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SOME 2-ARYL-5-AZAINDANDIONES-1, 3

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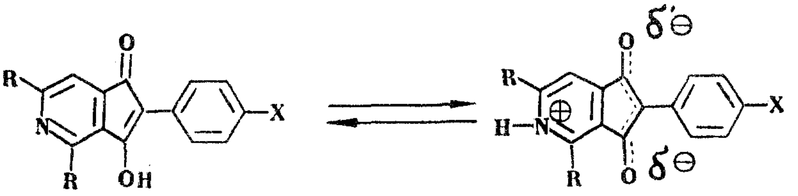
Condensation of cinchomeronic acid with p-nitrophenylacetic acid, of 2, 6-dimethylcinchomeronic acid with phenylacetic acid, and p-nitrophenylacetic acid in acetic anhydride solution in the presence of triethylamine followed by rearrangement of the condensation products with sodium methoxide gives 2-(p-nitrophenyl)-5-azaindandione-1, 3, 4, 6-dimethyl-2-phenyl-5-azaindandione-1, 3, and 4, 6-dimethyl-2-(p-nitrophenyl)-5-azaindandione-1, 3. Reaction of the alkali metal salts of these compounds with dimethyl sulfate leads to alkylation at the nitrogen atom, and formation of N-methyl betaines of the corresponding 5-azaindandiones. 2-Aryl-5-azaindandiones and their N-methyl betaines are dark in color (black to reddish brown), sparingly soluble, and decompose at 250-350°.

The present authors previously prepared 2-phenyl-5-azaindandione-1, 3 by condensing cinchomeronic acid with phenylacetic acid in acetic anhydride solution in the presence of triethylamine [1]. Now, with a view to extending the ambit of the method, cinchomeronic acid has been condensed with p-nitrophenylacetic acid and 2, 6-dimethylcinchomeronic acid with phenylacetic and p-nitrophenylacetic acids. The appropriate pyridine dicarboxylic and phenylacetic acids were reacted in equimolar proportions. Immediately before the condensation, the cinchomeronic acids were refluxed for some time (20-40 min) with acetic anhydride, to bring about formation of the anhydrides of the cinchomeronic acids, or of mixed anhydrides of those acids with acetic acid, and it can be assumed that these, under the action of triethylamine react with the phenylacetic acids. A two-fold excess of triethylamine is used, as one molecule is used up in neutralizing the acetic acid produced in anhydride formation from the cinchomeronic acids, and the second participates in condensation. As is usual in condensation of this type, the p-nitrophenylacetic acid reacts more readily, and gives much higher yields. Basically the condensation products are substituted α-phenyl-α-(5-azaphthalyl) acetic acids and the corresponding 1-benzal-5-azaphthalides. Previously when investigating the reaction between cinchomeronic and phenylacetic acids, the isolation of these compounds in a pure state was attempted, but here it was abandoned. Immediately after drying, the impure condensation products obtained were rearranged by treatment with sodium methoxide to the corresponding 2-aryl-5-azaindandiones-1, 3, and in that way the following were prepared: 2-(p-nitrophenyl)-5-azaindandione-1, 3 (I), 4, 6-dimethyl-2-phenyl-5-azaindandione-1, 3 (II), and 4, 6-dimethyl-2-(p-nitrophenyl)-5-azaindandione-1, 3 (III).



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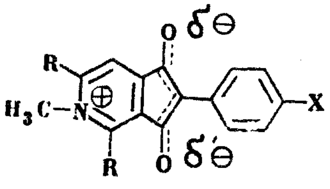
I R=H, X=NO_2; II R=CH_3, X=H; III R=CH_3, X=NO_2

All of these, like 2-phenyl-5-azaindandione-1, 3, are dark in color, do not have a sharp melting point, and decompose above 250°, but unlike that compound, they are sparingly soluble; they form red alkali metal salts which are readily soluble in water and ethanol. The sodium salt of compound II is very readily soluble, but is not easy to purify by crystallization.

