

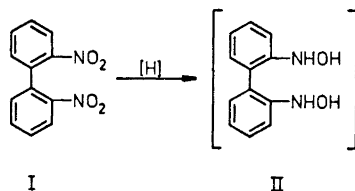
Reductive Cyclization of 2,2'-Dinitrobiphenyl to 5,7-Dihydroxy-6H-dibenzo[d,f][1,3]diazepines

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5,7-Dihydroxy-6H-dibenzo[d,f][1,3]diazepines have been prepared by reduction of 2,2'-dinitrobiphenyl with hydrogen under simultaneous addition of an aldehyde. The reduction could be carried out either catalytically or by hydrogen *in statu nascendi*. A more sterically hindered aldehyde does not yield any cyclic reaction products. Oxidation of the cyclic dihydroxylamines yielded a mixture of free radicals.

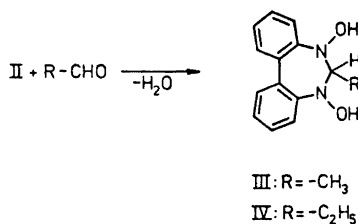
Moore and Furst¹ have proposed that biphenyl-2,2'-dihydroxylamine (II) might be an intermediate in the reduction of 2,2'-dinitrobiphenyl (I) to 2,2'-diaminobiphenyl (V).



So far all attempts to isolate this intermediate have been unsuccessful. However, if a dihydroxylamine is an intermediate, it should be possible to trap this *in situ* by an aldehyde. Similar reactions are known, *e.g.*, *N,N'*-(1,1,2,2-tetramethylethylene)dihydroxylamine (VII) reacts readily with aldehydes to give derivatives of 1,3-dihydroxy-4,4,5,5-tetramethyltetrahydroimidazoles (VIII) in good yield.^{2,3}

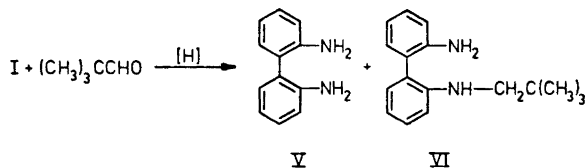
RESULTS

This paper describes the reduction of 2,2'-dinitrobiphenyl (I) and the simultaneous trapping of the expected dihydroxylamine by an aldehyde to form the hitherto unknown 5,7-dihydroxy-6H-dibenzo[d,f][1,3]diazepines (III and IV).



The reduction of I in dimethyl sulfoxide using either zinc or magnesium as reducing agent under simultaneous addition of acetaldehyde or propionic aldehyde (*method A*) yielded III or IV. Similarly reduction of I in ethanol in the presence of acetaldehyde with hydrogen, and palladium on barium sulfate as catalyst (*method B*), resulted in the formation of III. Thus the reaction seems to be general and the formation of III and IV as the main products strongly suggests the formation of II as an intermediate in the reduction of I.

The reaction between the aldehyde and the bis-hydroxylamine (II) must be relatively fast in order to compete with further reduction to the diamine. This is also indicated from the fact that when 2,2-dimethylpropanal was used in the reaction after *method B*, no cyclization took place. Instead 2,2'-diaminobiphenyl (V) and 2-(*N*-neopentylamino)-2'-aminobiphenyl (VI) were isolated.



The 2,2-dimethylpropanal is probably too hindered sterically to yield any cyclized product.

IDENTIFICATION OF PRODUCTS

The structure of III, IV, and VI were deduced from the spectroscopic and analytic data (see the experimental section for numerical values).

