Indane-1,3-dione, Phthalimidine and Phthalide Derivatives as Alkylating Agents

Pier Luigi Barili and Valerio Scartoni*

Istituti di Chimica Farmaceutica e di Chimica Organica, Università di Pisa,
via Bonanno 6, 56100 Pisa, Italy

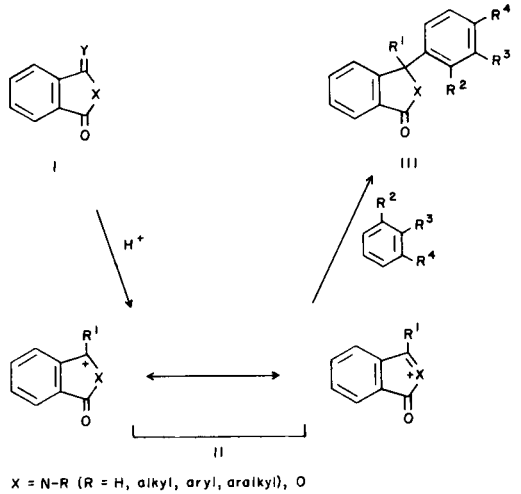
Received October 19, 1984

The title compounds gave carbocations in acid media. The electrophilic aromatic substitution of those carbocations was studied.

J. Heterocyclic Chem., **22**, 1199 (1985).

We wish to disclose our findings for utilizing a simple synthetic route which affords the construction of a carbon-carbon bond in nitrogen or oxygen heterocycles as shown in Scheme 1 [1].

Scheme I



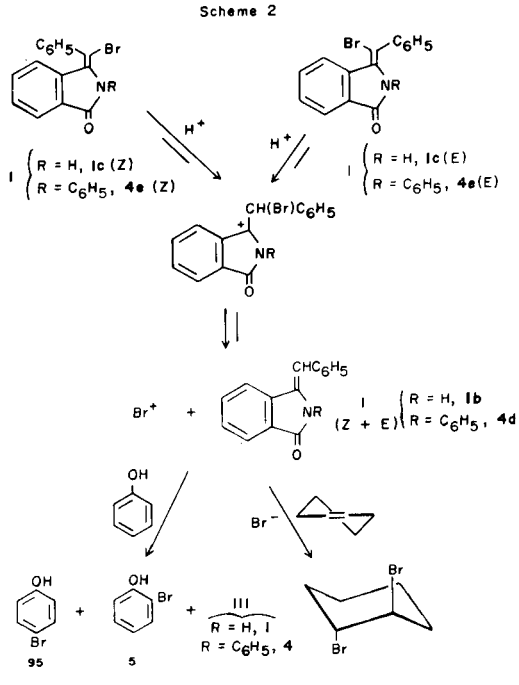
X = N-R (R = H, alkyl, aryl, aralkyl), O
Y = R + OH, R + OCH_3, R + NHC_6H_5, RCH (R = H, alkyl, aryl), RCBr (R = aryl)
R' = H, CH_3, C_6H_5, $CH_2C_6H_5$; R^2 = H, OCH_3; R^3 = H, OCH_3; R^4 = H, OH, OCH_3

The reactive acylimmonium or acyloxonium ions (II) were generated *via* protonation of cyclic enamides (3-alkylidene or aralkylidenephthalimidines) [2] and enesters (3-alkylidene or aralkylidenephthalides) or *via* acid catalysed elimination of HW (water, methanol or aniline) from -X-CW= substituted lactams and lactones [3].

Thus, treating a mixture of phthalimidine or phthalide derivative with the indicated structural requirements and phenol or phenol ether (anisole, veratrole) with a catalytic amount of an inorganic acid (perchloric acid, more generally) at 100° for 1-3 hours yielded the products III presented in Table 1 and Table 2. These may show interesting activity from a pharmaceutical point of view.

