SUBSTITUTION OF NH HYDROGEN IN NITROGEN DERIVATIVES OF POLYCYCLIC HYDROCARBONS AND QUINONES*

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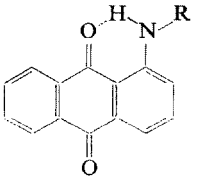
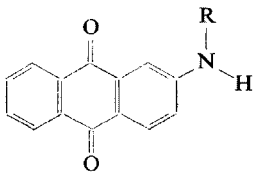
Polycyclic compounds containing NH groups have been converted into the respective sodium salts by action of sodium hydride in polar aprotic solvents, and the salts have been used for preparation of methyl derivatives of the starting substances.

Hydrogen atoms of the NH groups bound to aromatic nuclei of polycyclic hydrocarbons and quinones are relatively acidic in nature. Formation of coloured salts of these compounds on treatment of the substances with alcoholic potassium hydroxide in pyridine medium was described by Bradley[1]. The presence of a strong negative substituent at nitrogen enables the preparation of the salts even in aqueous medium and their application in synthesis of alkyl derivatives of the starting substances[2,3]. With the aim of extending the range of reactive substances we used the knowledge about sodium hydride and properties of strongly polar aprotic solvents. Besides its preparative importance, the study of reactions with sodium hydride is interesting, especially in the case of quinoid derivatives, with respect to their easy reducibility leading to possible side reactions with sodium hydride.

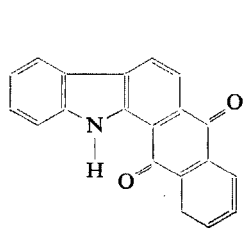


Ia, R = H
Ib, R = CH_3
Ic, R = C_6H_5
Id, R = 4-$C_6H_4NO_2$
Ie, R = 1-anthraquinonyl
If, R = 2-anthraquinonyl
Ig, R = COC_6H_5
Ih, R = $COCH_3$
Ii, R = 4-$SO_2C_6H_4CH_3$



IIa, R = H
IIb, R = CH_3
IIc, R = C_6H_5
IId, R = 2-anthraquinonyl
IIe, R = COC_6H_5
IIf, R = $COCH_3$
IIg, R = 4-$SO_2C_6H_4CH_3$

* Part XX in the series Anthraquinone Dyestuffs; Part XIX: This Journal *39*, 3117 (1974).



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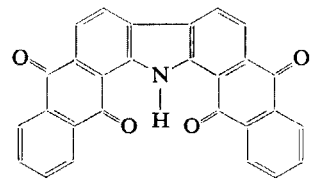
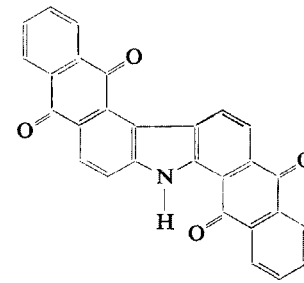


IV



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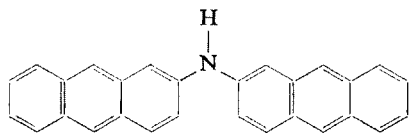
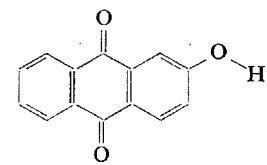


VI



VII

The preparation of sodium salts of polycyclic nitrogen derivatives has been studied in the series of model substances *Ia* – *VI*. The reactions were carried out in dimethylformamide or dimethyl sulphoxide. If the reaction is followed by the rate of formation of the characteristically coloured solution, it can be stated that the salts were formed smoothly from most substances at the room temperature except for 1-methylaminoanthraquinone (*Ib*) and 1,2,7,8-diphthaloylcarbazole (*IV*). The former substance reacts with difficulties due probably to that the acidity of the hydrogen is reduced by inductive effect of the methyl group at nitrogen and the whole system is stabilized by a strong hydrogen bond[4]. Obviously important is here the combined influence of the both effects, because both 1-phenylaminoanthraquinone (*Ic*), whose hydrogen is involved in a strong hydrogen bond, and 2-methylaminoanthraquinone (*IIb*) (containing the active hydrogen at a N—CH_3 group) form easily the respective salts on action of sodium hydride. 1,2,7,8-Diphthaloylcarbazole (*IV*) does not react due to sterical reasons, as it follows from the comparison with the reactivity of the corresponding 1,2,5,6-isomer *V* and from the consideration of steric arrangement of the molecule[5].