The sodium salt of 2-(p-nitrophenyl)-5-azaindandione-1, 3 reacts with dimethyl sulfate in methanol solution to give the N-methyl betaine of 2-(p-nitrophenyl)-5-azaindandione-1, 3 (IV)



IV R=H, X=NO_2
V R=CH_3, X=H
VI R=CH_3, X=NO_2

As might be expected, because of steric hindrance alkylation of II and III with methyl groups at positions 4 and 6 takes place only under drastic conditions, by heating the sodium or potassium salts with dimethyl sulfate in the absence of any solvent. The betaines IV, V, and VI prepared, are high-melting, sparingly soluble and deeply colored substances. In formic acid they form orange-red solutions, and evidently this is related to protonization of the oxygen atom, i.e., formation of salts of enol forms of N-methylated azaindandiones-1, 3 [2].

None of the IR spectra of the 2-aryl-5-azaindandiones described, show the characteristic diketo form frequencies at 1700-1760 cm^{-1}. The spectra of the azaindandiones I and III, which contain nitro groups, are markedly reminiscent of the absorption shown by their N-methyl betaines IV and VI, for which the minimum intensity maximum lies in the interval 1560-1580 cm^{-1}. So it is assumed that I and III in the crystalline state exist as internal salts (IB and IIIB). In the range 1480-1800 cm^{-1} the spectrum of II is clearly different from that of the N-methyl betaine (V), as well as from the spectra of I and III and other previously synthesized 2-arylazaindandiones [1, 3], as at 1683 cm^{-1} there is a maximum of the same intensity as that at 1568 cm^{-1}. This kind of absorption may indicate the presence of a slightly polarized enol form (IIE) [4].

Much of a general character was elucidated by comparing the IR spectra of the alkali metal salts of the 5-azaindandiones-1, 3 here prepared with the spectra of salts of 2-arylindandiones [5]. The anion of 4, 6-dimethyl-2-phenyl-5-azaindandione, like that of 2-phenylindandione-1, 3, is characterized by intense absorption in the range 1515-1532 cm^{-1}. In the spectra of the salts of I and III which contain a nitro group, as for that of the sodium salt of 2-(p-nitrophenyl) indandione-1, 3, this band is displaced towards higher frequencies, and appears in the region 1560-1580 cm^{-1}.

IR spectra were measured with an IKS-14 instrument; in the range 1480-1800 cm^{-1} a NaCl prism was used for the compounds suspended in vaseline, and in the range 2300-3600 cm^{-1} a LiF prism was used for the compounds suspended in hexafluorobutadiene.

Experimental

2-(p-Nitrophenyl)-5-azaindandione-1, 3 (I). A mixture of 1.67 g (0.01 mole) cinchomeronic acid and 7 ml acetic anhydride was heated and stirred for half an hour at 120-130°. After cooling to 70°, 1.81 g (0.01 mole) p-nitrophenylacetic acid was added. When the latter had dissolved, 2.8 ml (0.02 mole) triethylamine was added dropwise at such a rate that the temperature of the reaction mixture did not exceed 60°. After half of the requisite triethylamine had been added, the dark color of the solution changed to red. The temperature was held at 60° for another half an hour, after which the reaction products were left at room temperature. After 24 hr the products were poured onto 20 g crushed ice mixed with 5 ml ethanol and 2 ml concentrated HCl. A dark oil was formed, and after some time it crystallized, and the crystals were filtered off. A solution of sodium methoxide was prepared from 0.21 g (0.0093 g eq) sodium and 15 ml dry methanol, added to the dried material (2.5 g), the whole refluxed for half an hour, 3 ml water added, the mixture treated with activated carbon, and filtered. Addition of acetic acid precipitated I, yield 1.82 g (68%). It was sparingly soluble in ethanol, acetic acid, and dioxane. When heated with 20 ml dimethylformamide 0.4 g dissolved, but only a very small amount of fine crystalline material separated on cooling. So to purify I, 0.75 g was dissolved in 15 ml methanol, containing 0.12 g sodium hydroxide, the solution heated to boiling, and filtered. Acetic acid was added to the filtrate, when a black fine crystalline precipitate was formed, yield 0.71 g, mp 335-340° (decomp). Found: C 62.84; H 3.11; N 10.31%. Calculated for $C_{14}H_8N_2O_4$: C 62.69; H 3.01; N 10.46%. IR spectrum: 1488 (58); 1531(68); 1565 (73); 1584 (70); 1619 (41); inflection 1653 (23); 1666 (26) cm^{-1} (%).