In the case of 3-(α-bromobenzylidene)phthalimidines I, **1c** and **4e**, the isolation of *ortho* and *para*-bromophenol and III, **1** and **4**, or *trans*-1,2-dibromocyclohexane and 3-benzylidenephthalimidines I, **1b** and **4d** when treated with phenol or cyclohexene, respectively, in the presence of hydrobromic acid, denotes the formation of a bromonium ion as the first step of the reaction. In the past we observed the acid catalysed *cis-trans* isomerization of 3-(α-bromobenzylidene)phthalimidines [4]. Present results allow the understanding of the behaviour of these compounds with respect to acids, which can be used as a source of bromonium ion (Scheme 2).

Scheme 2



The previously reported analogous reactions are the well known α-amidoalkylation [5], and the Bistrzycki reaction [6], which we have reinvestigated to control the regiochemistry. Nearly all the investigated reactions showed a high regioselectivity and we were able to isolate *para*-substitution products in good yield. Reactants **5** and **10** gave both substitution products, whereas **2, 3** and **16** afforded only *ortho* isomers (Table 1). The assignment of the configurations was based on pmr and cmr spectroscopy. The pmr spectrum of the *para* isomers showed two doublets in almost all cases in the aromatic zone attributable to four symmetric protons. The cmr spectra instead allowed us to solve uncertain cases (Table 3).

Table 1

Reaction Conditions

Reactant No.	Starting product (I) X	Y	Reaction product (III) R^1	R^2	R^3	R^4	Reaction time hours/ml [a]
1a	NH	$C_6H_5CH_2$ + OH	$C_6H_5CH_2$	H	H	OH	2/0.2
1b	NH	C_6H_5CH	$C_6H_5CH_2$	H	H	OH	2/0.2
1c	NH	C_6H_5CBr	$C_6H_5CH_2$	H	H	OH	3/4 [b]
2	NCH_3	H + OH	H	OH	H	H	2.5/0.2
3	NC_6H_5	H + OH	H	OH	H	H	4/0.2
4a	NC_6H_5	$C_6H_5CH_2$ + OH	$C_6H_5CH_2$	H	H	OH	2.5/0.2
4b	NC_6H_5	$C_6H_5CH_2$ + OCH_3	$C_6H_5CH_2$	H	H	OH	2.5/0.2
4c	NC_6H_5	$C_6H_5CH_2$ + NHC_6H_5	$C_6H_5CH_2$	H	H	OH	3/2 [b]
4d	NC_6H_5	C_6H_5CH	$C_6H_5CH_2$	H	H	OH	2.5/0.2
4e	NC_6H_5	C_6H_5CBr	$C_6H_5CH_2$	H	H	OH	2/0.05
5	$NCH_2C_6H_5$	H + OH	H	H	H	OH	2.5/0.2
			H	OH	H	H	
6	$NCH_2C_6H_5$	CH_2	CH_3	H	H	OH	3/0.1 [b]
7	$NCH_2C_6H_5$	C_6H_5CH	$C_6H_5CH_2$	H	H	OH	2/0.2
8	$NCH_2CH_2C_6H_5$	C_6H_5CH	$C_6H_5CH_2$	H	H	OH	2/0.2
9	NCH_2CH_2OH	H + OH	H	H	OCH_3	OCH_3	12/5 [c]
10	NCH_2CH_2OH	CH_2	CH_3	H	H	OH	12/1 [c]
			CH_3	OH	H	H	
11	NCH_2CO_2H	C_6H_5CH	$C_6H_5CH_2$	H	H	OH	2/0.2
12	NCH_2CO_2H	C_6H_5CH	$C_6H_5CH_2$	H	OCH_3	OCH_3	3/0.2
13a	O	H + OH	H	H	H	OH	1.5/0.05
13b	O	H + OH	H	H	H	OH	23/2 [c]
14	O	H + OH	H	H	H	OCH_3	1.5/0.05
15	O	H + OH	H	H	OCH_3	OCH_3	1.5/0.05
16	O	CH_3 + OH	CH_3	OCH_3	H	H	2/0.05
17	O	C_6H_5 + OH	C_6H_5	H	H	OH	2/0.05
18a	O	$C_6H_5CH_2$ + OH	$C_6H_5CH_2$	H	H	OH	2.5/0.2
18b	O	C_6H_5CH	$C_6H_5CH_2$	H	H	OH	2.5/0.2

[a] Volume (ml) of 70% perchloric acid, unless otherwise indicated, for 1 g of the substrate (I). [b] 48% Hydrobromic acid. [c] 37% Hydrochloric acid.