The methylations were accomplished by addition of excess methyl iodide to the prepared solution of the salt. The conversion degree was followed visually by the change of the solution colour. Further details of the reaction progress were obtained from chromatographic evaluation of the composition of the isolated reaction product. Methylations of the salts prepared showed rather greater reactivity differences. High yields of the methyl derivatives were obtained from methylations of the substances *Ic*, *Id*, *If*, *IIb*, *IIc*, *IId*, *III*, *V*, *VI*, eventually also *Ii* and *IIg*, if the reaction time was prolonged. The methylation of the α-derivative *Ii* is accompanied by side

reactions; the pure product can be obtained by oxidation of the impurities with chromium trioxide in acetic acid.

Whereas the alkylation of 1-aminoanthraquinone (*Ia*) gave predominantly the corresponding monoalkyl derivative, alkylation of the 2-isomer *IIa* resulted in substitution of the both aminohydrogens. From the methylation reaction mixtures of 1-benzoylaminoanthraquinone (*Ig*) and the corresponding acetyl derivative *Ih* it was possible to isolate 1-methylaminoanthraquinone as the main product, whereas 2-di-

TABLE I

Methylation Results of Compounds *I*—*VII* with Methyl Iodide

Compound	Colour of the salt solution	Product[a]	Yield g	M.p.,[b] °C
Ia	green	1-$NHCH_3$—A	1·01	172—172·5[c]
Ib	—	—[d]	—	—
Ic	green	1-$N(CH_3)C_6H_5$—A	0·98	132·5—133[e]
Id	green	1-$N(CH_3)$4-$C_6H_4NO_2$—A	1·00	237—238[f]
Ie	green	—[d]	—	—
If	green	N—CH_3-1,2′-dianthraquinonylamine	1·02	288—289[g]
Ig	violet	1-$NHCH_3$—A	0·71	172—172·5[c]
Ih	violet	1-$NHCH_3$—A	0·65	172—172·5[c]
Ii	red	1-$N(CH_3)$4-$SO_2C_6H_4CH_3$—A	0·58[h]	197—199[i]
IIa	green	2-$N(CH_3)_2$—A	1·06	189—189·5[j]
IIb	green	2-$N(CH_3)_2$—A	1·07	189—189·5[j]
IIc	green	2-$N(CH_3)C_6H_5$—A	1·04	162·5—163[k]
IId	green	N—CH_3-2,2′-dianthraquinonylamine	0·91	339—340[l]
IIe	violet	2-$N(CH_3)_2$—A	0·73	189—189·5[j]
IIf	violet	2-$N(CH_3)_2$—A	0·88	189—189·5[j]
IIg	red	2-$N(CH_3)$4-$SO_2C_6H_4CH_3$—A	1·00	196·5—197·5[m]
III	green	N—CH_3-1,2-phthaloylcarbazole[n]	1·04	233—234
IV	—	—[o]	—	—
V	green	N—CH_3-1,2,5,6-diphthaloylcarbazole[p]	0·93	does not melt up to 360°C
VI	blue	N—CH_3-2,2′-dianthracenylamine[r]	1·02	304—306
VII	red	2-OCH_3—A	1·00	197·5—198[s]

