2-BENZOPYRYLIUM SALTS

XVII.* SYNTHESIS OF INDENO-2-BENZOPYRYLIUM SALTS AND INDENOISOQUINOLINES

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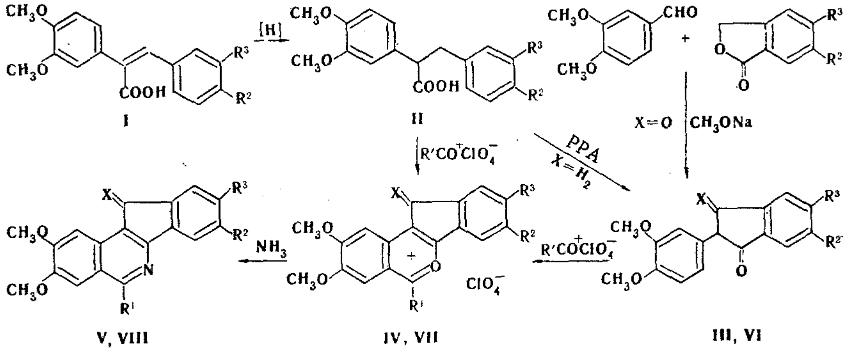
UDC 547.814:833.07

2-Veratryl-5,6-dimethoxyindanone and 2-veratrylindane-1,3-dione, respectively, were obtained by intramolecular acylation of α,β-diveratrylpropionic acid and condensation of veratraldehyde with phthalide in strongly alkaline media. A method was worked out for the synthesis of indeno[1,2-c]-2-benzopyrylium salts, from which indeno[1,2-c]isoquinolines are formed in good yields.

We have previously synthesized 11-aryl-11H-indeno[1,2-c]-2-benzopyrylium salts and have shown the possibility of preparation from them of 11-aryl-11H-indeno[1,2-c]isoquinolines [2], the structure of which is close to that of the opium alkaloid cryptopine [3]. The method differs favorably from the previously described syntheses of similar structures [4-6] with respect to its simplicity, the accessibility of the starting compounds, and the high yields.

In the present research we have extended the limits of applicability of the method by accomplishing the synthesis of indeno- and oxoindenoisoquinolines. For this, 2-veratryl-5,6-dimethoxyindanone (III) was obtained by reduction of α-(3,4-dimethoxyphenyl)-3,4-dimethoxycinnamic acid (I) and subsequent cyclization in polyphosphoric acid (PPA). Acylation of ketone III with aliphatic acid anhydrides in the presence of $HClO_4$ gave 4,5,8,9-tetramethoxyindeno[1,2-c]-2-benzopyrylium salts (IV) – brightly colored, high-melting substances, the IR spectra of which contain a number of characteristic absorption bands at 1620, 1600-1610, 1540-1547, 1460-1463, and 1429-1430 cm^{-1}.†

Like 11-aryl-11H-indeno[1,2-c]-2-benzopyrylium salts, salts IV exchange an oxonium oxygen atom for a nitrogen atom only on treatment with an alcohol solution of ammonia under pressure to give 1-alkyl-4,5,8,9-tetramethoxyindeno[1,2-c]isoquinolines (V).



III, IV, V $X=H_2$; VI, VII, VIII $X=O$

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* See [1] for communication XVI.

† Salts IV can be obtained in somewhat lower yields by direct acylation of acid II.

Rostov State University. Scientific-Research Institute of Physical and Organic Chemistry, Rostov-on-Don. Translated from Khimiya Geterotsiklicheskikh Soedinenii, No. 1, pp. 25-28, January, 1975. Original article submitted March 4, 1974.

