CONDENSATION OF o-PHENYLENE DIAMINE AND SUBSTITUTED ACROLEINS TO FORM MACROHETEROCYCLES

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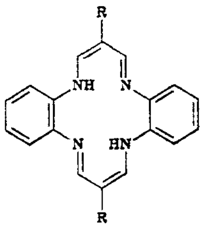
The reaction of o-phenylene diamine with β-alkoxy-, β-dimethylamino-, and β-acetoxy-α-alkyl- or α-arylacroleins has been studied. A new synthesis of 7,16-diaryl[5,14]dihydro[b,i]dibenzo-[5,9,14,18]tetraaza[14]annulenes was developed, and the syntheses of 5,14-dihydro[b,i]dibenzo[5,9,14,18]tetraaza-[14]annulene and 7,16-dialkyl[5,14]dihydro[b,i]dibenzo[5,9,14,18]tetraaza[14]-annulenes were improved. 5,14-Dihydro[b,i]dibenzo[5,9,14,18]tetraaza[14]-annulenes were synthesized with various substituents in the benzene rings and at positions 7 and 16.

5,14-Dihydro[b,i]dibenzo[5,9,14,18]tetraaza[14]annulenes of general formula I are chelating agents. Their metal chelates, like phthalocyanines and porphyrins, tend to undergo redox rearrangements and can catalyze redox reactions [1].

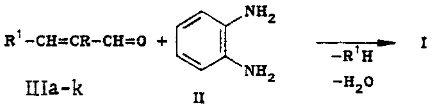


Ia-e

Ia R=H; b R=CH_3; c R=C_2H_5; d R=C_6H_5; e R=p-$C_6H_4CH_3$

Previous syntheses of compounds I have been based on condensation of o-phenylene diamine with propargyl aldehyde [2, 3], α-alkyl-β-ethoxyacroleins in DMFA [4], or 4-aryl[1,2]dithiolium hydrosulfates in dichloroethane [5]. The yields of compounds Ia-c are low (20-31%) [2-4],* and increase little when a catalyst is added [3]; the yields of Id, e are not mentioned [5]. Synthesis of the 4-aryl[1,2]dithiolium hydrosulfates used in the last method requires either a long time or starting materials that are hard to obtain.

We studied the reactions of o-phenylene diamine II with various substituted acroleins III:



III a R=H, R^1=OCH_3; b R=H, R^1=OC_2H_5; c R=CH_3, R^1=OC_2H_5; d R=C_2H_5, R^1=OC_2H_5; e R=C_6H_5, R^1=OC_2H_5; f R=H, R^1=$N(CH_3)_2$; g R=CH_3, R^1=$N(CH_3)_2$; h R=C_6H_5, R^1=$N(CH_3)_2$; i R=p-$C_6H_4CH_3$, R^1=$N(CH_3)_2$; j R=H, R^1=CH_3COO; k R=CH_3, R^1=CH_3COO

Starting from β-alkoxyacroleins IIIa, b one can synthesize Ia, and the yield in alcohol is higher (41-45%) than in DMFA. The yields of Ib, c from IIIc, d are better if quinoline is the solvent. Analogous results are obtained in the condensation of II with

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*Upon multiple repetition of the procedure of [4] we obtained yields an order of magnitude smaller; more concentrated solutions must be used.

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acrolein IIIe; in quinoline Id is formed. In alcohol, acroleins IIIc, e (IIIe also in DMFS) give the respective polymeric Schiff bases.

Direct use of the mixture of hydrolysis products of the malonic dialdehydes Va-e (obtained from alkenyl acetates IV) showed that compounds Ia-c can also be obtained from them:

$$\underset{\text{IVa,b}}{RCH{=}CHOOCCH_3} \xrightarrow{HC(OR^2)_3} \underset{\text{va,d}}{(R^2O)_2CH{-}CHR{-}CH(OR^2)_2} \xrightarrow{H_2O} [R^1{-}CH{=}CR{-}CH{=}O] + II \longrightarrow I$$

