

# On Phthalides and 1,3-Indandiones. XL. Reduction of the Nitrated 3-(Arylmethylene)phthalides by Hydroiodic Acid

L. KRASNEC, Jr., and P. HRNČIAR

*Department of Organic Chemistry, Faculty of Natural Sciences, Komenský University,  
Bratislava 1*

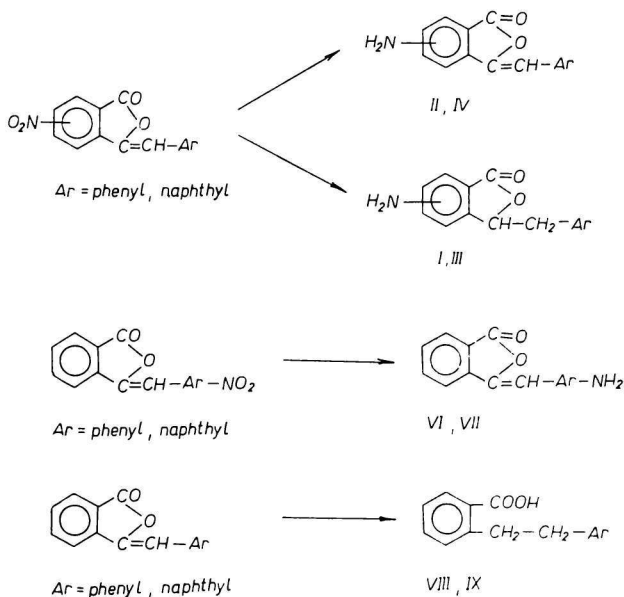
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Nitro group of the nitrated 3-(arylmethylene)phthalides was reduced to amino group by 57% hydroiodic acid. When the nitro group was in one of the positions 5, 6, or 7, the double bond between the carbon atoms was reduced, too. However, a dilute (35–40%) hydroiodic acid reduced the nitro group only.

Up to the present, stannous chloride [1–4], ferrous sulfate [5, 6], or iron [5] have been used for the reduction of nitrated 3-(arylmethylene)phthalides to the corresponding amines. In the nitrated 3-(arylmethylene)phthalides, there are besides nitro group also the C=C bond and the carbonyl group reducible. It is known that hydroiodic acid is most often used to replace hydroxyl or halogen by hydrogen, and to reduce double C=C bonds [7]. Hydroiodic acid was used by *Fels* [8] to reduce C=C bonds in similar structures as (arylmethylene)phthalides. Upon reduction with concentrated hydroiodic acid, he obtained 4-(2-phenylethyl)-3-pyridinecarboxylic acid from benzaleinchomeronide, *i.e.*, reduction of C=C bond proceeded at the simultaneous opening of the lactone ring which is obvious at the reduction of lactones by hydroiodic acid [9].

At determining the structure of positional isomers of 3-(1-naphthal)nitrophthalides we found [10] that in the presence of red phosphorus, the nitro group was preferentially reduced by 57% hydroiodic acid. We were interested in how the reduction of nitrated 3-(arylmethylene)phthalides with nitro group either on the phthalide skeleton or on the aryl (aryl = naphthyl, phenyl) by hydroiodic acid would proceed. It was apparent from the reduction products of (arylmethylene)phthalides (with nitro group on the phthalide skeleton) that the result of reduction depended on the position of nitro group (Scheme 1).

On reduction of 5-nitro-3-(1-naphthal)phthalide, 7-nitro-3-(1-naphthal)phthalide, and 7-nitro-3-benzalphthalide by concentrated hydroiodic acid, the nitro group to amino group as well as the double C=C bond were reduced. On the corresponding infrared spectra the bands of symmetric and asymmetric vibrations of the nitro group at 1340–1360  $\text{cm}^{-1}$  and at 1530–1540  $\text{cm}^{-1}$  disappeared, while the bands belonging to symmetric and asymmetric vibrations of amino group in the region of 3360–3380  $\text{cm}^{-1}$  and 3470–3480  $\text{cm}^{-1}$  respectively, appeared. Also the band of C=C vibration at 1650–1670  $\text{cm}^{-1}$  disappeared. Using a dilute hydroiodic acid (35–40%), only the nitro group of 7-nitro-3-(1-naphthal)phthalide and that of 7-nitro-3-benzalphthalide was reduced to amino group. We failed to reduce the C=C bond of 4-nitro-3-(1-naphthal)phthalide and that of 4-nitro-3-benzalphthalide by concentrated hydroiodic acid (probably owing to the steric effects of naphthalene



Scheme 1

and benzene rings respectively, and to the formed amino group in the neighbourhood of the  $\text{C}=\text{C}$  bond). From this we can assume that the position of nitro group and the concentration of hydroiodic acid play an important role in these reductions.

