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2-(p-NITROPHENYL)-AND 2-(p-DIMETHYLAMINOPHENYL)-4-AZA-5, 6-BENZINDANDIONES-1, 3

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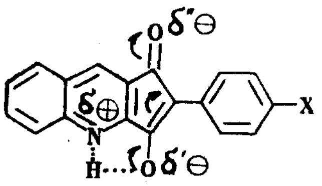
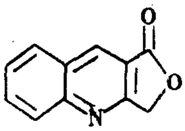
Condensation of the lactone of 2-hydroxymethylquinoline carboxylic acid with p-nitrobenzaldehyde in acetic anhydride solution gives 3-(p-nitrobenzal)-4-aza-5, 6-benzophthalide, rearranged by sodium methoxide to 2-(p-nitrophenyl)-4-aza-5, 6-benzindandione-1, 3. Condensation of the lactone of 2-hydroxymethylquinoline carboxylic acid with p-dimethylaminobenzaldehyde in ethyl acetate solution in the presence of sodium methoxide synthesizes 2-(p-dimethylaminophenyl)-4-aza-5, 6-benzindandione- 1, 4. It is a high-melting black compound. Reaction of the sodium salt of 2-(p-nitrophenyl)-4-aza-5, 6-benzindandione-1, 3 with dimethyl sulfate gives the N-methyl betaine of 2-(p-nitrophenyl)-4-aza-5, 6-benzindandione-1, 3. A description is given of the use of α, α'-isopropylidenetetronic acid, prepared from acetoacetic ester of diketene for synthesis of 2-hydroxymethylquinoline carboxylic acid.

Continuing the study of 2-arylazaindandiones-1, 3 [1, 2], the following compounds which are 2-phenyl-4-aza-5, 6-benzindandiones- 1, 3 substituted in the phenyl group have been synthesized by the present authors: 2-(p-nitrophenyl)-4-aza-5, 6-benzindandione-1, 3(I) and 2-(p-dimethylaminophenyl)-4-aza-5, 6-benzindandione-1, 3(II).

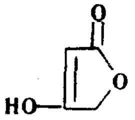


I $X=NO_2$
II $X=N(CH_3)_2$

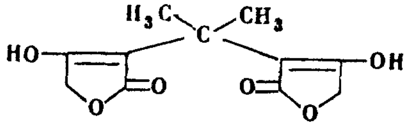
For this purpose use has been made of the condensation of the lactone of 2-hydroxymethylquinoline-3-carboxylic acid(III) with p-nitro- and p-dimethylaminobenzaldehydes.



III



IV



V

The literature [3] describes a method of preparing compound III by condensing tetronic acid(IV) with o-aminobenzaldehyde in ethanol solution. However, pure tetronic acid is accessible only with comparative difficulty. The present work used an aqueous solution of tetronic acid, which is readily prepared by a method developed by the present authors [4, 5] from ethyl acetoacetate or diketene. It has been shown that the lactone III is also formed by boiling α, α'-isopropylidenetetronic acid(V) [4, 5] with o-aminobenzaldehyde in ethanol solution in the presence of bases, triethylamine or pyridine. Apparently compound V under the action of the catalyst splits [6] into acetone and tetronic acid, which then reacts with the o-aminobenzaldehyde. This method gives purer III lactone than does condensation in aqueous solution, and it can be used directly, without being crystallized, for further syntheses.

Condensation of compound III with p-nitrobenzaldehyde in acetic anhydride solution leads to formation of 3-(p-nitrobenzal)-4-aza-5, 6-benzophthalide(VI).

Absorption characteristic of lactone carbonyl, at 1799 cm^{-1}, is observed in the IR spectrum of VI, and intense absorption at 1513 cm^{-1} is due to antisymmetric vibrations of the nitro group. Treatment of phthalide VI with sodium methoxide converts it into the sodium salt of 2-(p-nitrophenyl)-4-aza-5, 6-benzindandione-1, 3(VII).