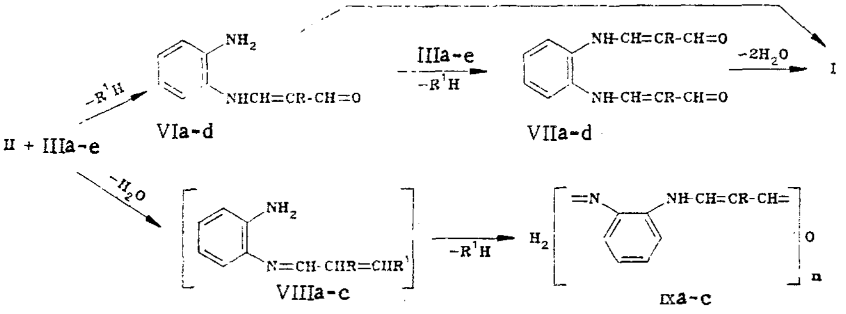
IV a $R=H$, b $R=CH_3$, c $R=C_2H_5$; V a $R=H$, $R^2=CH_3$; b $R=H$, $R^2=C_2H_5$; c $R=H$, $R^2=C_3H_7$; d $R=CH_3$, $R^2=C_2H_5$; e $R=C_2H_5$, $R^2=C_2H_5$

For acetals Va-c the Ia yields increase as the length of radical R^2 increases. For synthesis of Ia by the method given, the reaction product of vinyl butyl ether and ethyl orthoformate can be used without separation of the intermediate acetal. This route of Ia-c synthesis is of practical interest in connection with the availability of starting materials.

The replacement of the alkoxy group in the acrolein by dimethylamino changes the nature of the reaction substantially. In contrast to the corresponding alkoxyacroleins IIIb, the β-dimethylaminoacroleins IIIf, g in DMFA give compounds Ia, b only in low yield, whereas α-aryl-β-dimethylaminoacroleins IIIh, i give Ic, d in 30-45% yield; in quinoline the yields are lower. This reaction, studied by us for the first time, is convenient for the synthesis of Ic, d [6] because it insures the synthesis of the desired product in good yield from available materials in a shorter time and with fewer steps.

Under the conditions studied the condensation of β-acetoxy-acroleins IIIj, k with o-phenylene diamine II does not form compound I.

The general mechanism of the reaction of acroleins IIIa-e with compound II can be shown as follows:



VI, VII a $R=H$, b $R=CH_3$, c $R=C_2H_5$, d $R=C_6H_5$; VIII, IX a $R=CH_3$, b $R=C_2H_5$, c $R=C_6H_5$

The first step in the reaction of II with IIIa-e is the replacement of the alkoxy group to form β-(o-aminophenylamino)-acroleins VIa-d. A similar reaction is known specifically for aniline and β-methoxy-α-ethylacrolein [7]. As a result, the second amino group of VIa-d forms with IIIa-d the respective N,N'-di-(β-formylvinyl)-o-phenylene diamines VIIa-d, and then Ia-d. Compounds analogous to VIIb, c were isolated in [4] from the reaction of α-ethoxy-β-alkylacroleins with ethylene diamine. But further heating with diamine does not form a macrocycle, although compounds such as VII, obtained by the reaction of aromatic diamines with propargyl aldehyde, give annulene compounds upon further reaction with diamine [2, 3].

In special tests we demonstrated the formation of VIb and VIIb when o-phenylene diamine reacts with acrolein IIIc, and the conversions VIb → VIIb → Ib and VIb → Ib. Compounds VIb and VIIb were detected in the reaction mixture by TLC. It was determined by the same method that VIb reacts with IIIc to form VIIb.

The latter compound reacts with o-phenylene diamine in DMFA to give Ib in 20% yield. Moreover when acrolein VIb is heated it dimerizes and also forms Ib, but in low yield (5%). Thus VI → VII → I can be considered the fundamental course of the reaction.

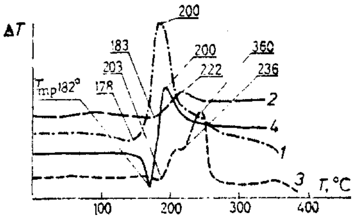


Fig. 1. DTA curves: 1, 2, 3) compounds IXa-c, respectively; 4) compound VIb.

Separate tests were carried out to demonstrate the structure and elucidate the formation of the polymeric Schiff bases IXa-c. We showed that boiling VIb in alcohol does not form base IXa, whereas when the latter hydrolyzes, VIb specifically is formed. Starting from this, we consider compounds VIIIa-c as alternative intermediates. The thermograms of IXa-c are compared with that of VIb in Fig. 1. The endothermic peak corresponding to the melting point of IX is absent from IXa-c, although there is some decrease in temperature before decomposition occurs. From these observations, combined with elemental analysis data and the extraction of small amounts of VIb from the reaction product of IXa, we can assign to IX the structure indicated in the diagram, with average n = 2-3. In view of the insolubility of the polymeric compounds in the usual organic solvents, a more detailed demonstration of their structure was not possible.