4, 6-Dimethyl-2-phenyl-5-azaindandione-1, 3 (II). Prepared similarly to compound I. Condensation of 3.9 g (0.02 mole) 2, 6-dimethylcinchomeronic acid with 2.7 g (0.02 mole) phenylacetic acid, followed by rearrangement of the crude product (2.8 g) with sodium methoxide (0.26 g sodium in 25 ml dry methanol) gave 2.0 g (40%) compound II in the form of violet-brown crystals sparingly soluble in water (orange solution), ethanol (violet solution), more soluble in acetic acid, which on heating dissolved 1.2% (violet solution). It was readily soluble in formic acid and in dimethylformamide. It was recrystallized from mixed formic-acetic acids (2 : 1), and vacuum-dried at 140°, mp 250-260° (decomp). Found: C 76.40; H 5.26; N 5.77%. Calculated for $C_{16}H_{13}NO_2$: C 76.48; H 5.21; N 5.57%. IR spectrum: 1493 (55); inflection 1529 (54); 1568 (62) 1617 (49); 1683 (67); 2650-3090 cm^{-1} (%).

4, 6-Dimethyl-2-(p-nitrophenyl)-5-azaindandione-1, 3 (III). Prepared similarly to compound I, from 3.9 g (0.02 mole) 2, 6-dimethylcinchomeronic acid and 3.6 g (0.02 mole) p-nitrophenylacetic acid. Yield 4.75 g (80%). The compound was sparingly soluble in water, ethanol, and acetic acid, but dissolved in formic acid, to give a brownish red solution; it was purified by recrystallizing from dimethylformamide, when it formed dark brown crystals; it was vacuum-dried at 140°, mp about 300° (decomp). Found: C 64.89; H 4.29; N 9.34%. Calculated for $C_{16}H_{12}N_2O_4$: C 64.86; H 4.08; N 9.46%. IR spectrum: 1523 (62); 1566 (70); inflection 1585, 1621 (50), inflection 1641 (38); 1672 (45); 2617 (38); 2926 (55); 3010-3095 (50) cm^{-1} (%).

Sodium salt of 2-(p-nitrophenyl)-5-azaindandione-1, 3. 0.27 g (0.001 mole) I was heated with 5 ml methanol containing 0.04 g (0.001 mole) sodium hydroxide to dissolve it, and the solution filtered. On cooling there was formed a precipitate of the sodium salt of 2-(p-nitrophenyl)-5-azaindandione-1, 3, yield 0.2 g (69%), which was dried at

70°. The sodium salt of I was soluble in ethanol and water. Found: N 10.03%. Calculated for $C_{14}H_7N_2NaO_4$: N 9.65%. IR spectrum: 1503(60); 1573(85); 1625(64); 1660(39) cm^{-1}(%).

Sodium salt of 4, 6-dimethyl-2-phenyl-5-azaindandione-1, 3. A solution of sodium methoxide prepared from 0.046 g (0.002 g eq) sodium and 5 ml methanol was added to 0.50 g (0.002 mole) II, the mixture heated to boiling and filtered. Addition of ether to the blood red filtrate precipitated the sodium salt of 4, 6-dimethyl-2-phenyl-5-azaindandione-1,3, yield 0.47 g (86%). The sodium salt of compound II was readily soluble in water and ethanol. Found: N 5.27%. Calculated for $C_{16}H_{12}NNaO_2$: N 5.13%. IR spectrum: 1495(82); 1515-1532(81); 1600(72); inflection 1612(68); 1631-1643(62) cm^{-1}(%).