Table 2

MP, Yields and Analytical Data

Compound III No.	Molecular Formula	Mp, °C [x]	Yield %	Analyses, Calcd./Found, % C	H	N
1	$C_{21}H_{17}NO_2$	273-275 [a]	78	79.98/80.12	5.43/5.57	4.44/4.27
2	$C_{15}H_{13}NO_2$	238-239 [a]	52	75.30/75.23	5.48/5.49	5.85/5.80
3	$C_{20}H_{15}NO_2$	295-297 [c]	61	79.71/79.92	5.02/5.05	4.65/4.44
4	$C_{27}H_{21}NO_2$	267-269 [a]	80	82.84/83.10	5.41/5.70	3.58/3.59
5 *p*-isomer	$C_{21}H_{17}NO_2$	237-239 [a]	51	79.98/80.12	5.44/5.64	4.44/4.18
5 *o*-isomer	$C_{21}H_{17}NO_2$	170-171 [a]	31	79.98/80.05	5.44/5.59	4.44/4.25
6	$C_{22}H_{19}NO_2$	266-268 [a]	53	80.22/80.46	5.77/5.59	4.25/4.48
7	$C_{28}H_{23}NO_2$	210-212 [b]	83	82.94/82.92	5.72/5.78	3.45/3.17
8	$C_{29}H_{25}NO_2$	222-224 [b]	81	83.03/82.95	6.01/6.25	3.34/3.36
9	$C_{18}H_{19}NO_4$	181-183 [b]	78	68.99/68.97	6.11/6.10	4.47/4.37
10 *p*-isomer	$C_{17}H_{17}NO_3$	247-249 [d]	32	72.07/71.93	6.05/6.02	4.94/4.92
10 *o*-isomer	$C_{17}H_{17}NO_3$	220-222 [d] + [e]	17	72.07/71.95	6.05/6.09	4.94/4.90
11	$C_{23}H_{19}NO_4$	271-273 [b]	75	73.98/74.14	5.13/5.03	3.75/3.78
12	$C_{25}H_{23}NO_5$	156-158 [b]	82	71.93/71.95	5.55/5.27	3.36/3.48
13	$C_{14}H_{10}O_3$	156-158 [b]	65	74.33/74.60	4.46/4.18	
14	$C_{15}H_{12}O_3$	115-117 [b]	70	74.99/75.07	5.03/5.01	
15	$C_{16}H_{14}O_4$	147-149 [b]	71	71.10/71.40	5.22/5.43	
16	$C_{16}H_{14}O_3$	144-145 [b]	15	75.57/75.33	5.55/5.69	
17	$C_{20}H_{14}O_3$	214-216 [b]	81	79.45/79.54	4.47/4.46	
18	$C_{21}H_{16}O_3$	187-189 [b]	83	79.73/80.01	5.10/5.31	

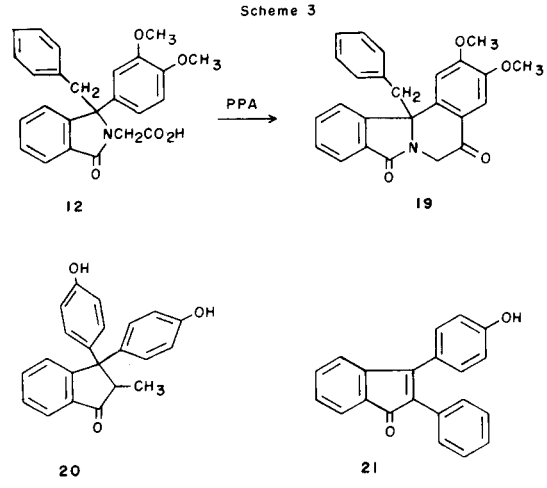
[x] Crystallization solvent. [a] Methanol. [b] Ethanol. [c] Ethyl acetate. [d] Ethyl ether.

