Jiří Grúz; Zdeněk Stránský

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Vedoucí katedry: prof. RNDr. Eduard Růžička, kandidát věd

CONTRIBUTIONFOR PREPARING PHENOXAZINE NITRODERIVATIVES

JIŘÍ GRÚZ AND ZDENĚK STRÁNSKÝ

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The nitroderivatives of phenoxazine can be prepared by three more general processes:

A. By the reaction of aromatic 1,2-dihalogenous compounds with 1,2-aminophenols in an acid medium (1)

B. Using Turpin' synthesis based on the reaction of 2-nitroarylchloride containing reactive halogen with 1,2-aminophenols in an alkaline medium (2)

C. By direct nitration of phenoxazine- derivatives.

More broader scope of application was found in two processes recently induced. The substituted 2-nitro-2′-hydroxydiphenylamines resulting with proper Turpin's reaction in intermediate states can be used as starting materials [3—5] too.

Misslin and Bau [6] made use of trinitroanisole as a reactive component instead of the reactive nitroarylhalide. The mechanism of Turpin' reaction [7—11] which was in the last time thoroughly clarified by Musso [12] was followed in details. It was no other than Musso who recommended to use the anhydrous dimethylsulphoxide or dimethylformamide as a reaction medium reaching in such a way excellent results even with such nitrophenoxazines which could not be prepared by any other modification of Turpin's reaction.

Table I

Preparation of nitrophenoxazines

Nr.	Nitrated phenoxazine	Process	Literature
1	1-nitro-	B	3, 4
2	3-nitro-	B, C	7, 9, 12
3	1,3-dinitro-	A, B	1, 2, 6, 14
4	3,7-dinitro-	C	13
5	1,3,7-trinitro-	B, C	6, 13
6	1, 3, 7, 9-tetranitro-	B, C	6, 13

There are especially polynitroderivatives of phenoxazine which are usualy prepared by nitration. Great attention was paid to the nitration of N-acetylphenoxazine [13] as well as to some nitrophenoxazines [6, 13].

The table I gives a review of nitrophenoxazines which have been prepared. Our aim was to use the nitrated phenoxazines as neutralizing indicators in non- aqueous media. For comparative studies it was necessary to prepare 1, 3, 9-trinitrophenoxazine as well as 1, 3, 7-trinitrophenoxazine and to produce 1, 3, 7, 9- tetranitrophenoxazine in an unambiguous way, because the processes formerly described result in some mixtures of derivatives which are uneasy to separate.

EXPERIMENTAL PART

1 — nitrophenoxazine	— was prepared according to Ullmann [3]
3 — nitrophenoxazine	— was prepared by two-hours boiling in dimethylformamide [12]
1, 3 — dinitrophenoxazine	— prepared with use of Musso' modification too [12]
3, 7 — dinitrophenoxazine	— prepared in the known way [13]

The crystallization of all the compounds was realized from benzene as well as from the glacial acetic acid. The purity was controlled by means of elementary analysis and by thin-layer-chromatography on silicagel using benzene as a system-.

5-nitro-2-acetaminophenol (I):

A mixture of 12.5 g 5-nitro-O, N-diacetyl-2-aminophenol (IA) and 3-nitro-O, N-diacetyl-2-aminophenol was obtained by nitration of 20 g O, N-diacetyl-2-aminophenol [15].

2g of less soluble IA (m.p. 190—191 °C), and through its saponification 1,8 g of I with m.p. 268 (*d*), was obtained with threefold crystallization of mixture with ethanol.

3-nitro-2-acetaminophenol (II):

The coupled mother liquors after IA-isolation were evaporated to dryness and the residue saponified with 2N sodium hydroxide at room-temperature. The separated mixture I with II was solved in benzene-cyclohexane and carried on a column of aluminium oxide (Reanal-Brockmann's II) desactivated with 5% weight of glacial acetic acid and eluated with the solvent just mentioned. From one more speedily flowing fraction was isolated 1,8g II after crystallization from water with m. p. 172—174 °C (Lit.: 169 °C [15]).

1, 3, 7-trinitrophenoxazine: 0,98g (0,005M) 1 and 1,25g (0,005M) picrylchloride (III) were heated in 8ml ethanol during one-hour-period under reflux-condenser. During this time 0,7g anhydrous sodium acetate was induced. The reaction-mixture was cooled, precipitated with water and the isolated product recrystallized from benzene; 0,83g-(52%).

The product was found to be chromatografically pure.