TABLE 1. Indeno[1,2-c]-2-benzopyrylium Perchlorate

Compound	X	R¹	R²	R³	mp, °C	Color	Empirical formula	Found, %			Calculated, %			Yield, %
								C	H	Cl	C	H	Cl	
IVa	H_2	CH_3	CH_3O	CH_3O	308—309	Orange	$C_{21}H_{21}O_3Cl$	55,8	4,9	7,6	55,7	4,7	7,9	87
IVb	H_2	C_2H_5	CH_3O	CH_3O	286	Bright-red	$C_{22}H_{23}O_9Cl$	56,7	4,9	7,1	56,6	5,0	7,6	80
IVc	H_2	C_3H_7	CH_3O	CH_3O	270	Dark-red	$C_{23}H_{25}O_9Cl$	57,3	5,0	6,9	57,5	5,2	7,4	75
IVd	H_2	C_4H_9	CH_3O	CH_3O	255—256	" "	$C_{24}H_{27}O_9Cl$	58,0	5,5	7,6	58,2	5,5	7,2	69
IVe*	H_2	3,4-$(CH_3O)_2$—C_6H_3	CH_3O	CH_3O	235—236	" "	$C_{28}H_{27}O_{11}Cl$	58,5	4,8	6,5	58,5	4,7	6,2	62
VIIa	O	CH_3	H	H	232—233	Light-brown	$C_{19}H_{15}O_8Cl$	56,3	4,1	8,5	56,1	3,7	8,1	90
VIIb	O	C_2H_5	H	H	223—224	" "	$C_{20}H_{17}O_8Cl$	57,3	4,6	8,2	57,0	4,4	8,4	70
VIIc	O	C_4H_9	H	H	214—215	Light-orange	$C_{22}H_{21}O_8Cl$	58,9	4,6	8,2	58,8	4,7	7,9	53

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*Salt IVe was obtained by acylation of indanone III with veratrylic acid in PPA.

TABLE 2. Indeno[1,2-c]isoquinolines

Compound	X	R¹	R²	R³	mp, °C	Color	Empirical formula	Found, %			Calculated, %			Yield, %
								C	H	N	C	H	N	
Va	H_2	C_8H_7	CH_3O	CH_3O	217—218	Colorless	$C_{23}H_{25}O_4N$	72,8	6,7	3,9	72,9	6,6	3,7	43
Vb	H_2	C_4H_9	CH_3O	CH_3O	214—215	Colorless	$C_{24}H_{27}O_4N$	73,3	6.9	3,4	73,3	6,9	3,6	57
VIIIa	O	CH_3	H	H	225—226	Yellow-orange	$C_{19}H_{15}O_3N$	74,9	5,1	4,7	74,8	4,9	4,6	91
VIIIb	O	C_2H_5	H	H	207—208	Orange	$C_{20}H_{17}O_3N$	74,9	5,1	4,5	75,3	5,3	4,4	93
VIIIc	O	C_4H_9	H	H	194—195	Light-brown	$C_{22}H_{21}O_3N$	75,8	5,8	4,3	76,1	6,1	4,1	83

Acylation of 2-veratrylindane-1,3-dione (VI) with aliphatic acid anhydrides in the presence of $HClO_4$ gives high yields of 1-alkyl-8,9-dimethoxy-11-oxoindeno[1,2-c]-2-benzopyrylium salts VII, which are brightly colored, high-melting substances, the IR spectra of which contain an intense absorption band at 1720-1730 cm^{-1} (C = O) and a number of characteristic bands at 1620-1625, 1597-1600, 1539-1540, and 1460-1465 cm^{-1}. It is interesting to note that, in contrast to salts IV, salts VII form isoquinolines VIII even when they are treated with ammonium hydroxide.

As compared with pyrylium salt VII, the absorption band of the carbonyl group in the IR spectra of isoquinolines VIII lies at 1695-1705 cm^{-1}; this can be explained by the absence of conjugation with the positively charged ring. This assumption is confirmed by the reverse shift of the C = O band to the shortwave region by 15-25 cm^{-1} in the case of quaternary salts obtained by the addition of 70% $HClO_4$ to a solution of isoquinoline VIII in chloroform.

The easier replacement of the oxonium oxygen atom by nitrogen in salts VII as compared with salts IV is explained, in our opinion, by conjugation of the carbonyl group and the absence of donor methoxy groups in the 4 and 5 positions; this leads to an increase in the positive charge of the cation and, on the whole, to facilitation of nucleophilic attack on the $C_{(1)}$ atom of the pyrylium ring.

EXPERIMENTAL

The IR spectra of mineral oil suspensions of the compounds were recorded with a UR-20 spectrometer.

