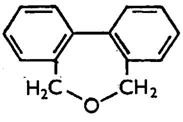
# **504.** *The Stereochemistry of the Bridged Quaternary Salts of 2,2′-Bipyridyl.*

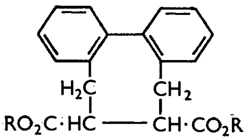
By R. F. Homer and T. E. Tomlinson.

The stereochemistry of a number of diquaternary salts of 2,2′-bipyridyl in which the quaternising group forms a bridge between the nitrogen atoms has been investigated by ultraviolet spectroscopy and by measurements of the redox potentials of the compounds. The results closely parallel those for the isosteric 2,2′-bridged biphenyls. In the compounds having bridging chains up to four carbon atoms long the presence of considerable inter-ring conjugation has been demonstrated. This conjugation present in the ethylene-bridged compound is little affected by the introduction of *oo*′-methyl groups, whereas conjugation in 2,2′-bipyridyl dimethiodide is much reduced.

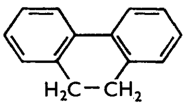
Beaven and his co-workers [1,2] examined the ultraviolet spectra of a series of biphenyl derivatives containing 2,2′-bridging groups with from two to four atoms in the bridge. On the basis of molecular models they concluded that there is a twist of 50° between the planes of the benzene rings in the dihydrodibenzoxepin (I), and they argued that the high degree of inter-ring conjugation revealed in the ultraviolet absorption spectrum of this molecule could only be explained on the assumption that " large departures from coplanarity may be accommodated [in bridged biphenyls] without complete loss of conjugation." This assumption was later [2] apparently substantiated by the finding of considerable conjugation between the benzene rings of the $C_4$-bridged compound (II). In order to account for the unexpectedly high degree of inter-ring conjugation in these twisted molecules Beaven and Johnson [3] subsequently produced evidence suggesting that possibly " the bridge atoms may be involved through hyperconjugation, in the interaction between the phenyl groups, in addition to their influence on the angle between the benzene ring planes."



(I)



(II)



(III)

Braude and Forbes,[4] on the other hand, produced evidence that the angle of twist in compound (I) was only about 21°, not significantly different from that of 9,10-dihydrophenanthrene (III) which is also conjugated and is generally agreed to be twisted through 18—20°. On the basis of their investigations of spectra they concluded that compounds such as (I) and (III) were non-planar in their ground state but were near-planar in the excited state.*

*ortho*-Substituted bridged compounds usually exhibit inter-ring conjugation,[4,5] while similarly substituted unbridged compounds do not. Beaven *et al.* explain this as due to the fact that the unsubstituted bridged molecule is already sufficiently twisted to accommodate these substituents without further twisting. Braude and Forbes explain it by postulating a " locking-effect " to be exerted by the bridge which limits further out-of-plane twisting of the rings; *ortho*-substituents are, in their view, accommodated in much less twisted molecules by distortion of the bond angles between the substituent and the ring.

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* Suzuki (*Bull. Chem. Soc. Japan*, 1959, **32**, 1340) has concluded, by calculation, that some conjugation is possible in twisted biphenyl systems.

[1] Beaven, Hall, Lesslie, and Turner, *J.*, 1952, 854.

[2] Beaven, Bird, Hall, Johnson, Lesslie, and Turner, *J.*, 1955, 2708.

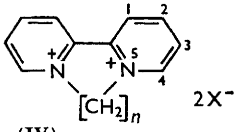
[3] Beaven and Johnson, *J.*, 1957, 651.

[4] Braude and Forbes, *J.*, 1955, 3776.

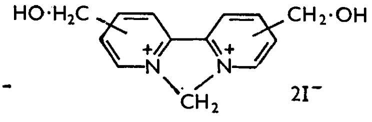
[5] Hall and Minhaj, *J.*, 1957, 4584.

Two schools of thought therefore exist and it appeared that a series of bridged diquaternary salts of 2,2'-bipyridyl (IV) would prove interesting. Whereas in the biphenyl field, the only readily available tool for configurational studies is ultraviolet spectroscopy, several bipyridyl compounds have redox properties which it will be shown depend on the degree of conjugation possible between the rings.

The compounds (IV; $n = 2$, 3, and 4) are readily available by treatment of 2,2'-bipyridyl with the appropriate polymethylene αω-dihalide. 6,7,8,9-Tetrahydrodipyrido-[1,2-*a*:2,1-*c*]-[1,4]-diazocinium dibromide (IV; $n = 4$) always crystallised with one-third of a mol. of hydrogen bromide, arising presumably by dehydrohalogenation of the tetramethylene dibromide used for quaternisation and revealed by titration and analysis.



