- 7. A. W. Baker, J. Phys. Chem., <u>62</u>, 744 (1958).
- 8. G. I. Kagan, V. A. Kosobutskii, V. K. Belyakov, and O. G. Tarakanov, Khim. Geterotsikl. Soedin., No. 8, 1048 (1972).
- 9. Yu. A. Zhdanov and V. I. Minkin, Correlation Analysis in Organic Chemistry [in Russian], Rostov-on-Don (1966), p. 384.
- M. M. Kremlev, N. E. Kul'chitskaya, A. D. Biba, and V. T. Dorofeev, Khim. Tekhnol. Resp. Mezhved. Temat. Nauchno-Tekhn. Sb., <u>23</u>, 27 (1971).
- 11. O. A. Yuzhanova, V. F. Bystrov, and R. G. Kostyanovskii, Izv. Akad. Nauk SSSR, Ser. Khim., 240 (1966).
- 12. A. Albert and E. Serjeant, Ionization Constants of Acids and Bases, Methuen (1962).
- 13. J. W. Emsley and L. Phillips, Mol. Phys., <u>11</u>, 437 (1966).

4,9-DIHYDROBENZ[f]INDOLE-4,9-DIONE DERIVATIVES SYNTHESIS AND PROPERTIES OF 2,3,4,9-TETRAHYDROBENZ[f]INDOLE-2,4,9-TRIONES AND 2,3,4,9-TETRAHYDROBENZ[f]INDOLE-2,3,4,9-TETRONES

B. V. Salov and A. I. Shakhnovich

UDC 547.756.757'759.5.07

Under the influence of amines, (3-chloro-1,4-naphthoquinon-2-yl)malonic ester is cyclized to 3-carbethoxy derivatives of 2,3,4,9-tetrahydrobenz[f]indole-2,4,9-trione, which were decarboxylated and then oxidized to 2,3,4,9-tetrahydrobenz[f]indole-2,3,4,9-tetrone derivatives. Methylation of 2,3,4,9-tetrahydrobenz[f]indole-2,4,9-triones leads to a mixture of O- and C-methyl derivatives.

It is known [1] that diethyl (3-bromo-1,4-naphthoquinon-2-yl)malonate is cyclized under the influence of ethylamine to ethyl 1-ethyl-2,3,4,9-tetrahydrobenz[f]indole-2.4,9-trione-3-carboxylate. This is one of the few examples [1-3] of the synthesis of benz[f]indole-4,9-quinone derivatives, whereas they are of interest for the synthesis of indigoid dyes.

We have synthesized a number of benz[f]indole-4.9-quinone derivatives and have investigated some of the physical and chemical properties of these compounds.

Ethyl 2,3,4,9-tetrahydrobenz[f]indole-2,4,9-trione-3-carboxylate (IIa) and its N-substituted derivatives (IIb-d) are obtained in good yields by reaction of (3-chloro-1,4-naphthoquinon-2-yl)malonic ester (I) with ammonia and amines. 3-Chloro-2-R-amino-1,4-naphthoquinones (where R is the corresponding amine residue) is formed as a side product in 2-10% yield; the formation of the latter is expressly a side reaction, but it is not due to a 2,3-dichloro-1,4-naphthoquinone impurity in starting I. Kitasato and Sone [2] isolated a side product, to which they assigned the (3-bromo-1,4-naphthoquinon-2-yl)acetic acid methylamide structure, when they carried out the reaction of (3-bromo-1,4-naphthoquinon-2-yl)malonic ester with methylamine. We have found that this side product is actually identical to 3-bromo-2-methylamino-1,4-naphthoquinone [4].

Our proposed method for the synthesis of IIa gives the desired product in higher overall yields and has fewer steps than the methods described in [3].

2,3,4,9-Tetrahydrobenz[f]indole-2,4.9-trione (IIIa) and its N-substituted derivatives (IIIb-d) are formed by treatment of IIa-d with boiling acetic acid.

Compounds IIa-d and IIIa-d are soluble in cold aqueous solutions of bases to give blue-violet enolates. The starting materials are regenerated when the solutions are acidified.

Scientific-Research Institute of Organic Products and Dyes, Moscow. Translated from Khimiya Geterotsiklicheskikh Soedinenii, No. 7, pp. 911-914, July, 1976. Original article submitted July 22, 1975.

This material is protected by copyright registered in the name of Plenum Publishing Corporation, 227 West 17th Street, New York, N.Y. 10011. No part of this publication may be reproduced, stored in a retrieval system, or transmitted, in any form or by any means, electronic, mechanical, photocopying, microfilming, recording or otherwise, without written permission of the publisher. A copy of this article is available from the publisher for \$7.50. 2,3,4,9-Tetrahydrobenz[f]indole-2,3,4,9-tetrone (IVa) and its N-substituted derivatives (IVb-d) are formed by oxidation of IIa-d with 70% nitric acid in concentrated sulfuric acid.