In p-dimethylaminobenzaldehyde the carbonyl group is less reactive than in p-nitrobenzaldehyde or benzaldehyde, so that the first-named does not react with lactone III on boiling in acetic anhydride; condensation was effected by Shapiro's method [7, 8], in the presence of sodium methoxide in ethyl acetate solution. There the sodium salt of 2-(p-dimethylaminophenyl)-4-aza-5, 6-benzindandione-1, 3(VIII) was isolated from the solution, and after acidification the filtrate also gave some quantity of compound II.

Compound I, like 2-phenyl-4-aza-5, 6-benzindandione-1, 3 [1], is sparingly soluble, lacks a sharp melting point, is dark red in color, and forms a well-crystallized orange sodium salt (VIII). Almost black, high-melting II gives a brownish-violet sodium salt. Thus compounds I and II show a property previously observed when investigating other 2-arylazaindandiones-1, 3, viz. formation of an anion which is not as deeply colored as the dicarbonyl compound itself. Investigation of the electronic spectra of 2-phenyl-4-azaindandione-1, 3 and 2-phenyl-4-azaindandione-1, 3 [9] showed that this phenomenon is apparently connected with formation of betaine forms.

Regarding IR spectra of the sodium salt VIII of compound II in the frequency range 1480-1800 cm^{-1}, its appearance is almost the same as that of the spectra of anions of other 2-arylindandiones-1, 3 [10]. In the 1510-1530 cm^{-1} region there is a wide intense absorption band which characterizes the equalizing of the electron system of the anion. In the IR spectrum of sodium salt VII of compound I this absorption band is displaced towards higher frequencies, and appears in the range 1548-1571 cm^{-1}.

As absorption above 1700 cm^{-1} is absent from compounds I and II in the crystalline state, they are not then in the diketo form. A strongly polarized enol form is most probable [10], and in the case of compound II it is characterized by an intense absorption maximum at 1548 cm^{-1} (68%) with an inflection about 1521 cm^{-1} (56%), and a less intense band at about 1662 cm^{-1} (23%). Somewhat enhanced frequency values are found for compound I: 1560 (83), 1589 (63), 1650 (17) and 1676 (30) cm^{-1} (%).

Reviewing the structural formulas of the enol forms of I and II it is evident that a hydrogen atom can be sterically close to a nitrogen atom in the pyridine ring. This facilitates polarization of the O–H bond, and formation of a system with an intramolecular hydrogen bond with the hydrogen atom simultaneously in the fields of the oxygen and nitrogen atoms. Some 2-arylindandiones-1, 3, for which intermolecular hydrogen bonding has been shown to exist in the crystalline state, absorb in the range 2400-2600 cm^{-1} [10]. It is considered that for compounds I and II formation of intermolecular hydrogen links of the type O=C–C=C–O– H...O=C– is improbable, since no absorptions are observed in the range 2400-2600 cm^{-1}, and the maxima in the range 2750-2940 cm^{-1} in the case of compound I, and in the range 2680-2920 cm^{-1} for compound II may be due to the presence of intramolecular hydrogen bonds. How then are the high melting points and quite limited solubilities of the compounds prepared, properties so uncharacteristic of compounds with intramolecular hydrogen bonds, to be explained? Can it be that here there is another kind of intermolecular interaction, viz donor-acceptor bonds, which also plays a part in the deep coloring of the azaindandiones? These are questions which it is at present difficult to answer.

Compound II has basic properties, and dissolves in formic acid, hydrochloric and other mineral acids to give comparatively stable red salts. The IR spectrum of the hydrochloride of 2-(p-dimethylaminophenyl)-4-aza-5, 6-benzindandione-1, 3 (IX) is clearly reminiscent of the absorption of base II; here is found very intense absorption in the range 1515-1551 cm^{-1} (73%), and low-intensity maxima about 1671 cm^{-1} (23%) and 1642 cm^{-1} (17%). So it is considered that formation of salt IX does not involve actual changes in the azabenzindandione group, i.e., the same strongly polarized enol form with an intramolecular hydrogen bond is preserved, and a proton of the acid is linked with the nitrogen of the dimethylamino group. Judging by its IR spectrum the hydrochloride of 2-(p-dimethylaminophenyl) indandione [11], unlike salt IX, is an enol of low polarity, as it has a characteristic absorption at 1689 and 1583 cm^{-1}.