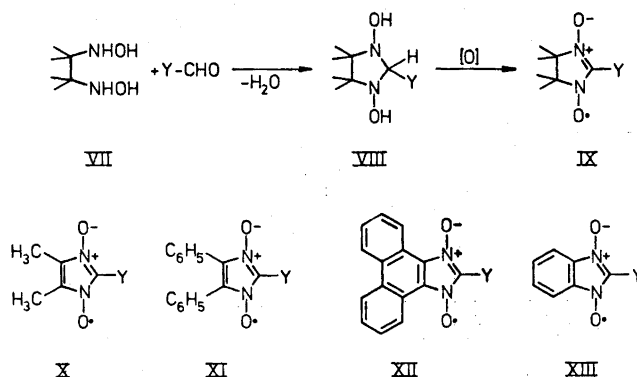
Strong absorption due to OH were seen in the IR spectra of III and IV. In the NMR spectra of III and IV the two OH groups were seen to be equivalent, and as expected, easily exchanged with D₂O. Furthermore the mass spectra of III and IV were very similar; both showed a strong molecular ion and a characteristic peak at *m/e* 180.*

In the IR spectrum of VI sharp absorption due to NH and NH₂ was seen, and in the NMR spectrum was seen a singlet due to the three NH protons. This peak disappeared after addition of D₂O. The rest of the NMR spectrum together with the mass spectrum and the elementary analysis showed VI to have the above depicted structure.

* The mass spectra of III and IV will be presented elsewhere.

OXIDATION

Recently hydroxylamine derivatives of imidazoles have been oxidized to free radicals containing the α -nitronyl nitroxide grouping.



Thus α -nitronyl nitroxides (IX) derived from the 1,3-dihydroxy-4,4,5,5-tetramethyltetrahydroimidazoles (VIII) prepared by Ullmann and Call³ are very stable, whereas the related nitroxides (X, XI, and XII) prepared by Volkamer and Zimmermann⁴ are stable.

Similarly, Balaban *et al.*⁵ found the radicals (XIII) prepared from 1-hydroxybenzimidazole-3-oxides to be stable; however, no information about the half life of XIII was given. Other radicals in the imidazole series have been prepared by Volodarsky *et al.*⁷ It was therefore of interest to see if the *N,N'*-dihydroxy diazepines (III and IV) could be converted into free radicals.

When benzene solutions of III and IV were treated with an excess of lead dioxide, the solutions turned red and ESR signals appeared. The ESR spectra indicated that a mixture of radicals was formed. However, since the ESR signals decayed in a few minutes at room temperature, the mixture of radicals was not separated and identified.

EXPERIMENTAL

Microanalyses were carried out in the Microanalytical Department of the University of Copenhagen by Mr. Preben Hansen. Melting points (uncorrected) were determined on a Büchi melting point apparatus.

Infrared spectra were recorded on a Perkin Elmer Model 457 grating infrared spectrophotometer either in KBr or in nujol. Ultraviolet spectra were recorded on a Beckman DB ultraviolet spectrophotometer. Proton magnetic spectra were recorded on a Jeol C-60H1 NMR spectrometer. The mass spectra were recorded by Drs. J. Møller and G. Schroll, University of Copenhagen, either on an MS 902 or a Finnigan 1015 mass spectrometer. The sample of 2,2'-diaminobiphenyl was prepared by Dr. N. Haunsø, University of Odense. The ESR spectra were recorded on a JES-ME-1X at the University of Copenhagen.

5,7-Dihydroxy-6-methyl-6H-dibenzo[d,f][1,3]diazepine (III). (Method A). 2,2'-Dinitrobiphenyl (I) (2.44 g) was dissolved in a mixture of 50 ml of dimethyl sulfoxide and 10 ml of water. Magnesium (2.0 g) and a solution of 10 ml of acetaldehyde in 20 ml of dimethyl sulfoxide were added simultaneously over a period of 2 h. With an automatic titrator (Radiometer 11) the pH of the reaction mixture was maintained at 5.5 during

the reaction by addition of 4 N hydrochloric acid. After this the reaction mixture was stirred for another 12 h. The reaction mixture was diluted with water followed by extraction with ether and separated by preparative layer chromatography on silica gel using ether-pentane (1 : 3) as eluent. The fraction which turned red when sprayed with a solution of sodium periodate was isolated to give 5,7-dihydroxy-6-methyl-6H-dibenzo[d,f][1,3]diazepine (III) as pale yellow crystals. Yield 1.1 g (46 %).

When magnesium was replaced by zinc, a similar yield of III could be obtained.

