

Synthesis, Metal Complex Formation, and Resolution of a New C₂ Diazabiaryl Ligand: Cyclo-octa[2,1-*b*:3,4-*b'*]dipyridine

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A new C₂ diazabiaryl ligand cyclo-octa[2,1-*b*:3,4-*b'*]dipyridine (**1**) has been prepared, and an X-ray crystallographic analysis of the tetracarbonyl molybdenum complex of (**1**) showed that the torsional angle between the alkenic bonds is 51°; attempted resolution of (**1**) with a chiral palladium complex apparently afforded a single diastereoisomer, whose stereochemical configuration was substantiated by one-dimensional and two-dimensional proton NMR studies.

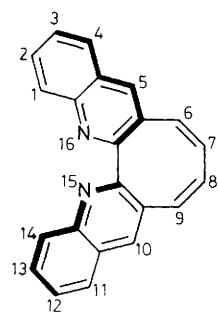
From a chemical perspective, the synthesis of metal complexes containing 2,2'-diazabiaryl ligands¹ seems especially worthy of study because these compounds have found applicability in the domains of host-guest chemistry, photochemistry, biochemistry, as well as organic synthesis.² Recently, we have prepared cyclo-octa[2,1-*b*:3,4-*b'*]diquinoline (**1**) and have accordingly proved that it functions as a new C₂ diazabiaryl ligand.³ However, the reactivity of (**1**) in this particular aspect is limited in a sense that H(1) and H(14) of (**1**) might be sterically detrimental to metal co-ordination.⁴ In the light of this fact, we reasoned that the parent compound of (**1**), namely cyclo-octa[2,1-*b*:3,4-*b'*]dipyridine (**2**) is a much better C₂ diazabiaryl ligand. Here we wish to report the synthesis, complex formation, and attempted resolution of (**2**).

Compound (**2**) was assembled as outlined in Scheme 1. Although the synthesis of (**5**) in two steps has been recorded,⁵ we discovered independently that direct condensation of β-aminoacrolein (**3**) and cyclo-octanone (**4**) in the presence of a catalytic amount of ammonium acetate and triethylamine also gave (**5**) in 25% yield. Condensation of (**5**) with benzaldehyde in acetic anhydride for 8 days provided the α-benzylidene derivative (**6**) in 83% yield, whose alkenic bond was cleaved by treatment with ozone and was followed by reduction of the resulting ozonide with dimethyl sulphide. In this manner, the pyridyl ketone (**7**) was isolated in 40% yield.⁶ The second pyridine ring was constructed by refluxing (**7**) with *O*-allylhydroxylamine hydrochloride (**8**),⁷ furnishing the allyl

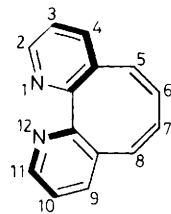
oxime (**9**) in 87% yield.⁶ The allyl oxime (**9**) was then heated at 180 °C for 52 h in a sealed tube to give the dipyridine (**10**) in 60% yield,⁵ m.p. 140–142 °C (from CHCl₃) [lit⁶ m.p. 140–142 °C]. Bromination with *N*-bromosuccinimide (NBS) in CCl₄ converted (**10**) to a mixture of dibromides (**11**) in 65% yield,[†] which was not separated and was allowed to undergo dehydrobromination with alcoholic KOH to afford the target molecule (**2**) in 70% yield.[†] The geometry of (**2**) is believed to resemble that of (**1**)³ as can be substantiated by the coupling constants of the alkenic protons.[†] It is of interest to note that