Potassium salt of 4, 6-dimethyl-2-(p-nitrophenyl)-5-azaindandione-1, 3. 0.87 g (0.003 mole) III was heated with 15 ml methanol containing 0.17 g (0.003 mole) potassium hydroxide. The mixture was heated to boiling, then filtered; on cooling there was precipitated the potassium salt of 4, 6-dimethyl-2-(p-nitrophenyl)-5-azaindandione-1, 3, yield 0.55 g (55%), which was vacuum-dried at 120°. Found: N 8.31%. Calculated for $C_{16}H_{11}KN_2O_4$: N 8.38%. IR spectrum: inflection 1501(71); 1521-1536(70); inflection 1547(68); 1560-1578(67); inflection 1601(60); inflection 1621(56); 1650 -1660(48) cm^{-1}(%).

2-(p-Nitrophenyl)-5-azaindandione-1, 3 N-methyl betaine (IV). 0.27 g (0.001 mole) I was dissolved in 5 ml methanol containing 0.16 g (0.004 mole) sodium hydroxide. 0.5 ml freshly-distilled dimethyl sulfate was added to this solution, and the whole heated at 40° for 30 min. A black precipitate formed. After 24 hr aqueous sodium hydroxide was added, and the solution filtered, the precipitate of IV on the filter was washed with methanol, yield 0.25 g (89%). It was recrystallized from formic acid. It did not melt up to 500°, and was sparingly soluble in most organic solvents. Found: N 9.92%. Calculated for $C_{15}H_{10}N_2O_4$: N 9.93%. IR spectrum: 1528 (41); 1567 (60); 1618 (28); 1641 (27); inflection 1665 (19) cm^{-1} (%).

4, 6-Dimethyl-2-phenyl-5-azaindandione-1, 3 N-methyl betaine (V). 3 ml freshly-distilled dimethyl sulfate was added to 0.27 g sodium salt of II, and the mixture heated on a boiling water bath for 30 min, cooled, an aqueous ethanolic solution of sodium hydroxide added until the reaction was strongly alkaline, and the solution filtered. The black precipitate of V was washed with methanol. Yield 0.17 g (64%). V was practically insoluble in water, sparingly soluble in ethanol, more soluble in dimethylformamide and acetic acid, and readily soluble in formic acid to give an orange solution. It was recrystallized from acetic acid, mp about 330° (decomp). Found: C 77.13; H 5.58; N 5.05%. Calculated for $C_{17}H_{15}NO_2$: C 76.96; H 5.70; N 5.28%: IR spectrum: 1493 (50); 1548 (66); inflection 1561 (62); inflection 1608; 1628 (48); 1655 (37) cm^{-1}(%).

4, 6-Dimethyl-2-(p-nitrophenyl)-5-azaindandione-1, 3 N-methyl betaine (VI). 0.55 g potassium salt of III was heated with 4 ml freshly-distilled dimethyl sulfate to dissolve it, then left overnight. A methanolic solution of alkali was added to the bright-red crystalline mass, which changed it to reddish brown. The solid was filtered off, and washed with methanol, yield 0.46 g (90%). The N-methyl betaine was practically insoluble in ethanol and acetic acid. It readily dissolved on heating with formic acid (bright red solution). It was recrystallized from dimethylformamide, mp about 310° (decomp). Found: N 8.86%. Calculated for $C_{17}H_{14}N_2O_4$: N 9.03%. IR spectrum: 1491 (75); inflection 1547 (79); 1563 (86); 1570-1581 (87); 1632 (70); inflection 1662 (52) cm^{-1}(%).

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