Polyaza Cavity Shaped Molecules. 5. Annelated Derivatives of 2,2'-Bipyridine

Randolph P. Thummel,* Francois Lefoulon, and Ramanathan Mahadevan

Department of Chemistry, University of Houston, Houston, Texas 77004

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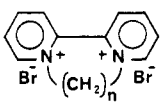
Friedländer condensation of β-aminoacrolein with α-oxo-2,3-cycloalkenopyridines or thermolysis of the *O*-allyloximes derived from these ketones leads to the formation of 3,3'-bridged-2,2'-bipyridines **2a–d**. Reaction of **2a–d** with 1,2-dibromoethane gives rise to the corresponding 1,1';3,3'-doubly bridged diquaternary salts. The NMR spectra of the dimethylene- and trimethylene-bridged compounds are consistent with structures which are conformationally mobile at room temperature, while the tetramethylene-bridged system is conformationally rigid up to 150 °C. The basicity and ultraviolet absorption spectra of **2a–d** may be related to the dihedral angle defined by the two pyridine rings and the resulting conjugative stabilization.

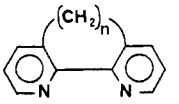
Biaryls have held a long time fascination for organic chemists. Mechanistic investigations have centered around the electronic and steric interactions of two covalently bonded aromatic rings where a principal consideration has been the relationship between the dihedral angle defined by the planes of these two rings and the degree of conjugative interaction between them. One convenient method available for such studies is to bridge the biaryl system and thus control the stereochemical relationship of the two planar ring systems. Early work in the 1950's on 2,2'-bridged biphenyls examined the electronic spectra of such molecules and drew sometimes conflicting conclusions regarding the prerequisite conformation.[1] The following decade brought forth elegant studies by Mislow and co-workers on 2,2';6,6'-doubly bridged biphenyls where the potential for optical activity was explored in detail.[2] Chemical reactivity of the aromatic rings themselves has been examined[3] as well as reactivity in side-chain derivatives.[4]

Unfortunately the chemistry of biphenyl itself is relatively uninteresting. By comparison, the diaza analogue, 2,2'-bipyridine, has a rich chemistry in which interest is currently growing. Most importantly, 2,2'-bipyridine is an effective ligand which coordinates a large variety of metals. By bridging 2,2'-bipyridine with ethylenedioxy units at the 6 and 6' positions, Newkome and co-workers have created a variety of new chelating systems.[5] Bridged diquaternary derivatives of 2,2'-bipyridine have been studied extensively[6] with diquat (**1a**) being a potent herbicide.[7] Homer and Tomlinson have studied the effect of varying the length of the diquaternary bridge in **1a–c** as a function of their reduction potential and electronic spectra.[8] Rebek and co-workers have bridged 2,2'-bipyridine at the 3 and 3' positions, again with ethylenedioxy units, to create macrocycles capable of demonstrating an allosteric effect by site-specific metal binding.[9]

For several years we have been interested in the effects of annelation on aromaticity and have prepared and studied a series of mono- and bis-annelated pyridines to establish the effects of annelating four- and five-membered rings to the pyridine nucleus.[10] As an extension of this work, we report the preparation and properties of series of 3,3'-annelated derivatives of 2,2'-bipyridine, **2a–d**, and their conversion of 1,1'-ethano-bridged diquaternary salts, **6a–d**.



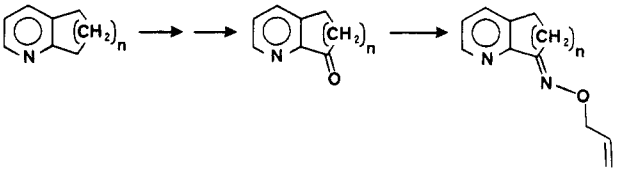
1a, $n = 2$
b, $n = 3$
c, $n = 4$



2a, $n = 1$
b, $n = 2$
c, $n = 3$
d, $n = 4$

Synthesis

Two different approaches to the preparation of 3,3'-annelated bipyridines have been developed. Both utilize the annelated pyridyl ketones **4a–d** as the key starting material. These ketones may be prepared by a previously described two-step route which involves conversion to the α-benzylidene derivative by condensation with benzaldehyde in acetic anhydride, followed by ozonolysis and reduction of the ozonide with methyl sulfide.[11]



3a, $n = 1$
b, $n = 2$
c, $n = 3$
d, $n = 4$

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5b, $n = 2$
c, $n = 3$
d, $n = 4$

The bridged bipyridines **2a–c** can be prepared by the Friedländer condensation of β-aminoacrolein with the

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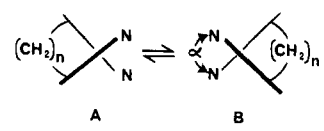


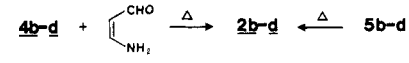
n	∝	Estimated Barrier
1	0°	0 Kcal/mole
2	20	≤4
3	55	≤13
4	80	

Figure 1.