Methylation of IIIa with dimethyl sulfate in the presence of 2,6-lutidine gives a mixture of 2-methoxy-1methyl-4,9-dihydrobenz[f]indole-4,9-dione (V) and 1,3-dimethyl-2,3,4,9-tetrahydrobenz[f]indole-2,4,9-trione (VI). A mixture of V and VI is also obtained under similar conditions from 1-methyl-2,3,4,9-tetrahydrobenz[f]indole-2,4,9-trione (VII)[2].



1-Methyl-2,3,4,9-tetrahydrobenz[f]indole-2,3,4,9-tetrone (VIII) [2] was isolated from the oxidation of V with a mixture of nitric and sulfuric acids. Compound VI is not oxidized under these conditions.

Compound IVa is also methylated by dimethyl sulfate in the presence of 2,6-lutidine to give VIII.

EXPERIMENTAL

The IR spectra of KBr pellets of the compound were recorded with a UR-20 spectrometer. The melting points were determined with a Kofler microscopic stage.

Ethyl 2,3,4,9-Tetrahydrobenz[f]indole-2,4,9-trione-3-carboxylate (IIa). A stream of dry ammonia was bubbled with cooling and stirring in the course of 2 h into a solution of 35.05 g (0.1 mole) of (3-chloro-1,4naphthoquinon-2-yl)malonic ester (I) [1] in 350 ml of ethanol, after which the mixture was allowed to stand overnight. The precipitated ammonium salt of IIa was removed by filtration and treated with 100 ml of a 10% solution of hydrogen chloride in 50% ethanol. Workup gave 21.5 g of ester IIa with mp 200° [from tetrahydrofuran (THF)] (mp 199-200° [3]). Workup of the mother liquor remaining after separation of the ammonium salt of IIa yielded 2.0 g (10%) of 3-chloro-2-amino-1,4-naphthoquinone [5], which was identified by a mixed-melting-point determination with an authentic sample and from its IR spectrum.

Ethyl N-isopropyl-, N-n-Dodecyl-, and N-Phenyl-2,3,4,9-tetrahydrobenz[f]indole-2,4,9-trione-3-carboxylates (IIb-d). These esters were similarly synthesized from 0.1 mole of I and 0.3 mole of the appropriate amine. Workup of the mother liquors gave 3-chloro-2-isopropylamino-1,4-naphthoquinone [6] in 8% yield, 3chloro-2-n-dodecylamino-1,4-naphthoquinone [7] in 4.7% yield, and 3-chloro-2-phenylamino-1,4-naphthoquinone [8] in 2% yield. The compounds were identified from mixed-melting-point determinations with authentic samples and from their IR spectra. IR spectra, cm⁻¹: IIb, 1665 s (quinone C = O); IIc, 1660 s (quinone C = O); IId, 1735 s (ester C = O); 1710 s ("amide I" C = O); 1670 s (quinone C = O); and 1158 vs (ester C = O).

2,3,4,9-Tetrahydrobenz[f]indole-2,4,9-trione (IIIa) and Its N-Isopropyl, N-n-Dodecyl, and N-Phenyl Derivatives (IIIb-d). A 0.05-mole sample of Ha-d was refluxed for 3 h with 150 ml of glacial acetic acid. after which the mixture was cooled and diluted with water (to 1.5-2 times its original volume), and the precipitates were removed by filtration, washed with water, and dried. IR spectra, cm⁻¹: IIIa, 3270 br (enol OH), 1710 w ("amide I" C = O), 1640 m (quinone C = O); IIIb, 3220 br (enol OH), 1700 w ("amide I" C = O), 1635 s (quinone C = O); IIIc, 3200 br (enol OH), 1720 w ("amide I" C = O), 1663 s (quinone C = O); IIId, 3200 br (enol OH), 1700 m ("amide I" C = O), and 1650 s (quinone C = O).