Reaction of the sodium salt VII with dimethyl sulfate leads to alkylation of the nitrogen atom of the pyridine ring and formation of a dark violet N-methyl betaine of 2-(p-nitrophenyl)-4-aza-5, 6-benzindandione-1, 3 (X). This latter, like other N-methylbetaines of azaindandiones-1, 3, gives, in its IR spectrum a very intense wide band in the range 1550-1580 cm^{-1} [1, 2].

Experimental

Lactone of 2-hydroxymethylquinoline-2-carboxylic acid (III). To 2.4 g (0.02 mole) o-aminobenzaldehyde and 2.4 g (0.01 mole) α, α'-isopropylidenetetronic acid (V) [4, 5] was added 20 ml ethanol, followed by a few drops of pyridine, and the mixture refluxed for 1 hr then left overnight. The crystals of the lactone III were filtered off, and washed with ethanol. Yield 2.6 g (70%) mp 217°. Mixed mp of lactone prepared thus with lactone III prepared by the method of [3], was undepressed.

3-(p-Nitrobenzal)-4-aza-5, 6-benzophthalide (VI). 1.85 g (0.01 mole) lactone III and 1.51 g (0.01 mole) p-nitrobenzaldehyde in 5 ml acetic anhydride were refluxed for 2 hr. On cooling crystals separated, they were filtered off, and washed with ether. Yield 2.4 g (75%) mp 236° (dioxane-ethanol). Found: N 8.69%. Calculated for $C_{18}H_{10}N_2O_4$: N 8.80%. IR spectrum: 1513 (78), inflection 1575 (48), inflection 1589 (56), 1597 (59), 1613 (49) 1668 (45), 1799 (83) cm^{-1} (%).

Sodium salt of 2-(p-nitrophenyl)-4-aza-5, 6-benzindandione-1, 3 (VIII). A solution of sodium methoxide was prepared from 0.06 g (0.0026 g eq) sodium and 10 ml methanol, and added to 0.8 g (0.0025 mole) VI. The mixture turned violet, and then, on heating, brownish red. An orange precipitate of salt VII formed. Heating time 30 min. The mixture was cooled, 2 ml water added, filtered, and the solid washed with methanol. Yield 0.8 g (94%). The sodium salt VII was sparingly soluble in ethanol and water. It was recrystallized from dimethylformamide (orange crystals), and vacuum-dried at 120°. Found: N 8.41%. Calculated for $C_{18}H_{19}N_2NaO_4$: N 8.23%. IR spectrum: 1502(60), 1548(74), inflection 1571(65), 1629(50), 1656(41) cm^{-1}(%).

2-(p-Nitrophenyl)-4-aza-5, 6-benzindandione-1, 3(I). 5 ml 6 N hydrochloric acid was added to a solution of 0.65 g sodium salt VII in 10 ml dimethylformamide. A dark red precipitate of I formed. The yield was almost quantitative. The compound was practically insoluble in ethanol, dioxane, nitrobenzene, and formic acid. It was recrystallized from dimethylformamide, the precipitate separated off by centrifuging and vacuum-dried at 120°. Mp 360-365° (decomp). Found: N 8.69%. Calculated for $C_{18}H_{10}N_2O_4$: N 8.80%. IR spectrum: 1497(52), 1560(82), 1589(63), 1618(25), 1650(17), 1676(30), 2750-2940(43), 2990-3030(35), inflection 3082(31), inflection 3140(27) cm^{-1}.*

N-Methylbetaine of 2-(p-nitrophenyl)-4-aza-5, 6-benzindandione-1, 3(X). 3 ml freshly-distilled dimethyl sulfate was added to 0.34 g sodium salt VII, and the mixture heated to boiling. After 24 hr it was diluted with aqueous ethanolic sodium hydroxide solution and filtered. The dark violet precipitate of compound X on the filter was washed with methanol, yield 0.25 g (75%). The N-methyl betaine X was sparingly soluble, even in hot dimethylformamide, which was used to recrystallize it. It was vacuum-dried at 140°, mp about 365°(decomp). Found: C 68.76; H 3.70; N 8.05%. Calculated for $C_{19}H_{12}N_2O_4$: C 68.67; H 3.64; N 8.43%. IR spectrum: 1489(63), 1527(39), 1577(75), 1639(58), 1657(45) cm^{-1}(%).