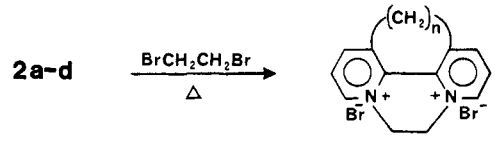
appropriate ketones **4**. In the case of **4b** and **4c** these condensations proceed to give moderate yields of **2b** and **2c**, respectively, while **4a** gives only low yields of **2a**, which is more easily obtained by the previously described Wolff–Kishner reduction of 1,8-diazafluorenone.[12]

An alternate two-step route from **4** to **2** proceeds more smoothly. Treatment of the ketones **4** with *O*-allylhydroxylamine lead to the corresponding *O*-allyloximes **5** in purified yields of 87–94%. Heating these materials in a sealed tube at 180 °C for 50 h results in the formation of bipyridines **2b–d** in yields of 36–66%.[13] By either method of synthesis, the 5,6-dihydro-1,10-phenanthroline (**2b**) is produced as a dark reddish oil, even after repeated column chromatography. Nevertheless, this material appears to be quite pure spectroscopically and by preparative gas chromatography it can be obtained as an off-white, low melting solid. A priori, facile oxidation to 1,10-phenanthroline might be invoked as the reason for these purification problems; however treatment of a $CHCl_3$ solution of **2b** with 2,3-dichloro-5,6-dicyano-1,4-benzoquinone at 25 °C for 24 h showed little or no oxidation to have occurred.

We have recently reported the synthesis of 3,3′-annelated 2,2′-biquinolines[14] and 2,2′-bi-1,8-naphthyridines[11] by a double Friedländer condensation of 2 equiv of o-aminobenzaldehyde or 2-aminonicotinaldehyde with 1,2-cycloalkanediones. Thus, it appeared that a similar condensation of β-aminoacrolein with these cyclic diketones might provide our desired bipyridines in a single reaction. Of the systems previously studied, yields have consistently been highest with 1,2-cyclooctanedione. When this material was reacted with 2 equiv of β-aminoacrolein, however, none of the desired bipyridine **2d** could be detected.



The diquaternary salts **6a–d** were readily prepared by heating **2a–d** in 1,2-dibromoethane for 2 h during which time the desired material precipitated from solution.



6a, $n = 1$
b, $n = 2$
c, $n = 3$
d, $n = 4$

Properties

There are two ways in which a 3,3′-bridge can affect the geometry of 2,2′-bipyridine. To relieve eclipsing interactions or torsional strain in the annelated bridge, there can be rotation about the 2,2′-bond causing the pyridine rings to be noncoplanar. The dihedral angle between these rings is governed by the length of the bridge, and values estimated from Dreiding models are given in Figure 1. Notice

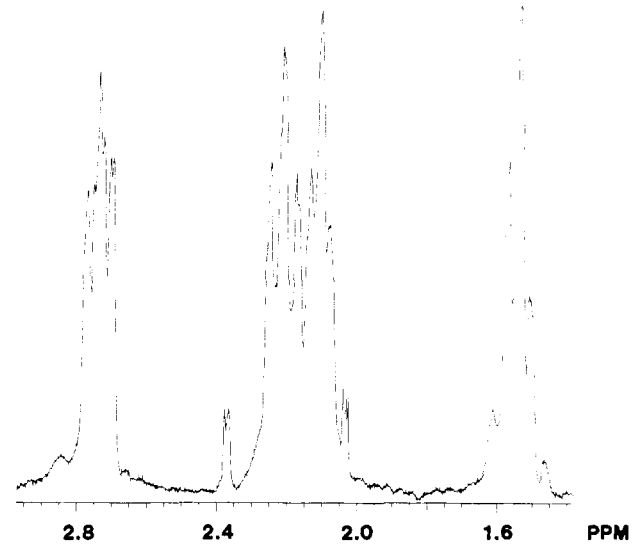
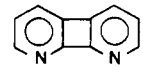


Figure 2. 300-MHz ^1H NMR spectrum of the upfield region of 3,3′-tetramethylene-2,2′-bipyridine (**2c**) [$CDCl_3$].

also that as the system interconverts between the two minimum energy conformations of the annelated ring conformational enantiomerism occurs. A sufficiently high barrier to such interconversion could lead to the isolation of optical isomers.