Table 3

Compound	IR ν (cm^{-1}), PMR and CMR δ (ppm) Data
1	ir: 3220 (NH + OH), 1660 (CO); pmr: 3.6 (s, CH_2, 2H), 6.83 (d, aromatic, 2H, J = 9 Hz), 6.82-7.2 (m, aromatic, 5H), 7.25-7.47 (m, aromatic, 4H), 7.37 (d, aromatic, 2H, J = 9 Hz), 8.8 (s, NH, 1 exchangeable H), 9.2 (s, OH, 1 exchangeable H)
2	ir: 3090 (OH), 1670 (CO); pmr: 2.97 (s, 3H, NCH_3), 5.95 (s, 1H, CH), 6.57-6.81 (m, aromatic, 2H), 6.85-7.16 (m, aromatic, 2H), 7.27-7.6 (m, aromatic, 3H), 7.93 (m, aromatic, 1H), 9.47 (s, OH, 1 exchangeable H); cmr: 167.69 (CO), 155.71, 146.70, 126.78 (3 quaternary aromatic C [a]), 131.50, 128.96, 127.85, 123.01, 122.88, 122.51, 119.42, 115.88 (8 aromatic C), 59.93 (1 quaternary aliphatic C), 27.13 (1 aliphatic C, CH_3)
3	ir: 3150 (OH), 1670 (CO); pmr: 6.33-8.0 (m, aromatic, 13H and aliphatic, 1H, CH), 9.8-10.0 (broad OH, 1 exchangeable H); cmr: 167.10 (CO), 155.33, 146.39, 137.85, 132.56, 123.69 (5 quaternary aromatic C), 128.82, 128.60, 128.27, 124.28, 123.25, 122.96, 121.71, 119.41, 115.89 (9 non equivalent aromatic C), 58.61 (1 quaternary aliphatic C)
4	ir: 3270 (OH), 1655 (CO); pmr: 3.73 (d, CH_2, 1H, J = 15 Hz), 4.06 (d, CH_2, 1H), 6.4 (m, aromatic, 2H), 6.87 (d, aromatic, 2H, J = 9 Hz), 6.97-7.9 (m, aromatic, 7H), 7.27 (d, aromatic, 2H), 7.30 (s, aromatic, 5H)
5	(*para*-isomer) ir: 3170 (OH), 1670 (CO); pmr: 3.77 (d, CH_2, 1H, J = 15 Hz), 5.07 (d, CH_2, 1H), 5.36 (s, CH, 1H), 6.72 (d, aromatic, 2H, J = 9 Hz), 6.91 (d, aromatic, 2H), 6.99-7.39 (m, aromatic, 6H), 7.46-7.58 (m, aromatic, 2H), 7.73-7.85 (m, aromatic, 1H), 9.53 (s, OH, 1 exchangeable H)
5	(*ortho*-isomer) ir: 3170 (OH), 1670 (CO); pmr: 3.83 (d, CH_2, 1H, J = 15 Hz), 5.15 (d, CH_2, 1H), 5.82 (s, CH, 1H), 6.70-7.41 (m, aromatic, 10H), 7.44-7.56 (m, aromatic, 2H), 7.72-7.84 (m, aromatic, 1H), 9.81 (s, OH, 1 exchangeable H); cmr: 167.85 (CO), 155.84, 146.84, 131.17, 122.62 (4 quaternary aromatic C [a]), 137.32, 131.86, 129.18, 128.53, 128.05, 127.66, 127.21, 123.12, 122.93, 119.51, 115.99 (11 non equivalent aromatic C), 57.53 (1 quaternary aliphatic C), 43.44 (1 aliphatic C, CH_2)
6	ir: 3100 (OH), 1635 (CO); pmr: 1.65 (s, CH_3, 3H), 3.91 (d, CH_2, 1H, J = 16.5 Hz), 5.04 (d, CH_2, 1H, J = 16.5 Hz), 6.8 (d, aromatic, 2H, J = 9 Hz), 7.15 (d, aromatic, 2H), 7.15-7.70 (m, aromatic, 3H), 7.35 (s, aromatic, 5H), 8.0 (m, aromatic, 1H), 9.5 (s, OH, 1 exchangeable H)
7	ir: 3050 (OH), 1640 (CO); pmr: 3.69 (d, CH_2, 1H, J = 15 Hz), 4.07 (d, CH_2, 1H), 4.53 (d, NCH_2, 1H, J = 16 Hz), 4.90 (d, NCH_2, 1H), 6.75 (d, aromatic, 2H, J = 9 Hz), 7.14 (d, aromatic, 2H), 7.30 (s, aromatic, 5H), 6.62-7.82 (m, aromatic, 9H), 9.5 (s, OH, 1 exchangeable H)
8	ir: 3100 (OH), 1640 (CO); pmr: 2.45-4.2 (two overlapped signals $3CH_2$, 6H), 6.5-7.75 (m, aromatic, 18H), 9.37 (s, OH, 1 exchangeable H)