Synthesis of compounds Ia, b, d, e by the reaction of β-dimethylaminoacroleins IIIf-i with o-phenylene diamine can proceed by a mechanism analogous to that for the alkoxyacroleins, with replacement of the dimethylamino group:

$$\mathrm{II} + \mathrm{III}\,\text{f-i} \xrightarrow[-\mathrm{NH(CH_3)_2}]{} \mathrm{VI}\,\text{b,d,e}\ \mathrm{III}\,\text{f-i} \xrightarrow[-\mathrm{NH(CH_3)_2}]{} \mathrm{VII}\,\text{b,d,e} + \mathrm{II} \xrightarrow[-2\mathrm{H_2O}]{} \mathrm{I}$$

$$\mathrm{VI}\,\text{e},\ \mathrm{VII}\,\text{e}\ \ \mathrm{R{=}p\text{-}C_6H_4CH_3}$$

Such a reaction is exemplified by the reaction of β-dimethylaminoacrolein with alkylamines [8], and in our case is confirmed by the evolution of dimethylamine already at the very start of the reaction for any compounds III.

It should be noted in conclusion that the determination of the reaction sequence in the formation of compound I has not only theoretical, but also synthetic value. Thus, starting from VIIb and VIb we synthesized not only compound If but also Ig; these are substances that contain various substituents in the benzene ring and at positions 7 and 16.

EXPERIMENTAL

IR spectra were obtained with a UR-20 spectrometer in mineral oil; UV spectra, with a Specord UV-VIS instrument in DMFA; PMR spectra, with a Tesla BS-567 instrument in DMSO-D_6 solution and TMS internal standard. Formation of compounds VIb and VIIb was monitored by TLC on Silufol UV-254 plates, with acetonitrile eluent. Thermograms were obtained with a Derivatograf instrument in air, at 5 deg/min heating rate.

The synthesis of malonaldehyde tetraethyl acetal [9] was modified and extended to tetraalkyl acetals of malonaldehydes.

Tetraalkyl acetals of malonaldehydes (Va-d). A mixture of 4 moles of alkyl orthoformate, 1 mole of alkenyl acetate (IVa-c) and 4 g of anhydrous ferric chloride was boiled under reflux for 2 h, cooled, stirred with 10 g of sodium bicarbonate at 20° for 2 h, and filtered. The filtrate was fractionally distilled in vacuum. Yield of Va, 36%, bp 66-67° (12 mm); Vb 56%, bp 87-88° (6 mm); Vc 50%, bp 120-122° (5 mm); Vd 50%, bp 98-100P (8 mm); Ve 52%, bp 101-103° (8 mm). Boiling points agree with data of [10, 11].

5,14-Dihydro[b,i]dibenzo[5,9,14,18]tetraaza[14]annulene (Ia). A. A mixture of 2.7 g (0.025 mole) of o-phenylene diamine, 0.025 mole of alkoxyacrolein (IIIa or IIIb), and 5 ml of alcohol or DMFA was boiled under reflux for 1-2 h. After cooling, the precipitate was filtered off, washed with ether, and dried. Yield of Ia: from IIIa, 41% in alcohol and 19% in DMFA; from IIIb, 46% in alcohol and 20% in DMFA. Mp 296-297° (from benzonitrile). According to [3], mp 296-299°. IR and UV spectra are identical with those described in [3].

B. A mixture of 0.025 mole of acetal Va-c and 0.48 ml of 1% H_2SO_4 was boiled under reflux with vigorous stirring until it became homogeneous, and then 5 min more. Then 2.16 g (0.02 mole) of o-phenylene diamine was added and the mixture was boiled for 1 h. After cooling the precipitate was filtered off, washed with ether, and dried. Yield of Ia: from Va 6; from Vb 12.5; from Vc 14%. According to IR spectra the products were identical with the material obtained by method (A).

C. To a mixture of 8.3 ml (0.05 mole) of ethyl orthoformate and 0.02 ml of boron trifluoride etherate at 35° was added 6.3 ml (0.05 mole) of vinyl butyl ether dropwise with stirring. The mixture was held at 40° for 1 h, treated with 0.95 ml of water, and boiled with vigorous stirring until it became homogeneous and then 5 min more. Then 5.4 g (0.05 mole) of o-phenylene diamine was added and the mixture was boiled under reflux for 1 h. After cooling, the precipitate was filtered off, washed with ether, and dried. Yield of Ia, 9%. The reaction product was identical with that obtained by methods (A) and (B).