From 3-(4-nitro-1-naphthal)phthalide and 3-(4-nitrobenzal)phthalide the corresponding 3-(4-amino-1-naphthal)phthalide and 3-(4-aminobenzal)phthalide respectively, were obtained on reduction with concentrated hydroiodic acid. The  $\text{C}=\text{C}$  bond was not reduced in these two cases (the reduction proceeded in a shorter period of time and at greater yields than in [5] where ferrous sulfate was used). We were unsuccessful in reducing 3-(1-nitro-2-naphthal)phthalide (see [5]). The nitro group was not reduced, nor was the  $\text{C}=\text{C}$  bond.

In most cases, the prepared amino derivatives precipitated from the reaction mixture as hydroiodides. However, these amino phthalides are such weak bases that already on crystallizing from dilute ethanol they hydrolyze giving the corresponding amines. In order to complete the hydrolysis, we boiled these hydroiodides with ammonia.

Reduction of the lactone ring of the mentioned substituted phthalides by concentrated hydroiodic acid has not proceeded. It was proved by infrared spectra of the reduction products which showed no absorption band belonging to the free carboxyl group; on the contrary, the band of  $\text{C}-\text{O}-\text{C}$  vibration at  $980-1000\text{ cm}^{-1}$  was visible. On reduction of 6-chloro-3-benzaldehyde, the double  $\text{C}=\text{C}$  bond was reduced only and the corresponding 6-chloro-3-benzylphthalide was obtained. However, the  $\text{C}=\text{C}$  bond of the unsubstituted 3-(1-naphthal)phthalide and 3-benzaldehyde was reduced by 57% hydroiodic acid and the lactone ring opened giving the appropriate substituted benzoic acids. It was proved by infrared spectra which showed a band at  $1700\text{ cm}^{-1}$  belonging to the stretching  $\text{C}=\text{O}$  vibration of carboxyl group; the band of  $\text{C}-\text{O}-\text{C}$  vibration on these spectra has not been observ-

ed. On reduction of 3-(2-naphthal)phthalide under the same conditions, the C=C bond was reduced, while the lactone ring was not opened.

Significant differences in the frequencies  $\nu(\text{CO})$  could be attributed to inter- and intramolecular interactions and to the effect of a substituent. Compounds *V* and *X* ( $\nu(\text{CO}) = 1753, 1760$ ) cannot form either inter- or intramolecular hydrogen bonds. With the compound *I* we take into consideration the intermolecular hydrogen bonds only of N—H...N and N—H...O types and the strong electron-donor effect of  $\text{NH}_2$  group in *p*-position regarding the C=O group what causes the decrease of  $\nu(\text{CO})$  in comparison with the unsubstituted compound *X*. With the compound *III*, in addition to the mentioned effects, the intramolecular hydrogen bonds of carbonyl group with amino group in *o*-position come into consideration. Owing to this fact the further decrease of  $\nu(\text{CO})$  was observed.

## Experimental

Melting points (Kofler) and the other analytical data of the prepared substances are given in Table 1.

Infrared spectra were recorded on a double-beam spectrophotometer UR-20 (Zeiss, Jena) in the region  $650\text{--}3600\text{ cm}^{-1}$ . The examination was carried out by making a fine suspension (mull) of compounds in liquid paraffin (nujol) (thickness 0.02 mm).

### *Reduction of substituted naphthalphthalides by 57% hydroiodic acid*

#### *Procedure A*

Into a 50-ml flask, 3.17 g (0.01 mole) of 5-nitro-3-(1-naphthal)phthalide, 0.6 g of red phosphorus, and 10 ml of 57% hydroiodic acid were introduced and refluxed for 2 hours. After 12 hours' staying, the precipitate was dissolved in dilute ethanol and red phosphorus was filtered by suction. 5-Amino-3-(1-naphthylmethyl)phthalide (*I*) was obtained after recrystallizing from dilute ethanol.