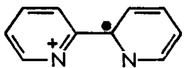
(IV)



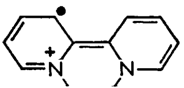
(V)

Several attempts to prepare the methylene compound (IV; $n = 1$) by treatment of 2,2'-bipridyl with a methylene dihalide gave no pure product. Use of methylene sulphate in nitrobenzene led to a quaternary salt, isolated as iodide, which appeared from analysis to be the required 6*H*-dipyrido[1,2-*c*:2,1-*e*]imidazolium dibromide with the addition of two formaldehyde residues. These were presumably combined as nuclear hydroxymethyl groups, since formaldehyde was not removed at 135°/0·001 mm. The bridged quaternary structure (V) suggested for this compound is strongly supported by its ultraviolet spectrum.

We reported recently [6] that 6,7-dihydrodipyrido[1,2-*a*:2,1-*c*]pyrazinium dibromide (IV; $n = 2$) reacts with strong reducing agents, *e.g.*, sodium dithionite, in aqueous solution, taking up a single electron and forming a free radical. The free radical is relatively stable, presumably owing to delocalisation of its odd electron over the whole molecule. The possibility of such delocalisation is illustrated by the eighteen possible resonance forms which can be written for the radical without postulation of charge separation. Some of these structures do not involve conjugation between the rings (*e.g.*, VI), but six of the structures (*e.g.*, VII) involve conjugation *via* a double bond between the rings.



(VI)



(VII)

Maximum stabilisation of the radical only occurs therefore when it is possible for conjugation to exist between the pyridine nuclei.

The stability of the original quaternary salt, however, is not dependent upon inter-ring conjugation; hence factors which tend to prevent ring coplanarity will tend to reduce the stability of the free radical relative to that of the unreduced salt. This relative stability may be measured by determining the reduction–oxidation potential of the reaction in which the radical is formed from the diquaternary salt; the smaller the relative stability of the radical the more difficult is the reduction and the more negative the redox potential. One factor which influences the value of the redox potential is, therefore, the degree of conjugation between the rings in the radical, which is related to the amount of steric hindrance in the molecule.

In the three compounds (IV; $n = 2$, 3, and 4), as the length of the bridging group increases, the redox potential associated with radical formation becomes more negative (cf. Table). This indicates that the longer the bridging group the less stable is the free radical

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[6] Homer and Tomlinson, *Nature*, 1959, **184**, 2012.

relative to its parent quaternary salt. This is most simply interpreted as reflecting an increased departure from coplanarity which decreases the ease with which the odd electron of the radical becomes delocalised, or increases the energy required to impose a conjugated structure on the molecule. An extreme example of the effect of restriction of conjugation on redox potential is provided by 2,2′-bipyridyl dimethiodide which cannot be reduced to a radical at potentials that can be attained in aqueous solution.

The methylene-bridged compound (V) is reduced in aqueous solution in a complex and irreversible manner and its behaviour cannot be interpreted in terms of redox properties.

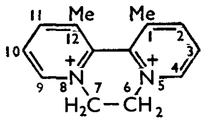
The absorption spectra and redox properties of the 1,12- (VIII), 2,11- (IX) and 3,10-dimethyl derivative (X) of the ethylene-bridged compound are summarised in the Table. In the 2,11- and the 3,10-compound the methyl groups would not be expected to influence inter-ring configuration, and the fact that the redox potentials of these compounds are ~120 mv more negative than that of the unsubstituted parent compound is probably due to the inductive effect of the methyl groups.

*Ultraviolet absorption spectra and redox potentials of bipyridyl salts.*

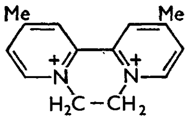
| Compound | $\lambda_{max.}$ | ε | Normal redox potential (mv) (H = 0) |
|---|---|---|---|
| (IV; *n* = 2) | 308—311 | 19,000 | −349 ± 3 |
| Monoprotonated bipyridyl | 302 | 14,700 [b] | |
| | 300 | 15,000 [a] | |
| Diprotonated bipyridyl | 290 | 15,200 [b] | |
| (IV; *n* = 3) | 287 | 15,600 | −548 ± 3 |
| 2,2′-Bipyridyl monomethochloride | 277 | 9,330 [b] | |
| (IV; *n* = 4) | 275 | 15,000 | ~−700 |
| 2,2′-Bipyridyl dimethiodide | 269 | 13,500 [a] | Not reduced |
| | 270 | 13,600 [c] | at −750 |
| Monoprotonated 2,2′-bipyridyl monomethochloride | 270 | 11,500 [b] | |
| (V) | 295 | 18,800 | Complex reduction |
| (VIII) | 307—310 | 15,600 | −580 ± 20 |
| (IX) | 305 | 16,700 | −487 ± 3 |
| (X) | 320—330 | 20,600—19,800 | −479 ± 3 |

[a] Krumholtz, *J. Amer. Chem. Soc.*, 1951, **73**, 3487. [b] Westheimer and Benfey, *ibid.*, 1956, **78**, 5309. [c] This work.