[a] A stands for anthraquinone nucleus; [b] after crystallization; [c] ref.[7] 170°C; [d] the product was not identified; [e] ref.[8] 130—131°C; [f] ref.[9] 233—234°C; [g] ref.[2] 284—285°C; [h] alkylation 24 hours, oxidation with CrO_3; [i] ref.[7] 198°C; [j] ref.[2] 185—186°C; [k] ref.[2] 163—164°C; [l] ref.[2] 332—333°C; [m] ref.[2] 195°C; [n] for $C_{21}H_{13}NO_2$ (311·3) calculated: 81·01% C, 4·21% H, 4·50% N; found: 80·85% C, 4·37% H, 4·57% N; [o] the reaction did not take place; [p] for $C_{29}H_{15}NO_4$ (441·4) calculated: 78·90% C, 3·43% H, 3·17% N; found: 78·43% C, 3·85% H, 3·20% N; [r] for $C_{29}H_{21}N$ (383·5) calculated: 90·83% C, 5·52% H, 3·65% N; found: 90·56% C, 4·92% H, 3·72% N; [s] ref.[10] 195 to 196°C.

methylaminoanthraquinone resulted from methylations of the isomeric 2-derivatives *IIe* and *IIf*. The difference in the alkylation degree of 1- and 2-isomers is due to the mentioned low reactivity of 1-methylaminoanthraquinone to sodium hydride. For the sake of explanation of the acyl splitting in methylations of benzoyl- and acetylaminoanthraquinones, the starting substances were exposed to a prolonged action of sodium hydride under the conditions of the above methylations. After decomposition of the formed salt solution with water only the unchanged starting substances were isolated, and the aminoanthraquinones formed on hydrolysis were present only in traces. Therefrom it follows that the splitting off of the acyl groups takes place first in the phase of N-methyl derivative of acylaminoanthraquinone. This reaction represents undoubtedly an analogy of "anhydrous hydrolysis" of esters[6]. The sodium hydroxide present originates from partial decomposition of sodium hydride.

According to chromatography the methylation of the sodium salt of the compound *Ie* with methyl iodide yields only traces of N-methyl derivative of 1,1'-dianthraquinonylamine, steric hindrance being obviously the reason of this fact. In contrast to the salts of most other substances, the salt of the compound *Ie* is very unstable in the reaction medium, and it decomposes on prolonged storage or heating. Also the salts of 1-aminoanthraquinone (*Ia*) and 1-methylaminoanthraquinone (*Ib*) decompose so that they give only small yields of dimethyl derivatives under more vigorous alkylation conditions. An increased inclination to side reaction was observed, if dimethyl sulphoxide was used as the solvent.

Thus according to the described method it is possible to methylate simply the polycyclic dyestuff intermediates and dyestuffs inclusive of the compounds having quinoid skeleton. Some 1-aminoanthraquinone derivatives make an exception, undergoing decomposition in the presence of sodium hydride. A possible use of other alkyl halogenides is illustrated by the alkylation of 1-aminoanthraquinone (*Ia*) with 1,4-diiodobutane. The reaction product did not contain any halogen, no bands corresponding to NH group were found in its IR and NMR spectra, and the character of the signal of CH_2 groups in NMR spectrum indicated the presence of a five-membered ring at nitrogen. The formula of 1-(1-pyrrolidino)anthraquinone was ascribed to the reaction product, and it was confirmed by comparison with the compound prepared from 1-chloroanthraquinone and pyrrolidine (melting point, IR spectrum).

The basicity differences between the compounds containing amino, monoalkylamino and dialkylamino groups enable their separation from the reaction mixtures using fractional precipitation of the solutions in strong acids. This method was adopted for isolation of 1-methylamino-, 1-dimethylamino- and 1-(1-pyrrolidino)anthraquinones.

Besides the alkylation of the NH-group-containing substances methylation of 1- and 2-hydroxyanthraquinones and benzoylation of 2-(4-toluenesulphonylamino)an-

thraquinone salt (*IIg*) were carried out, too. The salt of 1-hydroxyanthraquinone reacts very slowly with methyl iodide; the isomeric 2-derivative *VII* gives 2-methoxyanthraquinone in a high yield (Table I). Reaction of the salt of the compound *IIg* with benzoyl chloride gave 2-(N-benzoyl-N-4-toluenesulphonylamino)anthraquinone. Anthraquinone derivatives of this type have not yet been described.

The reference sample of 1-dimethylaminoanthraquinone was prepared by heating 1-nitroanthraquinone with dimethylformamide and sodium hydroxide solution. The necessary dimethylamine is generated *in situ* by partial decomposition of the solvent. The method is applicable for other analogous syntheses, too.