Similarly, 7-amino-3-benzylphthalide (*III*), 6-chloro-3-benzylphthalide (*V*), 2-(2-phenylethyl)benzoic acid (*VIII*), 2-(2-naphthylethyl)benzoic acid (*IX*), and 3-(2-naphthylmethyl)phthalide (*X*) were obtained from the corresponding 7-nitro-3-benzal-phthalide, 6-chloro-3-benzalphthalide, 3-benzalphthalide, 3-(1-naphthal)phthalide, and 3-(2-naphthal)phthalide, respectively.

#### *Procedure B*

Into a 50-ml flask, 2.67 g (0.01 mole) of 4-nitro-3-benzalphthalide, 0.6 g of red phosphorus, and 10 ml of 57% hydroiodic acid were introduced and refluxed for 2 hours. After cooling, the precipitate was sucked off, dissolved in the mixture of toluene—ethanol and red phosphorus was filtered by suction. Hydroiodide of 4-amino-3-benzalphthalide was obtained after evaporation of ethanol. Boiling of hydroiodide with ammonia gave the free amine. Crystallization from methanol afforded yellow crystals of 4-amino-3-benzalphthalide (*II*).

Similarly from 3-(4-nitro-1-naphthal)phthalide and 3-(4-nitrobenzal)phthalide, 3-(4-amino-1-naphthal)phthalide (*VI*) and 3-(4-aminobenzal)phthalide (*VII*) respectively, were obtained.

Table 1

Compound	Formula	<i>M</i>	Calculated/found			Yield [%]	M.p. [°C]	C=O [cm <sup>-1</sup> ]	C=C [cm <sup>-1</sup> ]	C—O—C [cm <sup>-1</sup> ]	NH <sub>2</sub> s/as [cm <sup>-1</sup> ]	
			[% C]	[% H]	[% N]							
<i>I</i>	C <sub>15</sub> H <sub>15</sub> O <sub>2</sub> N	289	78.89 78.50	5.22 5.46	4.82 5.04	78.1	187—189	1744	—	990	3360	3455
<i>II</i>	C <sub>15</sub> H <sub>11</sub> O <sub>2</sub> N	237	—	—	—	68.2	146—148*	1742	1649	1000	3343	3434
<i>III</i>	C <sub>15</sub> H <sub>13</sub> O <sub>2</sub> N	239	75.31 74.94	5.44 5.66	5.84 5.50	83.0	110—111	1722	—	993	3340	3460
<i>IV</i>	C <sub>15</sub> H <sub>11</sub> O <sub>2</sub> N	237	—	—	—	72.2	168—169**	1750	1665	1000	3346 3378	3470 3488
<i>V</i>	C <sub>15</sub> H <sub>9</sub> O <sub>2</sub> Cl	258.5	69.63 69.28	3.48 3.19	13.73 (Cl) 13.96	80.2	112—114	1753	—	998	—	—
<i>VI</i>	C <sub>15</sub> H <sub>13</sub> O <sub>2</sub> N	287	—	—	—	81.0	221—223***	1770	1660	979	3375	3470
<i>VII</i>	C <sub>15</sub> H <sub>11</sub> O <sub>2</sub> N	237	—	—	—	83.5	226—228****	1757	1670	988	3362	3440
<i>VIII</i>	C <sub>15</sub> H <sub>14</sub> O <sub>2</sub>	226	79.64 79.69	6.19 6.33	—	79.2	129—131	1695	—	—	—	—
<i>IX</i>	C <sub>15</sub> H <sub>16</sub> O <sub>2</sub>	276	82.60 82.86	5.80 5.68	—	77.1	148—149	1700	—	—	—	—
<i>X</i>	C <sub>15</sub> H <sub>14</sub> O <sub>2</sub>	274	83.21 83.21	5.10 5.38	—	86.1	125—126	1760	—	998	—	—

\* Ref. [4] gives 148—150°C.

\*\* Ref. [4] gives 168—170°C.

\*\*\* Ref. [3] gives 222—223°C.

\*\*\*\* Ref. [3] gives 228—229°C.

*7-Amino-3-benzalphthalide (IV)*

The starting 7-nitro-3-benzalphthalide was reduced as *I*; however, 35–40% hydroiodic acid was used. The precipitate was crystallized from ethanol and yellow crystals of 7-amino-3-benzalphthalide were obtained.

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