Com - pound	R	mp, [°] C (solvent), color	Empirical formula	Found, %			Calc., 7/0			d, º/o
				с	!1	N	с	н	Ň	Yiel
ЦЬ	CH(CH ₃)	175 (THF), vellow	C ₁₈ H ₁₇ NO-	66,2	5,4	4.1	66.1	5.2	4.3	75
llc Ild	n-C ₁₂ H ₂₅ C ₆ H	91 (hexane), yellow 126(methanol),	$C_{27}H_{35}NO_5 \\ C_{21}H_{15}NO_5$	71.3 71,5	7.9 4.1	$3,8 \\ 4,1$	71,5 71.8	$^{7,8}_{4,3}$	$3,1 \\ 4,0$	70 60
lila	Н	orange >360 (DMF),	C ₁₂ H ₇ NO ₂	67.9	2.9	6,9	67.6	3,3	6,6	97
H.b	CH(CH ₃) ₂	257 (acetic acid),	$C_{15}H_{13}NO_3$	70,3	5,0	õ,õ	70,6	5,1	5,5	90
IIIc	$n - C_{12}H_{25}$	193 (acetic acid),	$C_{24}H_{31}NO_2$	74,9	8,1	4.0	75.5	8,2	3,7	84
Illd	C_6H_3	293 (chloroform),	$C_{18}H_{11}NO_3$	74,5	3,5	4,6	74,7	3,8	4,9	80
IVa	н	>360 (dioxane),	C ₁₂ H ₅ NO ₄	63,1	2,2	6.3	63,4	2.2	6,2	90
IV b	CH(CH ₃) ₂	267 (chloroform),	$C_{15}H_{11}NO_4$	66.5	4,1	5,0	66,9	4,1	5,2	90
1Vd	C ₆ H ₃	240 (dec., chloroform),	C ₁₈ H ₉ NO ₄	71,1	2,7	4,4	71,3	3,0	4,6	60
V		331 (methanol),	$C_{14}H_{11}NO_3$	69.5	4,8	5.9	69.7	5,0	5,8	52*
VI	-	279 (methanol), violet	C ₁₄ H ₁₁ NO ₃	69,4	4,8	5.7	69,7	5,0	5,8	101 101

TABLE 1. Yields, Melting Points, Color, and Results of Elementary Analyses of II-VI

* By method A.

†By method B.

2.3,4,9-Tetrahydrobenz[f]indole-2,3,4,9-tetrone (IVa) and Its N-Isopropyl, N-n-Dodecyl, and N-Phenyl Derivatives (IVb-d). A 0.05-mole sample of IIIa-d was dissolved, with cooling, in 100 ml of 98% sulfuric acid, after which 9 g (0.1 mole) of 70% nitric acid was added dropwise. The mixture was then stirred for 30 min, after which it was poured into 750 ml of ice water. The precipitated IVa was removed by filtration, washed with water, and dried. Suspensions of IVb-d were extracted twice with 50-ml portions of chloroform, and the chloroform extracts were dried with anhydrous sodium sulfate. The chloroform was removed by vacuum distillation, and the residue was chromatographed with a column filled with L 100/160 μ silica gel with elution by chloroform-ethyl acetate (9:1). IR spectrum, cm⁻¹: IVa, 1790 m (C = O), 1735 s ("amide I" C = O), 1677 s (quinone C = O); IVb, 1770 m (C = O), 1720 m ("amide I" C = O), 1665 s (quinone C = O); IVc. 1770 m (C = O), 1713 s ("amide I" C = O), 1670 s (quinone C = O); IVd, 1783 m (C = O), 1732 s ("amide I" C = O), and 1681 s (quinone C = O).

2-Methoxy-1-methyl-4,9-dihydrobenz[f]indole-4,9-dione (V) and 1,3-Dimethyl-2,3,4,9-tetrahydrobenz[f]indole-2,4,9-trione (VI). A) A 5-g (23.5 mmole) sample of IIIa was methylated by refluxing for 4 h with 8.9 g (70.5 mmole) of dimethyl sulfate and 7.6 g (70.5 mmole) of 2,6-lutidine in 75 ml of absolute THF, after which the mixture was cooled, and V precipitated. The mother liquor was cooled and diluted to twice its volume with water to precipitate VI, which was purified by chromatography with a column filled with L 100/160 μ silica gel with elution by chloroform-ethyl acetate-acetic acid (10:10:1).

B) A 5.32-g (20.5 mmole) sample of VII [2] was methylated with 8.9 g (70.5 mmole) of dimethyl sulfate and 7.6 g (70.5 mmole) of 2,6-lutidine in 75 ml of absolute THF. The reaction conditions and the workup were the same as in experiment A. IR spectra, cm^{-1} : V, 1665 s (quinone C = O); VI, 1715 m ("amide I" C = O), and 1660 s (quinone C = O).

<u>Oxidation of V.</u> A solution of 0.5 g (2.1 mmole) of V in 5 ml of 98% sulfuric acid was treated, with cooling, with 0.5 g (5.6 mmole) of 70% nitric acid, after which the mixture was poured into 10 ml of water, and the aqueous mixture was extracted twice with 5-ml portions of chloroform. Workup of the extract gave 0.37 g (74\%) of tetrone VIII [2]. The tetrone was identified by a mixed-melting-point determination with an authentic sample and from its IR spectrum.

Methylation of IVa. A mixture of 1 g (4.4 mmole) of IVa, 0.55 g (4.4 mmole) of dimethyl sulfate, 0.47 g (4.4 mmole) of 2,6-lutidine, and 20 ml of absolute THF was refluxed for 1 h, after which the solvent was removed by vacuum distillation, and the residue was recrystallized from chloroform to give 0.35 g (37%) of tetrone VIII [2]. The product was identified by means of a mixed-melting-point determination with an authentic sample and from its IR spectrum.