2-(p-Dimethylaminophenyl)-4-aza-5,6-benzindandione-1,3(II) and its sodium salt(VIII). 5.55 g (0.03 mole) lactone III and 4.47 g (0.03 mole) p-dimethylaminobenzaldehyde were suspended in 15 ml dry ethyl acetate, and 1-2 ml solvent distilled off. A solution of sodium methoxide was prepared from 0.92 g (0.04 g eq) sodium and 11 ml dry methanol. 2 ml liquid was distilled off from the intensely red reaction mixture, which was then refluxed for 30 min. A violet brown precipitate of salt VIII formed. Most of the solvent was then distilled off, 5 ml water added, and the mixture filtered, when crystals of salt VIII remained on the filter. Yield 2.2 g(22%). Recrystallized from ethanol. Found: N 8.10%. Calculated for $C_{20}H_{15}N_2NaO_2$: N 8.28%. IR spectrum: 1510(74), inflection 1529(72), inflection 1599(36), 1611(37), inflection 1638(29) cm^{-1}(%).

50% acetic acid was added to the filtrate from filtering off sodium salt VIII. A black, finely divided crystalline precipitate of compound II was formed, yield 1.3 g (14%). It was sparingly soluble in most organic solvents, but readily soluble in formic acid to give a blood red solution from which it was reprecipitated by ethanol. To purify it, 0.7 g compound was recrystallized from 40 ml dimethylformamide, the precipitate centrifuged off, and vacuum-dried at 120°. Mp 315-320°(decomp). Found: C 75.67; H 5.04; N 8.95%. Calculated for $C_{20}H_{16}N_2O_2$: C 75.93; H 5.10; N 8.85%. IR spectrum: inflection 1521(66); 1548(68, 1601(48), inflection 1621(29), 1662(23), 2680-2920(45), 2996-3038(38) cm^{-1}(%).

2-(p-Dimethylaminophenyl)-4-aza-5, 6-benzindandione-1,3 hydrochloride(IX). 0.16 g compound II was dissolved in 5 ml concentrated hydrochloric acid, 4 ml 50% ethanol added, the mixture heated to boiling, and then filtered. On cooling red crystals of hydrochloride IX formed, and were dried over sulfuric acid in a desiccator, yield 0.11 g (61%). When IX was boiled with water or ethanol, or heated dry it was decomposed, giving the base II. Found: N 7.48, 8.43; Cl 10.10, 9.96%. Calculated for $C_{20}H_{17}ClN_2O_2$: N 7.94; Cl 10.05%. IR spectrum 1515(67), 1529-1551(73), 1617(22), 1642(19), 1671(23) cm^{-1}(%).

REFERENCES

1. L. E. Neiland and G. Ya. Vanag, DAN, 146, 615, 1962.
2. L. E. Neiland and G. Ya. Vanag, Izv, AN Latv. SSR, ser. khim., 203, 1964.
3. A. E. Fehnel, J. A. Deyrup, and M. B. Davidson, J. Org. Chem., 23, 1996, 1958.
4. L. E. Neiland, O. Ya. Neiland, and G. Ya. Vanag, Author's Certificate USSR, 164298, 1964.
5. L. E. Neiland, O. Ya. Neiland, and G. Ya. Vanag, DAN, 159, 1099, 1964.
6. L. Wolff and W. Schimpff, Ann., 315, 151, 1901.
7. S. L. Shapiro, R. Geiger, and U. Freedman, J. Org. Chem., 25, 1860, 1960.
8. S. L. Shapiro, K. Geiger, J. Youlus, and L. Freedman, J. Org. Chem., 26, 3580, 1961.
9. L. E. Neiland and G. Ya. Vanag, KhGS [Chemistry of Heterocyclic Compounds], 93, 1965.
10. O. Ya. Neiland and V. Kroge, Izv. Latv. SSR, ser. khim., 483, 1964.
11. O. Ya. Neiland and M. Ya. Tsirule, Izv. AN Latv. SSR, ser. khim., 65, 1963.

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*The (%) absorption over the range 1480-1800 cm^{-1} is not comparable with the (%) absorption over the range 2300-3600 cm^{-1}.