While the systems where $n = 2$ can relieve strain by twisting about the 2,2′-bond, the systems where $n = 0$ or $n = 1$ must remain coplanar and thus a distortion of the trigonal bond angles centered at C-2 and C-2′ must occur. By analogy with the known structure of fluorene,[15] the angle interior to the five-membered ring of **2a**, centered at C-2, is compressed to ca. 108° and the angle exterior to the two fused rings is expanded to ca. 131°. For 1,8-diazabiphenylene (**7**), these same two angles have been recently reported as 89.6° and 146.1°, respectively.[16]



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This type of in-plane distortion significantly increases the distance between the pyridyl nitrogen lone pairs and thus influences their cooperativity. One should also not overlook significant rehybridization changes at the bridgehead carbons of the $n = 0$ and $n = 1$ systems and resulting distortions in the pyridine ring geometry.[10]

Mislow and co-workers have calculated the conformational inversion barrier for 9,10-dihydrophenanthrene to be ca. 4 kcal/mol and that of the next higher homologue containing three methylene units to be ca. 13 kcal/mol.[2b] The corresponding bipyridine derivatives **2b** and **2c** should have similar or slightly lower inversion barriers by analogy with studies on [2.2]metacyclophane and its pyridine analogue.[17] The ^1H NMR spectrum of **2b** shows a sharp methylene singlet at 2.94 ppm, and it is unlikely that temperature-dependent behavior will be observed with this system.[18] At 300 MHz, **2c** shows a doublet of doublets

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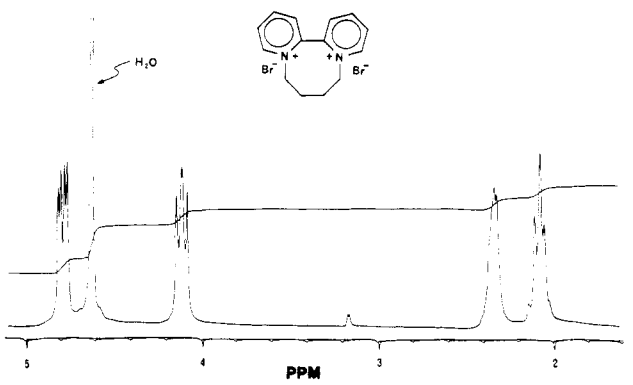

Figure 3. 400-MHz ^{1}H NMR spectrum of the upfield region of 1,1′-tetramethylene-2,2′-bipyridinium dibromide (**1c**) [D_2O].

(J = 6.7 Hz and J = 13.4 Hz) for the benzylic methylenes centered at 2.41 ppm and a triplet of triplets (J = 6.7 Hz and J = 13.4 Hz) centered at 2.12 ppm for the central methylene, indicating that molecule is conformationally mobile at 25 °C on the NMR time scale. Four signals of equal intensity in its aliphatic region (Figure 2) at 2.73, 2.21, 2.11, and 1.53 ppm indicate that **2d** is conformationally rigid. The two lower field signals are assigned to the α-methylene resonances while the higher field peaks belong to the β-methylenes. Examination of a molecular model reveals that one of the α-protons lies nearly in the plane of the adjacent pyridine ring and hence is shifted downfield to 2.73 ppm. On the other hand, one of the two nonequivalent β-protons points toward the shielding region of the more remote pyridine ring and hence is shifted upfield to 1.53 ppm. When a solution of **2d** in $C_6D_5NO_2$ is heated to 150 °C in the NMR, broadening of all four signals is observed but higher temperatures are apparently required for coalescence. The proton-decoupled ^{13}C NMR spectrum of this same molecule shows two clear carbon resonances at 31.0 and 28.3 ppm, verifying that **2d** does possess a C-2 symmetry axis. Similar behavior has been observed in the tetramethylene-bridged derivatives of 2,2′-biquinoline[14] and 2,2′-bi-1,8-naphthyridine.[11] The surprisingly high barrier to conformational inversion for **2d** should allow one to resolve the system into its optical antipodes. Efforts along these lines are being pursued.

A system related to **2d** would be the 1,1′-tetramethylene bridged diquaternary salt **1c** which was first reported by Calder and co-workers[6a] who saw evidence for magnetic nonequivalence of the bridge protons at 60 MHz. We prepared this compound by the reaction of 2,2′-bipyridine with 1,4-dibromobutane and examined its ^{1}H NMR spectrum at 400 MHz (Figure 3). As observed for **2d**, this system is clearly conformationally rigid, evidencing four well-separated resonances for the [A,A′,B,B′]$_2$ protons of the bridge. Notice that the α-methylene protons which are now adjacent to a quaternary nitrogen are shifted well downfield. These signals are also somewhat better resolved than the β-methylene signals which are only slightly shifted. We are also attempting to resolve this material.