EXPERIMENTAL

Methylation of 1-Benzoylaminoanthraquinone (*Ig*)

1 g 1-benzoylaminoanthraquinone was added to a suspension of 1 g sodium hydride in 50 ml dimethylformamide. Within 1 hour the former substance dissolved (purple solution) and, then, 2 ml methyl iodide was added, and the mixture was stirred for 1 hour. The temperature did not exceed 35°C, the solution colour changed to red. The excess hydride was removed by addition of ethanol, and the mixture was poured in 500 ml water. The product was collected by suction, washed and dried; yield 0·70 g. Thereafter it was dissolved in 50 ml warm conc. hydrochloric acid, filtered and reprecipitated with 200 ml water. Crystallization from n-butanol gave red needles melting at 172·0—172·5°C (ref.[7] 170°C).

Analogous methylations were used for compounds *Ia*—*VII*. At least a five-fold excess on sodium hydride was used compared to theoretical amount. The results are summarized in Table I.

Alkylation of 1-Aminoanthraquinone with 1,4-Diiodobutane

1 g sodium hydride was added to 2·2 g 1-aminoanthraquinone in 30 ml dimethylformamide. After 1 hour a solution of 4 g 1,4-diiodobutane in 10 ml dimethylformamide was added during 2 hours, and the mixture was further stirred at room temperature for 4 hours. Thereafter it was poured in 600 ml water, and the product precipitated was collected by suction, washed with water and dried; yield 2·35 g. The alkyl derivative was obtained either by chromatography on an alumina column using chlorobenzene as eluent (0·37 g from 1 g raw product) or by fractional precipitation from hydrochloric acid: a solution of 1 g raw product in 25 ml conc. hydrochloric acid was diluted with 100 ml water, and the precipitated fraction was removed by filtration with charcoal. The filtrate was neutralized with ammonia, the precipitated fraction was filtered off, washed with water and dried; yield 0·27 g. Crystallization from 65% aqueous ethanol gave red plates melting at 152—154°C. For $C_{18}H_{15}NO_2$ (277·3) calculated: 77·96% C, 5·45% H, 5·05% N; found: 76·8% C, 5·81% H, 5·29% N.

The same compound was synthetized by heating 1-chloroanthraquinone with pyrrolidine in dimethylformamide at 90°C. The reaction product was isolated as that obtained by the above alkylation.

2-(N-Benzoyl-N-4-toluenesulphonylamino)anthraquinone

3 ml benzoyl chloride was added to a suspension of 1 g potassium salt of 2-(4-toluenesulphonylamino)anthraquinone[2] in 25 ml pyridine and the mixture was heated to boiling until dissolution

of the starting substance and disappearance of red colour. The product was precipitated with water, the yield being practically quantitative, and after crystallization from acetic acid yellowish needles were obtained melting at 225–227°C. For $C_{28}H_{19}NO_5S$ (481·5) calculated: 69·84% C, 3·98% H, 2·91% N, 6·66% S; found: 69·62% C, 4·07% H, 3·07% N, 6·58% S.

1-Dimethylaminoanthraquinone

Within 6 hours 2·5 ml 2·5M-NaOH was added dropwise to a boiling solution of 1 g 1-nitroanthraquinone in 25 ml dimethylformamide. The mixture was diluted with water, the precipitated fraction was collected by suction and mixed with 25 ml conc. hydrochloric acid. After dilution with 100 ml water the insoluble fraction was removed by filtration with charcoal and the filtrate was alkalized with ammonia to give 0·4 g free base of 1-dimethylaminoanthraquinone. It was purified chromatographically (alumina–benzene) and recrystallized from ethanol, red needles, m.p. 142–143°C (ref.[11] 140·5°C).

Elemental analyses were carried out in Analytical Department of the Institute under the guidance of Dr L. Synek. We are indebted to Dr J. Knížek for IR spectra measurements and to Dr D. Šnobl for measurements and interpretation of NMR spectra in the case of identification of the reaction product of 1-aminoanthraquinone and diiodobutane; we are also indebted to Miss H. Faberová for technical assistance.

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