α,β-Diveratrylpropionic Acid (II). This compound was obtained in 93% yield by a method similar to that in [8]. The colorless crystals had mp 137° (alcohol). Found: C 65.6; H 6.4%. $C_{19}H_{22}O_6$. Calculated: C 65.9; H 6.4%. IR spectrum: 1700, 1589, and 1520 cm^{-1}.

5,6-Dimethoxy-2-veratrylindanone (III). A 6.9-g (0.02 mole) sample of acid II was heated in 60 g of PPA at 100° with vigorous stirring for 30 min. After hydrolysis of the reaction mixture, the resulting precipitate was removed by filtration and dried to give 6.5 g (95%) of colorless crystals with mp 134° (alcohol). Found: C 69.8; H 6.3%. $C_{19}H_{20}O_5$. Calculated: C 69.6; H 6.1%. IR spectrum: 1692, 1589, and 1503 cm^{-1}.

2-Veratrylindane-1,3-dione (VI). This compound was obtained in 89% yield by a method similar to that in [7]. The colorless crystals had mp 195-196° (alcohol). Found: C 72.0; H 5.4%. $C_{17}H_{14}O_4$. Calculated: C 72.4; H 5.0%. IR spectrum: 1737, 1695, 1585, and 1512 cm^{-1}.

1-Methyl-4,5,8,9-tetramethoxyindeno[1,2-c]-2-benzopyrylium Perchlorate (IVa). A) A 0.33-g (1 mmole) sample of III was dissolved in 5 ml of acetic anhydride, and 0.5 ml of 70% $HClO_4$ was added dropwise with cooling and stirring. The resulting precipitate was removed by filtration and washed with acetic acid and ether. The resulting orange crystals were recrystallized from nitromethane.

Salts IVb-d were similarly synthesized (Table 1).

B) A 0.345-g (1 mmole) sample of acid II was refluxed in 5 ml of acetic anhydride for 10 min, after which the mixture was cooled, and 0.5 ml of 70% $HClO_4$ was added dropwise with stirring and cooling. The resulting precipitate was removed by filtration and washed with acetic acid and ether to give 0.35 g (80%) of the salt.

1-Methyl-8,9-dimethoxy-11-oxoindeno[1,2-c]-2-benzopyrylium Perchlorate (VIIa). A 0.5-ml sample of 70% $HClO_4$ was added with stirring to a suspension of 0.5 g (17 mmole) of indanedione VI in 5 ml of acetic anhydride, and the mixture was heated for 10 min on a boiling-water bath. It was then cooled, and the precipitated salt was removed by filtration and washed with ether to give 0.65 g (90%) of light-brown crystals with mp 232-233° (glacial acetic acid).

Salts VIIb,c were similarly synthesized (Table 1).

1-Propyl-4,5,8,9-tetramethoxyindeno[1,2-c]isoquinoline. Ethanol (10 ml) was added to 0.48 g (1 mmole) of 1-propyl-4,5,8,9-tetramethoxyindeno[1,2-c]-2-benzopyrylium perchlorate, and the suspension was placed in an ampul, cooled (to −10°), and saturated with ammonia. The sealed ampul was heated at 100° for 6 h. It was then cooled and opened, and the resulting colorless crystals were removed by filtration. The yield of product with mp 217-218° (benzene) was 0.16 g (43%). IR spectrum: 1615, 1591, 1514, and 1425 cm^{-1}.

Isoquinoline Vb was similarly obtained (Table 2).

1-Methyl-8,9-dimethoxy-11-oxoindeno[1,2-c]isoquinoline. Concentrated ammonium hydroxide (5 ml) was added to 0.3 g (0.75 mmole) of 1-methyl-8,9-dimethoxy-11-oxoindeno[1,2-c]-2-benzopyrylium perchlorate. After a few minutes, a precipitate formed from the bright-red solution; the precipiate was removed by filtration, washed with water, and dried. The yield of yellow-orange crystals with mp 225-226° (glacial acetic acid) was 0.2 g (91%). IR spectrum: 1705, 1620, 1610, 1570, and 1510 cm^{-1}.

Isoquinolines VIIIb and VIIIc were similarly obtained (Table 2).

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