Next we examined the 1,1′-ethano-bridged salts **6a–d** in hopes that the second bridge would impose some additional rigidity on the system. The 3,3′-bridge for **6a–d** showed nearly the same NMR pattern as for **2a–d** except that most of the resonances were somewhat deshielded and shifted downfield by 0.4–1.0 ppm. For **6a–c**, the 1,1′-bridge showed a sharp singlet in the range of 5.3–5.56 ppm which indicated that for these systems all four methylene protons in the bridge were equivalent and conformational inversion was still rapid on the NMR time scale. For **6d**, however, we observed an A_2B_2 pattern centered at 5.06 ppm (Figure 4), indicating that the ethano-bridge protons were no longer equivalent and the molecule was conformationally rigid.

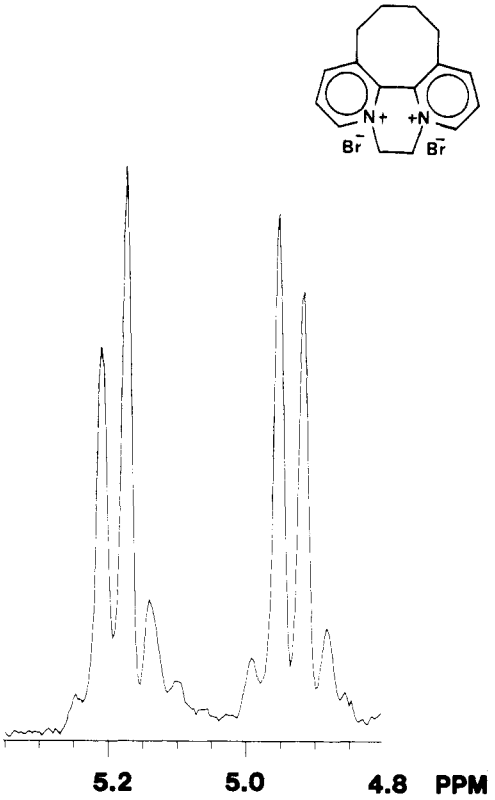

Figure 4. 300-MHz ^{1}H NMR spectrum of the ethano bridge of 9,10-dihydro-4,5-tetramethylene-8a,10a-diazoniaphenanthrene dibromide (**6d**) [D_2O].

Table I. Basicity[a] and Ultraviolet Absorption Data

compd	pK_1 (HNP, mV)	pK_2 (HNP, mV)	95% EtOH (ϵ)	λ_{max}
2,2′-bipyridine	4.44[b] (340)	−2.7 (793)	236 (11 500)	284 (15 000)
2a	4.0[c] (368)	−2.1[c] (743)	243 (7710)	313 (27 370) 305 (20 370) 298 (18 770)
2b	5.70 (255)	*d*	230 (6050)	280 (7700)
2c	4.75 (315)	−2.0 (748)	232 (6880)	279 (10 100)
2d	4.70 (326)	+0.1 (616)	218 (7800)	268 (7100)

[a] Determined as half-neutralization potential (HNP) by titration with 0.1 N $HClO_4$/HOAc in acetic anhydride. [b] Reference 19. [c] Reference 20. [d] A clear second equivalence point was not observed. If one assumes that this point occurs at twice the titrant volume of the first equivalence point, an HNP of 850 mV (pK_2 −3.6) may be estimated.

Table I summarizes the ultraviolet absorption data and basicities of **2a–d**. When 2,2′-bipyridine is bridged at the 3 and 3′ positions with a single methylene unit, the resulting diazafluorene exhibits a bathochromic shift as would be expected for a more rigid, planar molecule. As the bridge length is increased up to four methylene units the absorption maxima steadily shift to shorter wavelengths. This shift reflects diminished π-delocalization resulting from the concurrent increase in the bipyridine dihedral angle.

Considering the addition of the first proton to bipyridine, we observed that the change upon going from 2,2′-bipyridine to 4,5-diazafluorene (**2a**) is to lower the pK_a

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by 0.44 unit. The comparable change in going from 2-phenylpyridine (pK_a = 4.48) to 4-azafluorene (pK_a = 3.55) is about twice as much, which is to say that the prerequisite ciscoid disposition of the nitrogen lone pairs in **2a** augments the basicity of the molecule. In **2b** the lone pairs are still favorably disposed with respect to one another but noncoplanarity of the two pyridine rings retards delocalization and the pK_a increases to 5.70. In **2c** and **2d** the dihedral angle between the pyridine rings has increased substantially and the pK_a drops to 4.70–4.75, approximately the value expected for a 2-aryl-3-alkylpyridine. The low basicity of **2a** may also be due in part to rehybridization of C-2 (and C-2′) resulting from five-membered ring fusion.[10] As expected, the second protonation of bipyridine and its annelated derivatives is more difficult than the first as reflected by the lower pK_2 values. Electrostatic as well as steric effects inhibit addition of the second proton. It is interesting that for **2d** where the two pyridine rings are held nearly perpendicular (θ = 80°), the steric inhibition appears to be diminished and the pK_2 value increases substantially.