9	ir: 3425 (OH), 1640 (CO); pmr, 3.85 (s, OCH_3, 3H), 3.97 (s, OCH_3, 3H), 3.7-4.25 (m, CH_2CH_2, 4H), 5.7 (s, CH, 1H), 6.65 (s, aromatic, 1H), 7.0 (s, aromatic, 2H), 7.2-7.45 (m, aromatic, 1H), 7.45-7.75 (m, aromatic, 2H), 7.9-8.15 (m, aromatic, 1H), 9.31 (s, OH, 1 exchangeable H)
10	(*para*-isomer) ir: 3150 (OH), 1650 (CO); pmr: 1.9 (s, CH_3, 3H), 3.27-3.73 (m, CH_2CH_2, 4H), 6.73 (d, aromatic, 2H, J = 9 Hz), 7.0 (d, aromatic, 2H), 7.13-7.93 (m, aromatic, 4H), 9.3 (s, OH, 1 exchangeable H); cmr: 167.46 (CO), 157.06, 152.53, 130.06, 129.57 (4 quaternary aromatic C), 132.37, 128.01, 127.48, 122.79, 122.24, 115.46 (6 non equivalent aromatic C), 66.84 (1 quaternary aliphatic C), 41.55, 40.71 (2 aliphatic C, CH_2CH_2), 23.17 (1 aliphatic C, CH_3)
10	(*ortho*-isomer) ir: 3130 (OH), 1640 (CO); pmr: 1.9 (s, CH_3, 3H), 3.3 (s, OH, 1 exchangeable H), 3.1-3.8 (m, CH_2CH_2, 4H), 6.46-7.93 (m, aromatic, 8H), 9.03 (s, OH, 1 exchangeable H); cmr: 168.52 (CO), 155.68, 151.69, 131.56, 124.61 (4 quaternary aromatic C), 131.65, 129.72, 128.85, 127.44, 122.28, 121.41, 118.24, 116.24 (8 non equivalent aromatic C), 66.01 (1 quaternary aliphatic C), 41.93, 40.74 (2 aliphatic C, CH_2CH_2), 25.67 (1 aliphatic C, CH_3)
11	ir: 3020 (OH), 1640, 1700 (CO); pmr: 3.72 (s, CH_2, 2H), 4.3 (d, NCH_2, 1H, J = 15 Hz), 4.9 (d, NCH_2, 1H), 6.77 (d, aromatic, 2H, J = 9 Hz), 7.27 (d, aromatic, 2H), 6.5-7.75 (m, aromatic, 9H), 9.1 (broad s, 2 OH, 2 exchangeable H)
12	ir: 3250 (OH), 1660, 1740 (CO); pmr: 3.75 (s, 2 OCH_3, 6H), 3.91 (s, CH_2, 2H), 3.79 (d, NCH_2, 1H, J = 17 Hz), 4.37 (d, NCH_2, 1H), 4.85 (s, OH, 1 exchangeable H), 6.5-7.85 (m, aromatic 12H)
13	ir: 3100 (OH), 1700 (CO); pmr: 6.6 (s, CH, 1H), 6.92 (d, aromatic, 2H, J = 9 Hz), 7.21 (d, aromatic, 2H), 7.37-8.2 (m, aromatic, 4H), 9.3 (s, OH, 1 exchangeable H)
14	ir: 1725 (CO); pmr [b]: 3.92 (s, OCH_3, 3H), 6.55 (s, CH, 1H), 7.07 (d, aromatic, 2H, J = 9 Hz), 7.62 (d, aromatic, 2H), 7.35-8.42 (m, aromatic, 10H)
15	ir: 1720 (CO); pmr [b]: 3.88 (s, OCH_3, 3H), 3.96 (s, OCH_3, 3H), 6.5 (s, CH, 1H), 6.82 (s, aromatic, 1H), 7.0 (s, aromatic, 2H), 7.35-7.6 (m, aromatic, 1H), 7.6-7.9 (m, aromatic, 2H), 8.0-8.25 (m, aromatic, 1H)
16	ir: 1735 (CO); pmr [b]: 2.01 (s, CH_3, 3H), 3.54 (s, OCH_3, 3H), 6.88-7.09 (m, aromatic, 2H), 7.26-7.90 (m, aromatic, 6H); cmr: 169.56 (CO), 157.17, 154.24, 127.58, 125.48 (4 quaternary aromatic C), 134.17, 130.33, 128.90, 126.77, 124.54, 121.92, 120.44, 112.69 (8 non equivalent aromatic C), 86.43 (1 quaternary aliphatic C), 55.41 (1 aliphatic C, OCH_3), 26.16 (1 aliphatic C, CH_3)
17	ir: 3250 (OH), 1705 (CO); pmr [b]: 6.87 (d, aromatic, 2H, J = 9 Hz), 7.2 (d, aromatic, 2H), 7.4 (s, aromatic, 5H), 7.5-8.15 (m, aromatic, 4H)
18	ir: 3250 (OH), 1680 (CO); pmr: 3.72 (s, CH_2, 2H), 7.0 (d, aromatic, 2H, J = 9 Hz), 7.55 (d, aromatic, 2H), 6.97-7.95 (m, aromatic, 9H), 9.37 (s, OH, 1 exchangeable H)