Substituted 5,14-dihydro[b,i]dibenzo[5,9,14,18]tetraaza[14]annulenes (Ib-d). A. A mixture of 0.025 mole of ethoxyacrolein IIIc, d, 2.7 g (0.025 mole) of o-phenylene diamine, and 3 ml of DMFA or quinoline was boiled under reflux for 3 h. After cooling, the precipitate was filtered off, washed with ether, and dried. Yield: Ib 20% in DMFA and 39% in quinoline; mp 291-292° (from DMFA) [1]; Ic 20% in DMFA and 53% in quinoline; mp 200° (from DMFA) [1]; Id 53% in quinoline; mp 316° (from DMFA) . The IR spectrum of Id agrees with that described in [5].

B. A mixture of 0.025 mole of acetal (Vd or Ve) and 0.48 ml of 1% H_2SO_4 was boiled under reflux with vigorous stirring until it became homogeneous and then 5 min more. Then 5 ml of DMFA was added, the alcohol was quickly distilled off, 2.16 g (0.02 mole) of o-phenylene diamine was added, and the mixture was again boiled under reflux for 3 h. After cooling the precipitate was filtered off, washed with ether, and dried. Yield: Ib 16%, Ic 16%. According to the IR spectra the products were identical with those obtained by method A.

C. A mixture of 0.2 mole of β-dimethylaminoacrolein (IIIg-i*), 21.6 g (0.2 mole) of o-phenylene diamine, and 45 ml of DMFA or quinoline was boiled under reflux for 2 h. After cooling the precipitate was filtered off, washed with ether, and dried. Yield: Ib 4-7% in DMFA and traces in quinoline; Id 45% in DMFA and 33% in quinoline; according to the IR spectra the products are identical with those obtained by methods (A) and (B); Ie 30% in DMFA, mp 317° (from DMFA). UV spectrum of Ie agrees with that described in [5].

Reaction of o-phenylene diamine with β-ethoxyacroleins IIIc-e in alcohol. A mixture of 1.08 g (0.01 mole) of o-phenylene diamine and 0.01 mole of the β-ethoxyacrolein in 5 ml of alcohol was boiled for 1 h. Yellow or red insoluble infusible powders — polymeric Schiff bases — were obtained. Yield of IXa 0.9 g. IR spectrum: 1635 (C=N), 3315 cm^{-1} (N—H). Found, %: C 72.1, H 6.8, O 4.5 (here and subsequently, oxygen by direct determination). $C_{20}H_{22}N_4O$. Calculated, % (for n = 2): C 71.8, H 6.6, N 16.8, O 4.8. Yield of IXb 0.9 g. IR spectrum: 1630 (C=N), 3310 cm^{-1} (N—H). Found, %: C 73.0, H 7.5, N 15.3, O 4.5. $C_{22}H_{26}N_4O$. Calculated, % (for n = 2): C 72.9, H 7.2, N 15.5, O 4.4. Yield of IXc 2 g. IR spectrum: 1630 (C=N), 3350 cm^{-1} (N—H). Found, %: C 79.5, H 5.5, N 12.7, O 2.3. $C_{45}H_{38}N_6O$. Calculated, % (for n = 3): C 79.6, H 5.6, N 12.4, O 2.4.

β-(o-Aminophenylamino)-α-methylacrolein (VIb). o-Phenylene diamine, 10.8 g (0.1 mole) was dissolved in 50 ml of water and 5.7 g (0.05 mole) of α-methyl-β-ethoxyacrolein was added. The mixture was shaken several times to dissolve the latter, and was let stand for 1-3 days. The precipitate was filtered off, washed with water, alcohol, and ether, and dried. Yield of VIb 78-87%, mp 182°. IR spectrum: 1657 (C=O), 3220 (N—H), 3330, 3410 cm^{-1} (NH_2). PMR spectrum: 1.73 (3H, s, CH_3); 7.05 and 7.78 (1H, 2d, s-cis and s-trans, CH—N); 9.09 ppm (1H, s, CH=O). Found, %: C 68.3, H 6.9, N 15.8. $C_{10}H_{12}N_2O$. Calculated, %: C 68.2, H 6.9, N 15.9.

Hydrolysis of Polymeric Schiff Base (IXa). Sodium acetate trihydrate, 0.3 g, was dissolved in 7.5 ml of water containing 0.03 ml of glacial acetic acid. To the solution were added 18 ml of alcohol and 0.66 g of polymeric Schiff base IXa, synthesized above. The mixture was boiled under reflux with stirring for 4 h. It was cooled and filtered from unreacted polymer, and 50 ml of water was added to the filtrate. The mixture was left overnight to crystallize. The precipitate was filtered off and dried. Yield of VIb 0.15 g. According to the IR spectrum the product was identical with that obtained above.