Results from polarography are consistent with two one-electron transfers to the diquaternary salts **6a–d** where the measured standard half-wave potentials for the first reduction step are 0.36, 0.39, 0.47, and 0.54 V, respectively.[21] The decrease in the ease with which these salts will accept an electron reflects their diminished ability to effectively delocalize this electron. These values compare well with the reported values of 0.35 V for diquat (**1a**) and 0.58 V for the corresponding 4,5-dimethyl derivative.[22]

We are continuing our examination of the properties of annelated 2,2′-bipyridines and their salts as well as extending our studies to metal complexes of these systems.

Experimental Section

Nuclear magnetic resonance spectra were obtained on a Varian Associates FT-80 or XL-100 or a Nicollet NT-300 WB spectrometer, and chemical shifts are reported in parts per million downfield from Me_4Si. Infrared spectra were obtained on a Beckman IR-4250 or a Perkin Elmer 1330 spectrometer. Ultraviolet spectra were obtained on a Cary 14 spectrometer. Mass spectra were obtained by direct sample introduction into a Hewlett-Packard 5933A GC–mass spectrometer. Basicities were determined according to the method of Markgraf and Katt[23] by potentiometric titration with a Radiometer RTS 622 recording titration system. All solvents were freshly distilled reagent grade. 2,3-Cyclooctenopyridine (**4d**) was prepared by the method of Kakisawa et al.[13a] and also obtained as a generous gift from Prof. Jan Epsztajn.[24] All melting points are uncorrected.

10-Benzylidenecycloocta[*b*]pyridine. A mixture of 5.86 g (0.04 mol) of 2,3-cyclooctenopyridine, 7.5 g (0.07 mol) of benzaldehyde, and 10 mL of Ac_2O was heated to reflux with stirring under N_2 for 8 days. Benzaldehyde, Ac_2O, and AcOH were then removed by distillation under reduced pressure. The residue was fractionally distilled to give 8.3 g (83%) of 10-benzylidenecycloocta[*b*]pyridine, bp 140–160 °C (0.3 mm): ^{1}H NMR (80 MHz, $CDCl_3$) δ 8.46 (dd, H_2, $J_{2,3}$ = 7.0, $J_{2,4}$ = 1.8 Hz), 7.42 (dd, H_4, $J_{3,4}$ = 5.0 Hz), 7.33 (br s, Ar H), 7.08 (dd, H_3), 6.49 (s, C*H*-ϕ), 2.71 (m, 4 H), 1.48 (m, 6 H); IR (thin film) 3050, 3020, 2920, 2850, 1580, 1565, 1490, 1433, 800, 780, 754, and 700 cm^{-1}.

Cycloocta[*b*]pyridin-10-one (4d). A solution of 1.5 g (6 mmol) of 10-benzylidenecycloocta[*b*]pyridine in 120 mL of CH_2Cl_2 was treated with a mixture of oxygen and ozone at −40 °C until the solution became blue, indicating that it was saturated with ozone. The dissolved ozone was purged by bubbling N_2 through the solution; 8 mL of methyl sulfide were added, and the mixture was stirred for 0.5 h at −35 °C. After being warmed to 25 °C and stirred overnight, the solution was washed with water and 5% NaOH, dried over K_2CO_3, and concentrated to give a yellow oil. Chromatography on 40 g of silica gel, eluting with EtOAc–hexane (1:1), provided 0.42 g (40%) of **4d**, bp 105–110 °C (0.2 mm): ^{1}H NMR (80 MHz, $CDCl_3$) δ 8.44 (dd, H_2, $J_{2,3}$ = 4.7, $J_{2,4}$ = 1.4 Hz), 7.55 (d, H_4, $J_{3,4}$ = 7.9 Hz), 7.26 (dd, H_3), 2.78 (br s), 1.64 (br s); ^{13}C NMR (20 MHz, $CDCl_3$) 208.3, 156.4, 146.3, 137.0, 132.8, 123.6, 44.0, 30.3, 27.6, 26.1, 22.5; IR (thin film) 2880, 2840, 1675, 1555, 1425, 1270, 1170, 1032, 968, 891, 796 cm^{-1}; MS, *m/e* (relative intensity) 176 (12), 175 (M^+, 24), 147 (85), 146 (64), 138 (28), 132 (100), 131 (82), 130 (91).