[a] One quaternary aromatic C signal is casually overlapped. [b] Deuteriochloroform as the solvent.

Scheme 3



In some instances reaction products III may be important as synthons to achieve bridgehead nitrogen heterocycles: 3-benzyl-3-(3',4'-dimethyloxyphenyl)phthalimidin-2-ylacetic acid (**12**) was easily converted into the 13-benzyl-5,6-dihydro-2,3-dimethoxy-8*H*-isoindolo[1,2-*a*]isoquinoline-5,8-dione (**19**) (Scheme 3). This method represents an alternative to a Pictet-Spengler type ring closure which starts from 3-benzylidene-2-(β-phenylethyl)phthalimidines [7].

With the aim of extending the field of this reaction we have tried to employ 2-substituted indane-1,3-diones as substrates. First, we chose the 2-methyl and 2-phenylindane-1,3-diones from which compounds **20** and **21** were obtained respectively as the predominant products in the reaction with phenol. Interestingly, the absence in these structures of the heteroatom which exerts a stabilizing effect on the intermediate carbocation II, does not hinder the alkylation. However this argument would deserve further investigation.

EXPERIMENTAL

All melting points are taken on a Kofler apparatus and are uncorrected. The ir spectra were determined in nujol mulls with a Perkin-Elmer 197 spectrometer. The nmr spectra were obtained with a Varian EM 360 and CFT 20 spectrometers. A deuteriochloroform and DMSO-d_6 mixture was used as the solvent in the pmr spectra unless otherwise indicated with TMS as an internal standard. For the cmr spectra DMSO-d_6 was the solvent.

