, B. E. Graham, and H. G. Kolloff, *J. Org. Chem.*, **9**, 380 (1944).

[13] O. Wallach and E. Beschke, *Ann.*, **336**, 2 (1904).

double beam operation and matched cells. The instrument was operated according to the manufacturer's recommendations. The data obtained are listed in Table I.

Ultraviolet Spectra. The ultraviolet spectra were determined using a Cary Model 14 double-beam recording instrument. The solutions were freshly prepared in 95% ethanol and kept in the dark until used. Concentrations were 10^{-3} and 10^{-4} molar. Matched cells were used. The instrument was operated according to manufacturer's recommendations. Extinction coefficients were determined in the usual manner (ref. 11, p. 181). The data obtained are listed in Table II.

Fading absorbance was noted in alcohol solutions of II and III on standing. The 3430 Å band of II decreased to 20% of its initial intensity in 17 hr. on standing in the dark at room temperature. The 3400 Å band of III decreased to 76% of its initial intensity on standing 17 hr. in the dark at room temperature.

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

Some New Anil Derivatives of Gossypol[1]

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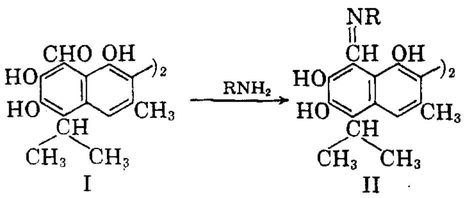
The scope of the reaction of Schiff base (anil) formation between gossypol and primary amines has been investigated. Seventeen primary amines of widely varying types were reacted with gossypol and the anil derivates isolated.

It has recently been demonstrated[2] in this laboratory that aliphatic amines form stable derivatives (II) of gossypol (I) analogous to the long known[3] dianilinogossypol (II,R=phenyl) and related aromatic anil derivatives.[4]



We have prepared a variety of new anil derivatives of gossypol in order to determine the scope of the reaction and to obtain potentially useful gossypol derivatives. The amines selected for anil formation with gossypol were in general of the following types: (1) amines containing other functional groups which should permit further reactions of the gossypol anils, (2) physiologically active amines which might impart biological activity to the anil formed, (3) azo dyes containing amino groups, and (4) amino acid and dipeptide esters.

Of particular interest were the anils with the methyl esters of lysine, glycine and the dipeptide glycylglycine. It has been proposed that gossypol becomes chemically bound with protein during the processing of cottonseed meal.[5] The site of the binding is the free amino groups present in the cottonseed protein and the terminal amino groups of lysine has seemed to be a likely spot. While the preparation of these amino acid ester anils does not offer any direct evidence for the site of binding, it demonstates that moderately stable anils of this type may be formed. The reaction product of lysine methyl ester and gossypol contained a 1:1 ratio of the two reactants indicating either anil formation at both amino groups in the lysine molecule (resulting in a polymeric type material) or reaction at only one carbonyl site in the gossypol molecule with one amine function (probably the terminal amino group[6]) in the lysine methyl ester molecule. The analytical data on the product agree more closely with the latter possibility.

The normal product (II,R=CH_2COOCH_3) was obtained from the reaction of gossypol and glycine methyl ester. The product from the reaction of glycylglycine methyl ester and gossypol was identical (analytical data and infrared spectra comparison) with that from glycine methyl ester and gossypol. Hydrolysis of the dipeptide apparently occurred during its liberation from the hydrochloride or during the anil formation.

Gossypol acetic acid complex[7] was used for all reactions. The yields of anils were generally quite satisfactory as indicated in Table I.

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(1) A report of work conducted under contract with the U. S. Department of Agriculture and authorized by the Research and Marketing Act. The contract is being supervised by the Southern Utilization Research and Development Division of the Agricultural Research Service.

(2) D. A. Shirley and W. C. Sheehan, *J. Org. Chem.*, **21**, 251 (1956).

(3) F. E. Carruth, *J. Am. Chem. Soc.*, **40**, 647 (1918).

(4) J. M. Dechary and L. E. Brown, *J. Am. Oil Chemists Soc.*, **33**, 76 (1956).

(5) E. P. Clark, *J. Biol. Chem.*, **76**, 229-235 (1928).

(6) B. Witkop and T. W. Beiler, *J. Am. Chem. Soc.*, **76**, 5589 (1954).

(7) Supplied by Southern Utilization Research and Development Division Laboratory, Agricultural Research Service.