5,6,7,8-Tetrahydro-8-quinolone Oxime *O*-(Allyl ether) (5b). A solution of 1.6 g (11 mmol) of ketone **4b**,[11] 1.05 g (11 mmol) of *O*-allylhydroxylamine hydrochloride,[13b] 1.2 g of anhydrous NaOAc, and 1.2 g of anhydrous Na_2CO_3 in 25 mL of EtOH was refluxed for 2 h. After evaporation of the solvent, the residue was extracted with $CHCl_3$. The $CHCl_3$ solution was washed with water, dried over $MgSO_4$, and concentrated to give an oil which was purified by Kügelröhr distillation to afford 2.08 g (94%) of **5b**, bp 123 °C (0.1 mm): ^{1}H NMR (80 MHz, $CDCl_3$) δ 8.53 (dd, H_2), 7.38 (d, H_4), 7.09 (dd, H_3), 6.3–5.9 (m, —CH=), 5.24 (m, =CH_2), 4.83 (d of t, -OCH_2-), 2.77 (m, 4 H), 1.68 (quintet, 2 H); IR (thin film) 1430, 1020, 1000, 860, and 780 cm^{-1}.

Cyclohepta[*b*]pyridin-9-one Oxime *O*-(Allyl ether) (5c). According to the procedure outlined above, 0.805 g (5 mmol) of ketone **4c**[11] were treated with 0.548 g (5 mmol) of *O*-allylhydroxylamine hydrochloride to provide 0.96 g (92%) of **5c**, bp 100–120 °C (0.15 mm): ^{1}H NMR (80 MHz, $CDCl_3$) δ 8.49 (dd, H_2), 7.41 (dd, H_4), 7.18 (dd, H_3), 6.2–5.8 (m, =CH—), 5.23 (m, =CH_2), 4.78 (m, -OCH_2-), 2.70 (m, 4 H), 1.69 (m, 4 H); IR (thin film) 1425, 1090, 1010, 990, 790, 770, and 720 cm^{-1}.

Cycloocta[*b*]pyridin-10-one Oxime *O*-(Allyl ether) (5d). According the the procedure outlined above, 0.875 g (5 mmol) of ketone **4d** were treated with 0.548 g (5 mmol) of *O*-allylhydroxylamine hydrochloride to provide 1.0 g (87%) of **5d**, bp 130 °C (0.2 mm); ^{1}H NMR (80 MHz, $CDCl_3$) δ 8.44 (dd, H_2), 7.46 (dd, H_4), 7.17 (dd, H_3), 6.2–5.5 (m, —CH=), 5.29 (m, =CH_2), 4.67 (d of t, -OCH_2-), 2.75 (m, 4 H), 1.52 (m, 6 H); IR (thin film) 1430, 1020, 990, 910, and 770 cm^{-1}.

4,5-Diazafluorene (2a). A mixture of 3 g (16.7 mmol) of 4,5-diazafluoren-9-one[25] and 0.92 g (18.3 mmol) of $NH_2NH_2{\cdot}H_2O$ was heated at 200 °C for 6 h. After cooling, the mixture was extracted with CH_2Cl_2 (4 × 150 mL) and the extracts were dried over anhydrous $MgSO_4$ and concentrated to give a solid. This material was chromatographed on silica gel, eluting with EtOAc, to give 1.25 g (45%) of 4,5-diazafluorene, mp 170–171 °C; lit.[12] mp 172 °C.

5,6-Dihydro-1,10-phenanthroline (2b). Method A. A mixture of 1.0 g (6.8 mmol) of **4b**,[11] 0.65 g (9.15 mmol) of β-aminoacrolein,[10] and 25 mg of anhydrous NH_4OAc in 30 mL of ethylene glycol was heated at 140 °C for 19 h. After cooling, this mixture was poured into 200 mL of water and extracted with CH_2Cl_2 (5 × 50 mL). The organic extracts were combined, washed well with water, dried, and concentrated to give 1.1 g of a reddish solid which was chromatographed on 40 g of silica gel, eluting with CH_2Cl_2 (500 mL), 1:1 EtOAc–CH_2Cl_2 (100 mL), and EtOAc (700 mL). From the EtOAc fraction was obtained 0.43 g of 5,6-dihydro-1,10-phenanthroline as a reddish oil. This material showed a single peak by VPC (0.25 in. × 4 ft column of 10% Carbowax 20 M and 10% KOH on Chromsorb W, 60–80 mesh, at 185 °C and 35 mL/min of He) at a retention time of 16 min. Isolation of this peak gave a solid, mp 32–33 °C: ^{1}H NMR (100 MHz, $CDCl_3$) δ 8.67 (dd, $H_{2,9}$, $J_{2,3}$ = 4.60, $J_{2,4}$ = 1.50 Hz), 7.51 (dd, $H_{4,7}$, $J_{3,4}$ = 7.62 Hz), 7.18 (dd, H_5), 2.94 (s, 4H, -CH_2-); ^{13}C NMR (20 MHz, $CDCl_3$) δ 151.8 (C-2), 148.8 (C-6), 135.8 (C-4), 133.6 (C-3), 123.5 (C-5), and 27.3 (-CH_2-); IR (thin film) 1580, 1565, 1444, 1422, 809, 775, and 749 cm^{-1}; MS, *m/e* (relative intensity) 182 (100, M), 181 (99), 105 (47), 77 (82), 63 (67), 51 (71). The molecule formed a nonstoichiometric hydrate which would not analyze correctly.