Calc.:	45,28 % C	1,89% H	17,61% N
Found:	44,98% C	2,06% H	17,32% N

1, 3, 9-trinitrophenoxazine:

0,98 g II was heated with 1,24 g III for four hours in 30 ml ethanol under reflux. During the first hour 0,9 g anhydrous sodium acetate was added to the reaction-mixture. After cooling and diluting with water 1,3 g (82%) of the crude product was obtained which was dissolved in 5 ml 10% KOH and heated to a boiling piont. After adding the diluted hydrochloric acid (colour-bridge from blue to red) the product was separated giving after recrystallization from benzene and acetic acid 0,70 g (44%) red crystalls. This product was chromatographically pure.

Calc.:	45,28% C;	1,89% H;	17,61% N
Found:	45,70% C;	1,91% H;	17,35% N

1, 3, 7, 9-tetranitrophenoxazine:

0,5 g 1, 3, 9-trinitrophenoxazine was mixed thoroughly in 10 ml glacial acetic acid and cautiously under refrigeration 15 ml HNO_3 (68 %) was added. The reaction-mixture was left to stand under occassionally mixing for 45 minutes at room temperature and then diluted with water. The separated product was recrystallized from benzene and from acetic acid-(66 %) and found to be chromatographically pure.

Calc.:	39,67% C;	1,38% H;	19,28% N
Found:	39,38% C;	1,30% H;	19,41% N.

DISCUSSION

All the mixtures of 1, 3, 7-trinitrophenoxazine and 1, 3, 7, 9-tetranitrophenoxazine originate with the nitration of 1, 3-dinitrophenoxazine [13], whereas under modification of Turpin's reaction just described it is possible to prepare 1, 3, 7-trinitrophenoxazine using the reaction I with III in an unambiguous way.

Relatively pure 1, 3, 7-trinitroderivative can be obtained also by way of nitration 1, 3-dinitrophenoxazine with 65% nitric acid in acetic acid. After two-hours reaction period at room temperature the product comes to be contamined with very few traces of starting compound and of tetranitroderivative as well.

1, 3, 9-Trinitrophenoxazine cannot be prepared by nitration at all, because in the positions 3 and 7 the nitration is preferentiated. The positions 1 and 9 are nitrated only unwillingly. That's why the unambiguous way of reaction II with III was chosen again.

1, 3, 9-Trinitrophenoxazine was chosen also as starting material for preparing 1, 3, 7, 9-tetranitrophenoxazine to enable an easier electrophile substitution in the position 7. It is true that the tetranitroderivative can be prepared by nitration of 3, 7-dinitrophenoxazine or by the nitration of 1, 3-dinitroderivative [13, 6] too, but not in such a high degree of purity. The solubilities of 1, 3, 7-trinitro- as well as 1, 3, 7, 9-tetranitroderivatives are alike and they can be mutually separated very uneasily. An attempt was made also to prepare the tetranitroderivative by means of reaction between 3, 5-dinitro-2-acetaminophenol with picrylchloride which reaction however does not occur under normal

pressure-conditions. The electronegative substituents appearing in molecules of substituted aminophenols restrain the course of reaction.

Just described chromatographic isolation of hardly accessible 3-nitro-2-acetaminophenol is essentially more simple than the twentyfold fractional crystallization [15] formerly described. The difference between the chromatographical properties of I and II is high so that it is possible to separate the two substances practically in the form of frontal chromatography. The substance I is seized totally in the upper part of the column and the column's capacity in separation is high. With 20 cm high columm 5 gramms of isomer II can be easily obtained by means of single operation. Isomer I caught on the column can be then washed out with ethanol.

Summary

The preparation of **1, 3,** 9-trinitrophenoxazine by means of modified Turpin's reaction has been described. A new unambiguous synthesis of **1, 3, 7** trinitrophenoxazine as well as **1, 3, 7,** 9-tetranitrophenoxazine has been just clarified. With use of frontal column-chromatography it was not difficult to gain the starting materials of 3-nitro as well as 5-nitro-2-acetoaminophenols.

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Zusammenfassung

BEITRAG ZUR HERSTELLUNG VON PHENOXAZINE-NITRODERIVATEN

Jiří Grúz und Zdeněk Stránský

Die Zubereitung von 1, 3, 9-Trinitrophenoxazin unter Benutzung von einer modifizierten Turpin's Reaktion wird beschrieben. Ferner wird in dieser Arbeit eine neue eindeutige Synthesis von 1, 3, 7- Trinitrophenoxazin sowie **1, 3, 7, 9** Tetranitrophenoxazin angeführt. Mit Hilfe einer frontalen Säulenchromatographie wird es erleichtert Ausgangsprodukte von 3-Nitro sowie 5-Nitro-2-acetaminophenolen zu gewinnen.