α-Carbinol Lactams I, **2**, **3**, **5**, **9**.

These compounds were obtained by sodium borohydride reduction of the appropriate phthalimide according to Speckamp [3].

3-Methylidenephthalimidines I, **6**, **10**.

These compounds were prepared by heating *o*-acetylbenzoic acid and the appropriate amine for 30 minutes at 150°.

General Procedure for the Preparation of Compounds III.

To a mixture of compound I (1 g) and phenol or phenol ether (2 g) the inorganic acid indicated in Table 1 was added at 100°. Reaction times are also listed in Table 1. Reaction mixtures containing phenol were diluted and repeatedly washed with water, whereas those of phenol ether (1:10 v/v) with dichloromethane-petroleum ether. Successive addition of crystallization solvent to the oily residue allowed us to obtain the products III.

Reaction of 3-(α-Bromobenzylidene)phthalimidines with Acids.

1) In the Presence of Phenol.

The reaction mixture obtained by heating **1c** (1.5 g, 5 mmoles), phenol (2 g, 21.3 mmoles) and 48% hydrobromic acid (6 ml) for 2 hours at 100°, was evaporated at reduced pressure. The mixture was then treated with dimethyl sulfate (3.3 ml) in methanol (30 ml) in the presence of potassium carbonate (6.7 g) and stirred for 30 minutes at room temperature. Filtration, evaporation and dilution of the residue with ethyl ether and elution on alumina (II-III) with dichloromethane-petroleum ether (1:1 v/v) gave from the first collected fractions *ortho* and *para*-bromanisole (5:95, gc analysis, 0.34 g, 36%).

2) In the Presence of Cyclohexene.

Compound **1c** (0.3 g, 1 mmole), cyclohexene (1.65 g, 2 mmoles) and 48% hydrobromic acid (1.2 ml) were heated in a sealed tube at 100° for 3 hours. Dilution with petroleum ether gave 3-benzylidenephthalimidine (I, **1b**) (0.21 g, 95%). The organic layer was washed with water and evaporated at reduced pressure. The oily residue was eluted on alumina with petroleum ether obtaining *trans*-1,2-dibromocyclohexane (0.22 g, 84%, gc analysis).

13-Benzyl-5,6-dihydro-2,3-dimethoxy-8*H*-isoindolo[1,2-*a*]isoquinoline-5,8-dione (**19**).

A mixture of finely ground **12** (5.0 g, 12 mmoles) and polyphosphoric acid (100 g) was heated at 100° for 1.5 hours. After cooling, the reaction mixture was poured into water (1 ℓ) causing the separation of crude **19** which was recrystallized from ethanol (4.3 g, 90%), mp 229-231°; ir: 1650, 1665 (CO); pmr: δ 3.51 (s, CH_2, 2H), 4.0 (s, OCH_3, 3H), 4.05 (s, OCH_3, 3H), 4.06 (d, NCH_2, 1H, J = 19 Hz), 5.35 (d, NCH_2, 1H), 6.7-8.2 (m, aromatic, 11H).

Anal. Calcd. for $C_{25}H_{21}NO_4$: C, 74.40; H, 5.46; N, 3.62. Found: C, 74.67; H, 5.38; N, 3.41.

2-Methyl-3,3-di-(4'-hydroxyphenyl)indan-1-one (**20**).

2-Methylindane-1,3-dione (1 g, 6.25 mmoles) and phenol (4 g, 42.5 mmoles) were treated with 70% perchloric acid (0.2 ml) and heated at 100° for 2.5 hours. Dilution with water and stirring left an oily residue which solidified with ethanol giving a white solid (1.5 g, 72%), mp 222-224°; ir: 3275 (OH), 1630 (CO); pmr: δ 0.96 (d, CH_3, 3H, J = 7.5 Hz), 3.5 (q, CH, 1H), 6.75 (s, aromatic, 4H), 6.9 (d, aromatic, 2H, J = 7.5 Hz), 7.36 (d, aromatic, 2H), 7.40-7.70 (m, aromatic, 4H), 9.05 (s, OH, 1 exchangeable H), 9.15 (s, OH, 1 exchangeable); cmr: 206.32 (CO), 158.31, 134.61, 127.96, 127.08 (4 quaternary aromatic C), 156.06, 155.73 (2 aromatic C, C-OH), 135.55, 135.10, 134.94, 130.11, 128.97, 122.75, 115.19, 114.61 (8 non equivalent aromatic C), 58.67 (1 quaternary aliphatic C), 54.38 (1 aliphatic C, CH), 12.41 (1 aliphatic C, CH_3).