Method B. A glass tube (1 cm × 20 cm) containing 2.08 g (10 mmol) of **5b** was sealed and heated at 180 °C for 50 h. After

(21) Half-wave potentials were measured vs. the standard calomel electrode and assume a reversible electron transfer.
(22) Reference 7, p 58.
(23) Markgraf, J. H.; Katt, R. J. *J. Org. Chem.* **1972**, *37*, 717.
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(25) (a) Kloc, K.; Mlochowski, J.; Szulc, Z. *J. Prakt. Chem.* **1977**, *319*, 959. (b) Eckhard, I. F.; Summers, L. A. *Aust. J. Chem.* **1973**, *26*, 2727.

cooling, the resulting dark oil was dissolved in $CHCl_3$ and washed with 5% HCl. The HCl washings were made basic with Na_2CO_3 and then extracted with $CHCl_3$. The extracts were washed with water, dried over anhydrous K_2CO_3, and concentrated. Chromatography on alumina, eluting with EtOAc, gave 0.72 g (40%) of **2b** as an oil which showed spectral properties identical with the material obtained by method A above.

3,3′-Trimethylene-2,2′-bipyridine (2c). Method A. In the manner described above for **2b**, a mixture of 2.0 g (12.4 mmol) of **4c**,[11] 1.3 g (18.3 mmol) of β-aminoacrolein, and 30 mg of anhydrous NH_4OAc in 20 mL of ethylene glycol was heated at 140 °C for 19 h. After this time an additional 50 mg of NH_4OAc was added, and the mixture was heated at 150 °C for 5 h. Workup provided 2.1 g of a reddish oil which was chromatographed on 40 g of silica gel, eluting with CH_2Cl_2 (1L), 1:1 EtOAc–CH_2Cl_2 (200 mL), and EtOAc (1 L). From the EtOAc fraction was obtained 0.29 g (12%) of a solid which showed a single peak by VPC (same conditions as for **2b** at a retention time of 26 min). Isolation of this peak gave pure **3c**, mp 140–141 °C: ^1H NMR (100 MHz, $CDCl_3$) δ 8.71 (dd, $H_{6,6'}$, $J_{5,6}$ = 4.7, $J_{4,6}$ = 1.3 Hz), 7.57 (dd, $H_{4,4'}$, $J_{4,5}$ = 7.6, $J_{5,6}$ = 1.3 Hz), 7.24 (dd, $H_{5,5'}$), 2.41 (dd, α-CH_2-, J = 6.7, J = 1.3 Hz), 2.12 (t of t, β-CH_2-, J = 6.7, J = 13.4 Hz); ^{13}C NMR (20 MHz, $CDCl_3$) δ 156.9 (C-2), 148.4 (C-6), 136.6 (C-4), 135.2 (C-3), 123.2 (C-5), 32.4 (α-C), and 29.8 (β-C); IR (KBr) 2932, 1562, 1422, 900, 820, 803, and 758 cm^{-1}; MS, m/e (relative intensity) 196 (35, M), 195 (30), 178 (12), 139 (18), 117 (88), 115 (100), 91 (76). Anal. Calcd for $C_{13}H_{12}N_2$: C, 79.57; H, 6.16; N, 14.27. Found: C, 79.80; H, 5.90; N, 14.20.

Method B. Following the same procedure outlined above for **2b**, 0.94 g (4.3 mmol) of **5c** was heated at 180 °C for 50 h, and the crude product was chromatographed on alumina, eluting with EtOAc, to provide 0.3 g (36%) of **2c**. Recrystallization from EtOAc/hexane provided a solid, mp 136–138 °C, which showed identical spectral properties with the material obtained by method A above.

3,3′-Tetramethylene-2,2′-bipyridine (2d). Following the procedure described as method B for **2b** above, 1.0 g (4.3 mmol) of **5d** was heated at 180 °C for 50 h and the crude product chromatographed on 30 g of alumina, eluting with EtOAc, to provide 0.6 g (66%) of **2d** which gave white crystals upon recrystallization from $CHCl_3$, mp 140–142 °C: ^1H NMR (300 MHz, $CDCl_3$), 8.62 (H_2), 7.59 (H_4), 7.29 (H_3) [the typical pyridyl H–H splittings are complicated by long range couplings], 2.73 (m, α-CH), 2.21 (m), 2.11 (m), 1.53 (m, β-CH); ^{13}C NMR (75 MHz, $CDCl_3$), 155.6 (C-2), 147.0 (C-6, J_{CH} = 179 Hz), 137.0 (C-3), 137.0 (C-4, J_{CH} = 166 Hz), 123.1 (C-5, J_{CH} = 162 Hz), 31.0 (α-C, J_{CH} = 128 Hz), 28.3 (β-C, J_{CH} = 131 Hz); IR (thin film) 3050, 2910, 2925, 2850, 1564, 1420, 1138, 1092, 1075, 788, and 758 cm^{-1}; MS, m/e (relative intensity) 211 (M + 1, 24), 210 (M, 84), 195 (18), 182 (54), 181 (100); m/e calcd for $C_{14}H_{14}N_2$ 210.1157, found 210.1148.