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*When compound IIIf was used, only traces of Ia formed in any of the solvents mentioned.

N,N'-Di(β-formyl-β-methylvinyl)-o-phenylene diamine (VIIb). In 15 ml of methanol were dissolved 0.54 g (5 mmole) of o-phenylene diamine, then 0.23 g (10 mmole) of sodium and 1.14 g (10 mmole) of α-methyl-α-ethoxyacrolein. The mixture was left over night. Then 0.57 ml (10 mmole) of acetic acid was added and the mixture was again left over night. The precipitate was filtered quickly through a porous filter (grade No. 1). The finely dispersed polymer IXa passed through the filter, and large well-formed crystals were left on the filter. The latter were washed with ether, dried and sieved to remove fine dark crystals of compound Ib. Yield of VIIb 0.25 g (20%), mp 192°. IR spectrum: 1615 (C=O), 3255 cm^{-1} (N—H). PMR spectrum: 1.75 (6H, s, CH_3); 7.52 and 8.73 (2H, 2d, s-cis and s-trans, CH—N); 9.16 ppm (2H, s, CH O). Found, %: C 69.0, H 6.7, N 11.4. $C_{14}H_{16}N_2O_2$. Calculated, %: C 68.8, H 6.6, N 11.5.

Self condensation of β-(o-aminophenylamino)-α-methyl-acrolein (VIb). A solution of 0.44 g (2.5 mmole) of β-(o-aminophenylamino)-α-methylacrolein in 0.6 ml of DMFA was boiled for 1 h. After cooling the precipitated dimerization product was filtered off, washed with ether, and dried, giving 0.02 g (5%) of Ib. According to the IR spectrum the product was identical with that obtained above.

Analogous treatment of the sample amount of VIb in the same amount of alcohol yielded the starting materials.

Condensation of N,N'-di(β-formyl-β-methylvinyl)-o-phenylene diamine (VIIb) with o-phenylene diamine. A mixture of 0.11 g (1 mmole) of o-phenylene diamine and 0.24 g (1 mmole) of N,N'-di(β-formyl-β-methylvinyl)phenylene diamine in 0.6 ml of DMFA was boiled for 1 h, giving 0.063 g (20%) of Ib, According to the IR spectrum the product was identical with that obtained above. Condensation could not be carried out in alcohol because of the low solubility therein of VIIb.

7,16-Dimethyl[11,12]dimethoxy[5,14]dihydro[b,i]dibenzo[5,9,14,18]tetraaza[14]annulene (If). A mixture of 0.49 g (2 mmole) of VIIb and 0.34 g (2 mmole) of unpurified 4,5-dimethoxy-o-phenylene diamine [12] in 1.2 ml of DMFA was heated for 1 h, cooled, treated with 1.2 ml of acetonitrile, and left over night to crystallize. The precipitate was filtered off, washed with ether, and dried. Yield of If 35 mg (4.6%). Mp 295-296°. UV spectrum, λ_{max} (log ε): 374 (3.67), 391 (3.73), 455 (3.51), 480 nm (3.46). PMR spectrum: 1.92 (6H, s, CH_3); 3.74 (6H, s, OCH_3); 7.84 (4H, s, CH of positions 6, 7, 15, 17); 13.64 and 13.94 ppm (CH, 2 t, NH). Found, %: C 70.2, H 6.4, N 14.9. $C_{22}H_{24}N_4O_2$. Calculated, %: C 70.1, H 6.4, N 14.8.

7-Methyl[16]phenyl[5,14]dihydro[b,i]dibenzo[5,9,14,18]tetraaza[14]annulene (Ig). A mixture of 1.76 g (0.01 mole) of VIb and 2.38 g (0.01 mole) of α-phenyl-β-ethoxyacrolein in 5 ml of DMFA was heated for 1 h at 80°. Then 1.08 g (0.01 mole) of o-phenylene diamine was added and the mixture was boiled for 1 h, then cooled. The precipitate was filtered off, washed with ether, and dried to give 0.88 g (23%) of Ig; mp 314°. UV spectrum, λ_{max} (log ε): 305 (4.51), 394 (4.50), 432 (4.06), 452 nm (4.04). PMR spectrum: 1.95 (3H, s, CH_3); 7.86 and 8.16 (4H, 2 t, CH at positions 6, 8, 15, 17); 13.59 and 14.18 ppm (2H, 2 t, NH). Found, %: C 79.3, H 6.0, N 14.9. $C_{25}H_{22}N_4$. Calculated, %: C 79.3, H 5.9, N 14.8.

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