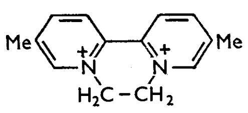
In the 1,12-dimethyl compound (VIII), however, the methyl groups would be expected to interfere with the configuration of the molecule owing to the increased twist necessary to accommodate them. It is noteworthy, therefore, that the redox potential of this compound is only some 100 mv more negative than those of the 2,11- and the 3,10-compound and is in fact almost the same as that of the trimethylene-bridged compound (IV; *n* = 3). The reduction of this compound is in marked contrast to the non-reducibility of 2,2′-bipyridyl dimethiodide in which one would expect a comparable degree of non-planarity. It appears, therefore, that the ethylene bridge largely overcomes the steric interference of the methyl groups in this compound. Braude and Forbes [4] observed a similar effect in the isosteric biphenyl, and Hall and Minhaj [5] found a comparable effect on introducing a bridge into a chlorobiphenyl.



(VIII)



(IX)



(X)

Krumholtz,[7] examining the ultraviolet spectra of 2,2′-bipyridyl, its monoprotonated ion, and its dimethiodide, and the spectra of other isomeric bipyridyl dimethiodides and salts, concluded that " some kind of electronic interaction involving a double (or π-)bond

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[7] Krumholtz, *J. Amer. Chem. Soc.*, 1951, **73**, 3487.

between the rings is related to the characteristic spectral behaviour of the polynuclear compounds," and further, " that in all α-substituted quaternary compounds the absorption spectrum consists of a unique band of reduced oscillator strength as compared with the spectra of the free bases and their NH ions. The absorption maximum of the biquaternary ions of the α,*x*-bipyridyls is located at a shorter wavelength than that of the long wavelength band of the free bases and their NH ions. This behaviour indicates strongly that steric hindrance by the α-NMe group prevents coplanarity of the rings, and hence structures involving a double bond between the rings."

Westheimer and Benfey [8] found that the ultraviolet spectra suggested that neither diprotonated 2,2'-bipyridyl nor the monoprotonated monomethiodide was flat, and ascribed this to twisting of the molecule by electrostatic repulsion of the charged nitrogen atoms. In the non-planar compounds the absorption maximum was less intense and at shorter wavelength than in the planar compounds.

The Table lists figures given by these workers and others obtained during the present work. Although embodying results from three different sources the figures appear to be comparable as the results of Krumholtz and of Westheimer and Benfey for the monoprotonated base agree well, as do ours and Krumholtz's for the dimethiodide. It is clear from the Table that of all the unsubstituted compounds examined the ethylene-bridged one shows the highest intensity and longest-wavelength absorption and is therefore presumably the most highly conjugated. That it is more conjugated than the diprotonated base is explicable on the basis of twisting of the latter by electrostic repulsion of the charged nitrogen atoms. As the chain length of the bridge is increased the intensity of the absorption falls and the maximum shifts to a shorter wavelength. It appears from the spectra, as from the redox data, that there is still slightly more conjugation in the tetramethylene-bridged compound than in the dimethiodide. As no criterion for complete non-conjugation can be deduced for these compounds, since no absorption which can be attributed to non-conjugated pyridine chromophores appears, it cannot be decided whether any residual conjugation remains in the dimethiodide.

The intensity of the absorption of the dimethyl ethylene-bridged salt (VIII) fits well with the closeness of its redox potential to that of the trimethylene compound (IV; $n = 3$), which has a similar ultraviolet absorption spectrum. The comparatively long wavelength of the absorption maxima of the methyl-substituted compounds is presumably due to the bathochromic effect of the methyl groups since, *e.g.*, β-picoline methiodide absorbs at 2650 Å compared with 2580 Å for pyridine methiodide. Both the intensity and the position of the peak for the compound obtained from bipyridyl and methylene sulphate are strong arguments for the correctness of formula (V), despite the complex behaviour on reduction.