Anal. Calcd. for $C_{22}H_{18}O_3$: C, 79.98; H, 5.49. Found: C, 79.71; H, 5.60.

2-Phenyl-3-(4'-hydroxyphenyl)indan-1-one (**21**).

2-Phenylindane-1,3-dione (1 g, 4.5 mmoles) and phenol (1 g, 10.6 mmoles) were treated with 70% perchloric acid (0.5 ml). The mixture was heated at 100° for 2.5 hours, then diluted with dichloromethane (50 ml) and washed with sodium bicarbonate and dried over anhydrous sodium sulfate. After removal of the solvent, the residue was recrystallized from ethanol giving 0.95 g (70%) of red prisms, mp 289-291° [8]; ir: 3180 (OH), 1660 (CO); pmr: δ 6.97 (d, aromatic, 2H, J = 9 Hz), 7.2-7.5 (m, aromatic, 6H), 7.45 (s, aromatic, 5H), 9.67 (s, OH, 1 exchangeable).

Anal. Calcd. for $C_{21}H_{14}O_2$: C, 84.54; H, 4.73. Found: C, 84.79; H, 4.51.

REFERENCES AND NOTES

[1] A part of this work was presented at the IVth Convegno Nazionale, Divisione di Chimica Farmaceutica, Palermo, 18-22/10/1983.

[2] V. Scartoni and T. Tognetti, *J. Heterocyclic Chem.*, **21**, 1499 (1984).

[3] J. C. Hubert, W. N. Speckamp and H. O. Huisman, *Tetrahedron Letters*, 4493 (1972); J. B. P. A. Wijnberg, W. N. Speckamp and H. E. Schoemaker, *Tetrahedron Letters*, 4073 (1974); J. B. P. A. Wijnberg and W. N. Speckamp, *Tetrahedron Letters*, 3963 (1975); J. B. P. A. Wijnberg and W. N. Speckamp, *Tetrahedron Letters*, 4035 (1975); J. J. J. de Boer and W. N. Speckamp, *Tetrahedron Letters*, 4039 (1975); J. Dijkink, H. E. Schoemaker and W. N. Speckamp, *Tetrahedron Letters*, 4043 (1975); J. Dijkink and W. N. Speckamp, *Tetrahedron Letters*, 4047 (1975); J. C. Hubert, J. B. P. A. Wijnberg and W. N. Speckamp, *Tetrahedron*, **31**, 1437 (1975).

[4] A. Marsili and V. Scartoni, *Gazz. Chim. Ital.*, **102**, 806 (1972).

[5] H. E. Zaugg, *Synthesis*, **2**, 85 (1984); H. E. Zaugg, *Synthesis*, **3**, 181 (1984).

[6] A. Bistrzycki and S. Zen-Ruffinen, *Helv. Chim. Acta*, **6**, 750 (1923) and references cited therein; J. Gronowska, *Rocz. Chem.*, **39**, 245 (1965); *Chem. Abstr.*, **63**, 11737f (1965).

[7] V. Scartoni, R. Fiaschi, E. Napolitano, L. Pistelli and A. Marsili, *Atti I Convegno Nazionale Divisione Chimica Farmaceutica S.C.I.*, 13-15/12/1979, p 100.

[8] D. Dalev and L. Velichkov, *Nauch. Trudove Visshiya Med. Inst. Sofiya*, **6**, 11 (1959); *Chem. Abstr.*, **54**, 18453 (1960), mp 248-249°.