(*Method B*). A mixture of 1.22 g of 2,2'-dinitrobiphenyl (I), 1 ml of acetaldehyde, 0.2 g of 10 % palladium on barium sulfate, and a drop of 4 N sulfuric acid in 150 ml of absolute ethanol was shaken in a hydrogen atmosphere (1.5 atm) at room temperature for 3 h. After this 1 ml of acetaldehyde was added and the shaking continued for 15 h. Potassium carbonate (0.2 g) was added and the reaction mixture filtered through celite and concentrated *in vacuo*. The resulting pale yellow oil was separated by preparative layer chromatography, yielding 0.51 g (37 %) of III.

A sample of III recrystallized from ether-pentane gave colourless crystals, *m.p.* 168–170°C. (Found: C 69.40; H 5.92; N 11.46. Calc. for $C_{14}H_{14}N_2O_2$: C 69.40; H 5.83; N 11.56.)

IR: ν_{\max} (nujol) 3235 (s) (OH) cm^{-1} . NMR: (DMSO- d_6) τ 8.64 (d, $J = 5$ cps, 3H, CH₃); τ 5.31 (q, $J = 5$ cps, 1H, CH); τ 3.08–2.39 (m, 8H, aromatic protons); τ 1.25 (s, 2H, NOH). MS: *m/e* (intensity, %): M^+242 (100). UV: (96 % EtOH) ν_{\max} 291 nm (log $\epsilon = 3.46$), 231 nm (log $\epsilon = 4.45$).

5,7-Dihydroxy-6-ethyl-6H-dibenzo[d,f][1,3]diazepine (IV). IV was prepared by *method A* using propionic aldehyde. Yield 26 % of IV as pale yellow crystals. IV recrystallized from ether-pentane yielded colourless crystals, *m.p.* 139–142°C. (Found: C 70.25; H 6.20; N 11.00. Calc. for $C_{15}H_{16}N_2O_2$: C 70.29; H 6.29; N 10.93.)

IR: ν_{\max} (nujol) 3230 (s) (OH) cm^{-1} . NMR: (DMSO- d_6) τ 8.97 (t, $J = 6$ cps, 3H, CH₃); τ 8.12 (m, 2H, CH₂); τ 5.49 (t, $J = 6$ cps, 1H, CH); τ 3.11–2.48 (m, 8H, aromatic protons); τ 1.33 (s, 2H, OH). MS: *m/e* (intensity, %): M^+256 (40). UV: (96 % EtOH) λ_{\max} 296 nm (log $\epsilon = 3.44$), 232 nm (log $\epsilon = 4.48$).

2-(N-Neopentylamino)-2'-aminobiphenyl (VI). VI was prepared by *method B* using 2.44 g of 2,2'-dinitrobiphenyl (I) and 3 ml of 2,2-dimethylpropanal added in two portions.

Preparative layer chromatography gave two fractions *a* and *b*. Fraction *a* was a colourless oil (b.p. 90°, 0.3 mm) identified as VI. Yield 1.05 g (41 %). (Found: C 80.40; H 8.76; N 10.93. Calc. for $C_{17}H_{22}N_2$: C 80.27; H 8.72; N 11.01.)

IR: ν_{\max} (KBr) 3350, 3400 (m) (NH) cm^{-1} . NMR: (CDCl₃) τ 9.14 (s, 9H, CH₃); τ 7.12 (s, 2H, CH₂); τ 6.41 (s, 3H, NH); τ 3.45–2.74 (m, 8H, aromatic protons). MS: *m/e* (intensity, %): M^+254 (12) (Finnigan 1015). UV: (96 % EtOH) λ_{\max} 299 nm (log $\epsilon = 3.69$), 235 nm (sh) (log $\epsilon = 4.17$).

Fraction *b* was identified as 2,2'-diaminobiphenyl (V) by mixed melting point and identical IR and NMR with that of an authentic sample,⁶ yield 0.77 g (42 %).

Oxidation of III and IV. The oxidation of III and IV was carried out by adding an excess of lead dioxide to dilute solutions of either III or IV in benzene. The mixtures were shaken for a few minutes at 15° and then centrifuged. In both cases a strong red colour was seen, and the ESR spectra indicated that a mixture of radicals was formed.

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