The figures given by Westheimer and Benfey for the monoquaternary monoprotonated ion and for the monoquaternary ion itself are as expected for a slightly sterically hindered molecule (interference between the *N*-Me and the *o'*-H), which in the former case is intensified by additional twisting due to electrostatic repulsion.

It is clear then that the redox potentials of the compounds, and their ultraviolet absorption spectra, are both influenced by conjugation, which is related to the degree of departure from coplanarity of the unexcited molecule. Hence, in considering their stereochemistry, deductions from both types of evidence may be used. The two methods are however independent, for excitation and reduction are different processes and the similarity between the results arises because in both processes the stability of the final form of the molecule, the excited or the reduced state, depends more upon conjugation than does the stability of the ground state. Both redox potentials and ultraviolet absorption spectra indicate a lessening of conjugation between the pyridine rings as the length of the bridging chain is increased. On the basis of ultraviolet absorption the effect of a 4-carbon chain is approximately as great as that of a single *o*-methyl substituent, the effects of 2- and 3-carbon

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[8] Westheimer and Benfey, *J. Amer. Chem. Soc.*, 1956, **78**, 5309.

chains being less. Both spectra and redox potentials show that steric effects of bridging groups up to $C_4$ are less than those introduced by two *o*-methyl substituents. More conjugation, therefore, is present in the bridged compounds than seems probable at first sight and this is emphasised by the effect revealed both by spectra and redox measurements of a 2-carbon bridge in overcoming the greater part of the restriction of conjugation normally associated with *o*-methyl substituents.

It may be concluded, therefore, that the dependence of conjugation upon stereochemistry which is so well established in the biphenyl series by ultraviolet-spectral investigations, is closely paralleled in the bipyridyl series, where redox potential measurements may be used to confirm deductions from spectral studies. Unfortunately, however, like spectral studies, redox potential determinations cannot be used to distinguish unambiguously between the alternative ideas of Beaven *et al.* and Braude and Forbes; the conflict might be resolved most simply by crystallographic investigations.

## EXPERIMENTAL

*Determinations of Ultraviolet Spectra.*—Ultraviolet absorption spectra were determined for $10^{-4}$M-aqueous solutions at 200—400 mμ, by means of a Unicam S.P. 500 spectrophotometer.

*Determinations of Reduction–Oxidation Potentials.*—A solution of the quaternary salt, freed from oxygen by a stream of oxygen-free nitrogen, was titrated at 30° with sodium dithionite solution. The potential of the system was measured between either of two gold electrodes and a saturated calomel electrode (assumed 0·238 v at 30°) after addition of each aliquot part of reductant, and again after the lapse of one minute to ensure that potential drift due to contamination with traces of oxygen was less than 1 mv/min. Each determination was carried out several times, with good agreement between replicates. The redox potentials were calculated from these results by the standard procedure.

As the redox potentials of the compounds were shown to be independent of pH the determination was carried out in a buffer solution at as high a pH as was consistent with the stability of the compound, in most cases at pH 10, to avoid exceeding the hydrogen potential. In the case of the tetramethylene-bridged compound it was not possible to obtain a complete reduction curve owing to interference by the hydrogen potential. The figure of approx. $-700$ mv is deduced from the first part only of the curve, which by analogy with the behaviour of the other compounds allows extrapolation to a figure which is probably within $+50$ to $-100$ mv of the true value.

6,7-*Dihydrodipyrido*[1,2-a:2,1-c]*pyrazinium Dibromide.*—2,2'-Bipyridyl (20 g.) was stirred under reflux with ethylene dibromide (100 c.c.) for 16 hr. The mixture was cooled, and the solid filtered off and washed with acetone and ether to give the anhydrous quaternary salt (31 g., 69%). Recrystallisation from aqueous acetone yields the *monohydrate*, m. p. 340° (decomp.) varying with the rate of heating (Found: C, 40·0; H, 3·5; Br, 44·6; $H_2O$, 5·1. $C_{12}H_{12}N_2Br_2,H_2O$ requires C, 39·8; H, 3·7; Br, 44·2; $H_2O$, 5·0%).

6,7-*Dihydro*-1,12-*dimethyldipyrido*[1,2-a:2,1-c]*pyrazinium Dibromide.*—3,3'-Dimethyl-2,2'-bipyridyl (1·8 g.) and ethylene dibromide (10 c.c.) were heated under reflux for 12 hr. To the cooled mixture was added acetone (20 c.c.), and the solid was filtered off and washed with acetone. The crude material was treated with carbon in water (10 c.c.) and reprecipitated with acetone (100 c.c.), to give the *quaternary salt monohydrate* (2·8 g.), m. p. >380° (Found: C, 43·2; H, 4·5; N, 7·0. $C_{14}H_{16}N_2Br_2,H_2O$ requires C, 43·1; H, 4·6; N, 7·2%).