9,10-Dihydro-4,5-methylene-8a,10a-diazoniaphenanthrene Dibromide (6a). A solution of 28 mg (0.165 mmol) of **2a** in 1.5 mL of freshly distilled 1,2-dibromoethane was stirred and heated to reflux for 2 h during which time a precipitate formed. The mixture was cooled and filtered, and the solid thus obtained was washed with acetone and then with ether to afford 54 mg (92%) of **6a** as a green solid, mp >300 °C; ^1H NMR (100 MHz, D_2O) δ 9.19 (d, $H_{1,8}$, $J_{1,2}$ = 6.0 Hz), 9.04 (d, $H_{3,6}$, $J_{2,3}$ = 7.9 Hz), 8.38 (dd, $H_{2,7}$), 5.56 (s, $H_{9,10}$), 4.72 (s, 4, 5-CH_2-).

9,10-Dihydro-4,5-dimethylene-8a,10a-diazoniaphenanthrene Dibromide (6b). Following the procedure described above for **6a**, 30 mg (0.165 mmol) of **2b** afforded 47 mg (77%) of **6b** as a green solid, mp >300 °C; ^1H NMR (100 MHz, D_2O) δ 9.04 (dd, $H_{1,8}$, $J_{1,2}$ = 6.0, $J_{1,3}$ = 1.2 Hz), 8.74 (d, $H_{3,6}$, $J_{2,3}$ = 8.1 Hz), 8.25 (dd, $H_{2,7}$), 5.34 (s, $H_{9,10}$), 3.45 (s, 4,5-CH_2CH_2-).

9,10-Dihydro-4,5-trimethylene-8a,10a-diazoniaphenanthrene Dibromide (6c). Following the procedure described above for **6a**, 32 mg (0.163 mmol) of **2c** afforded 52 mg (83%) of **6c** as a cream color solid, mp >300 °C: ^1H NMR (100 MHz, D_2O) δ 9.18 (dd, $H_{1,8}$, $J_{1,2}$ = 5.9, $J_{1,3}$ = 1.3 Hz), 8.84 (dd, $H_{3,6}$, $J_{2,3}$ = 8.2 Hz), 8.30 (dd, $H_{2,7}$), 5.30 (s, $H_{9,10}$), 2.85 (br m, 4,5-$CH_2CH_2CH_2$-).

9,10-Dihydro-4,5-tetramethylene-8a,10a-diazoniaphenanthene Dibromide (6d). Following the procedure described above for **6a**, 50 mg (0.24 mmol) of **2d** afforded 58 mg (63%) of **6d** as a yellow solid, mp >300 °C: ^1H NMR (300 MHz, D_2O) δ 8.99 (d, $H_{1,8}$, $J_{1,2}$ = 5.8 Hz), 8.72 (dd, $H_{3,6}$, $J_{2,3}$ = 8.3, $J_{1,3}$ = 1.0 Hz), 8.16 (dd, $H_{2,7}$), 5.05 (d of q, $H_{9,10}$), 3.14 (dd, 2H), 2.21 (t, 2 H), 2.12 (t, 2H), 1.66 (quintet, 2H).

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Regiochemistry and Stereochemistry of Nickel-Promoted, Carbon–Carbon Bond-Forming Reactions of Cyclic Sulfur Compounds

Marcello Tiecco* and Marco Tingoli

Istituto di Chimica Organica, Facoltà di Farmacia, Università degli Studi, Perugia, Italy

Ernest Wenkert*

Department of Chemistry (D-006), University of California—San Diego, La Jolla, California 92093

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Reactions of methylmagnesium iodide and phenylmagnesium bromide with thianaphthene, dibenzothiophene, thianthrene, and 2,3-dihydrothiapyran in the presence of [1,3-bis(diphenylphosphino)propyl]nickel dichloride have been shown to yield, regioselectively in most cases, ring-opened products in which the carbon–sulfur bonds have been replaced by carbon–carbon bonds. Stereospecific carbon–carbon bond formation has taken place in the reactions of thianaphthene and 2,3-dihydrothiapyran, the products having maintained the cis-olefin configuration of the starting sulfur compounds. Isomerization into the more stable compounds has been observed in some cases.

The last five years have witnessed the discovery[1,2] and subsequent general study[3-13] of carbon–carbon bond-forming reactions between alkenyl or aryl sulfides and Grignard reagents in the presence of phosphine-ligated

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