The yields of the compounds, the melting points. and the results of elementary analyses are presented in Table 1.

The authors thank N. S. Dokunikhin for his valuable directions and interest in this research.

LITERATURE CITED

- 1. C. Liebermann. <u>32</u>. 262 (1899).
- 2. Z. Kitasato and C. Sone, Bull. Chem. Soc. Japan. <u>5</u>. 348 (1930).
- 3. G. Cajipe, D. Rutolo. and H. W. Moore. Tetrahedron Lett., 4695 (1973).
- 4. Ôsterreichiche Stickstoffwerke A. -G., Austrian Patent No. 217777 (1961); Ref. Zh. Khim., 12L354 (1962).
- 5. J. R. E. Hoover and A. R. Day. J. Am. Chem. Soc.. 76, 4148 (1954).
- 6. I. Oeriu, Acad. Rep. Populare Romine. Studii Cercetari Chim., 9, 315 (1961).
- 7. R. V. Acharya and B. D. Tilak, J. Sci. Ind. Res. (India). 14, 219 (1955).
- 8. F. Krollpfeifer. G. Wolf, and H. Walbrecht. Ber., 67, 908 (1934).

NUCLEOPHILIC SUBSTITUTION REACTIONS

OF 2,4,6-TRIS(METHYLSULFONYL)-3.5-DICHLOROPYRIDINE

S. D. Moshchitskii, G. A. Zalesskii, and V. P. Kukhar' UDC 547.822.5.6

It was established that hard bases replace the methylsulfonyl groups and that soft bases replace the chlorine atoms in 2,4,6-tris(methylsulfonyl)-3,5-dichloropyridine.

In the present communication we present the results of studies of the competitive nucleophilic substitution of the chlorine atoms and methylsulfonyl groups in sulfone I [1]. Because of the strong electron-acceptor effect of three methylsulfonyl groups and a nitrogen heteroatom, the electron densities on the carbon atoms in the 2, 4, and 6 positions are lower than in the 3 and 5 positions. The 2-C. 4-C. and 6-C atoms should therefore act as hard acids, and the 3-C and 5-C atoms should act as soft acids. In fact, hard bases (sodium methoxide and phenoxide, potassium fluoride, sodium hydroxide, sodiomalonic ester, etc.) react at the 2, 4, and 6 positions, whereas soft bases (ammonia, aniline, morpholine, piperidine, malonic ester, ethanol, etc.) react at the 3 and 5 positions; this is in conformity with Pearson's principle of the reaction of hard and soft acids and bases [2].

The reaction of sulfone I with ammonia and amines at low temperature leads to replacement of one chlorine atom to give the corresponding 3-amino-substituted 5-chloro-2,4,6-tris(methylsulfonyl)pyridines (IIa-d, Table 1). At room temperature the reaction of I with morpholine and aniline gives rise to replacement of two chlorine atoms to give. respectively, 3,5-dimorpholino- and 3.5-bis(phenylamino)-2.4,6-tris(methyl-sulfonyl)pyridines (IIIa, b). The second chlorine atom in any of the products of replacement of one chlorine atom in IIa-d is also replaced by the further action of a soft nucleophile. Thus amine IId reacts with aniline or p-nitrophenol at room temperature to give, respectively, product IIIb and 3-phenylamino-5-(p-nitrophenoxy)-2,4,6-tris(methylsulfonyl)pyridine (IIIc).

An attempt to obtain the corresponding isocyanate by reaction of sulfone I with potassium cyanate yielded amine IIa, the synthesis of which evidently includes the formation of an intermediate reactive isocyanate, which reacts with water to give amine IIa.

The reaction of sulfone I with malonic ester and ethanol also leads to replacement of one chlorine atom to give, respectively, diethyl[2,4.6-tris(methylsulfonyl)-5-chloro-3-pyridyl]malonate (IIe) and 3-ethoxy-5-chloro-2,4,6-tris(methylsulfonyl)pyridine (IIf).

Institute of Organic Chemistry, Academy of Sciences of the Ukrainian SSR. Kiev. Translated from Khimiya Geterotsiklicheskikh Soedinenii. No. 7, pp. 915-919, July, 1976. Original article submitted July 22, 1975.

This material is protected by copyright registered in the name of Plenum Publishing Corporation, 227 West 17th Street, New York, N.Y. 10011. No part of this publication may be reproduced, stored in a retrieval system, or transmitted, in any form or by any means, electronic, mechanical, photocopying, microfilming, recording or otherwise, without written permission of the publisher. A copy of this article is available from the publisher for \$7.50.