6,7-*Dihydro*-2,11-*dimethyldipyrido*[1,2-a:2,1-c]*pyrazinium Dibromide.*—4,4'-Dimethyl-2,2'-bipyridyl (1·6 g.), nitrobenzene (10 c.c.), and ethylene dibromide (1·5 c.c.) were heated at 170—180° for 7 hr. The solid product was filtered off, treated with carbon in a small volume of water, and precipitated with acetone, to give the *quaternary salt monohydrate* (1·1 g.), m. p. 268—270° (Found: C, 43·0; H, 4·5; N, 7·0%).

6,7-*Dihydro*-3,10-*dimethyldipyrido*[1,2-a:2,1-c]*pyrazinium Dibromide.*—5,5'-Dimethyl-2,2'-bipyridyl (4·0 g.), nitrobenzene (20 c.c.), and ethylene dibromide (5 c.c.) gave, as above, the *quaternary salt* (6·8 g.), m. p. 330—335° (decomp.) (Found: C, 40·3; H, 4·6; N, 6·65; Br, 38·2. $C_{14}H_{16}N_2Br_2,2{\cdot}5H_2O$ requires C, 40·3; H, 5·0; N, 6·7; Br, 38·4%).

7,8-*Dihydro*-6H-*dipyrido*[1,2-a:2,1-c]-[1,4]-*diazepinium Dibromide.*—2,2'-Bipyridyl (6·0 g.) and trimethylene dibromide (20 c.c.) were heated under reflux for 16 hr. Isolation as above gave the *quaternary salt* (9·75 g.), m. p. >300° (Found: Br, 42·7. $C_{13}H_{14}N_2Br_2,H_2O$ requires Br, 42·6%).

6,7,8,9-*Tetrahydrodipyrido*[1,2-a:2,1-c]-[1,4]-*diazocinium Dibromide*.—2,2′-Bipyridyl (5·0 g.) and tetramethylene dibromide (20 c.c.) were heated at 140° for 6 hr. The solid was filtered off, washed with acetone, and treated with carbon in methanol (150 c.c.), and hot acetone (100 c.c.) was added. The *quaternary salt* (4·5 g.), m. p. 265° (decomp.), separated on cooling. Further crystallisation from aqueous ethanol failed to raise the m. p. [Found: C, 40·4; H, 4·3; N, 7·0; Br, 43·8; titratable acidity as $Br^-$, 6·2; O (by combustion), 4·65. $C_{14}H_{16}N_2Br_2,H_2O,\frac{1}{3}HBr$ requires C, 40·4; H, 4·4; N, 6·8; Br, 44·7; acidity, 6·4; O, 3·8%].

x,x′-*Bishydroxymethyl*-6H-*Dipyrido*[1,2-c:2,1-e]*imidazolium Di-iodide*.—Methylene sulphate (11 g.) was stirred in nitrobenzene (100 c.c.) at 100°, and 2,2′-bipyridyl (15·6 g.) in hot nitrobenzene (50 c.c.) was added. The mixture was heated at 150—160° for 3 hr. and a dark solid separated. After cooling, the nitrobenzene was decanted and the solid residue was boiled with water (100 c.c.) for 1 hr. to decompose unchanged methylene sulphate. The aqueous solution was treated with carbon, filtered, cooled, and neutralised with an excess of calcium carbonate. After filtration from inorganic material the filtrate was evaporated in a vacuum to a reddish oil which was dissolved in hot water (20 c.c.) and treated with sodium iodide (5 g.) in hot water (10 c.c.). The salt which separated on cooling was filtered off and recrytallised from aqueous ethanol in red needles (1·8 g.), m. p. 280° (decomp.) (Found: C, 32·0; H, 2·6; N, 5·65; I, 52·8. $C_{13}H_{14}O_2N_2I_2$ requires C, 32·2; H, 2·7; N, 5·8; I, 52·5%).

The authors are indebted to Dr. R. L. Jones for the method of synthesis of 6,7-dihydrodipyrido[1,2-*a*:2,1-*c*]pyrazinium and 7,8-dihydro-6*H*-dipyrido[1,2-*a*:2,1-*c*]-[1,4]-diazepinium dibromide.

Imperial Chemical Industries Limited,
Jealott's Hill Research Station,
Bracknell, Berks.

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