† Selected data for (**11**): m.p. 180–181 °C (from EtOAc/EtOH); *m/z*: 366 (*M*⁺); ¹H NMR (CDCl₃) δ 2.02 (m, 1H), 2.30 (m, 2H), 2.60 (m, 1H), 4.92 (dd, *J* 9, 11 Hz, 1H), 5.36 (dd, *J* 5, 13 Hz, 1H), 7.39 (dd, *J* 5, 7 Hz, 1H), 7.49 (dd, *J* 5, 8 Hz, 1H), 7.78 (dd, *J* 1.5, 8 Hz, 1H), 8.14 (dd, *J* 1.5, 7 Hz, 1H), 8.79 (m, 2H). For (**2**): m.p. 194–195 °C (from EtOAc/C₆H₁₄); *m/z*: 206 (*M*⁺); ¹H NMR (C₆D₆) δ 5.71, 6.20 [AA'BB', *J*_{5,6} 11 Hz, *J*_{5,7} -1.2 Hz, *J*_{6,7} 2.5 Hz, 4H, H(5,6,7,8)], 6.64 [dd, *J*_{3,4} 7.8 Hz, *J*_{2,3} 4.6 Hz, 2H, H(3,10)], 6.83 [dd, *J*_{3,4} 7.8 Hz, *J*_{2,4} 1.6 Hz, 2H, H(4,9)], 8.56 [dd, *J*_{2,3} 4.6 Hz, *J*_{2,4} 1.6 Hz, 2H, H(2,11)]. For (**12**): m.p. 215 °C (decomp.) (from xylenes/C₅H₁₂); ¹H NMR (C₆D₆) δ 5.33, 5.59 [AA'BB' *J*_{5,6} 10.3 Hz, *J*_{5,7} -0.2 Hz, *J*_{6,7} 3 Hz, 4H, H(5,6,7,8)], 6.17 [dd, *J*_{3,4} 7.8 Hz, *J*_{2,3} 5.2 Hz, 2H, H(3,10)], 6.48 [dd, *J*_{3,4} 7.8 Hz, *J*_{2,4} 1.4 Hz, 2H, H(4,9)], 8.63 [dd, *J*_{2,3} 5.2 Hz, *J*_{2,4} 1.4 Hz, 2H, H(2,11)]. For (*R,R,R*)-(14): m.p. 198–200 °C (from MeOH/Et₂O); ¹H NMR (CDCl₃) δ 1.14 (d, *J* 6.6 Hz, 3H, Me_a), 1.48 (d, *J* 6.5 Hz, 3H, Me_b), 2.34 (s, 3H, Me_c), 2.50 (s, 3H, Me_d), 2.53 (s, 3H, Me_e), 2.84 (s, 3H, Me_f), 3.54 (q, *J* 6.5 Hz, 1H, H_g), 3.70 (q, *J* 6.6 Hz, 1H, H_h), 5.51 (d, *J* 7.8 Hz, 1H, H_i), 5.63 (d, *J* 7.1 Hz, 1H, H_j), 6.18 [ABCD, *J*_{5,6} 11.2 Hz, *J*_{5,7} -2.4 Hz, *J*_{6,7} 2.8 Hz, *J*_{6,8} -2.4 Hz, *J*_{7,8} 12.0 Hz, 4H, H(5,6,7,8)], 6.69–6.78 (m, 4H, H_{1,j}), 6.96 (m, 2H, H_{k,k'}), 7.80 [m, 4H, H(3,4,9,10)] 9.13 [dd, *J*_{2,3} 5.1 Hz, *J*_{2,4} 1.6 Hz, 1H, H(2)], 9.19 [dd, *J*_{10,11} 6.9 Hz, *J*_{9,11} 1.5 Hz, 1H, H(11)].

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(1)



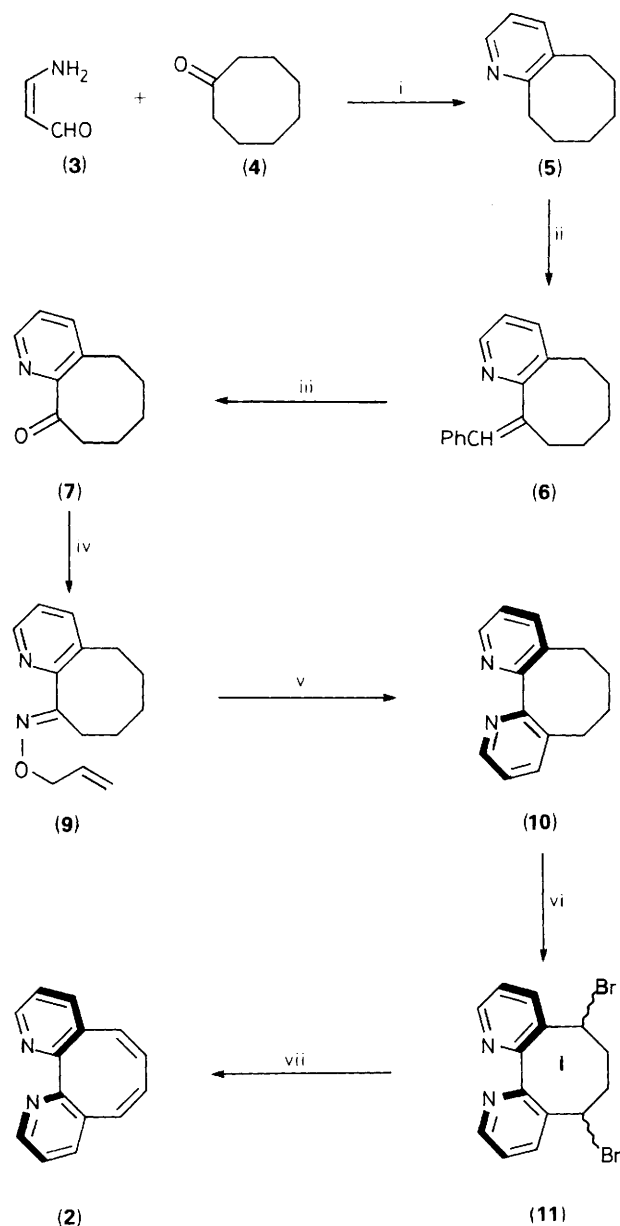
(2)

the 4J coupling constant between H(5) and H(7) has been calculated to be -1.2 Hz by NMR spectrum simulation studies. As such, the torsional angle C(5)–C(6)–C(7)–C(8) is approximately 60° which is commensurate with the expected C_2 symmetry of (2).⁸

In order to put to test the metal complex formation capability of (2), we refluxed a mixture of (2) and one equivalent of $\text{Mo}(\text{CO})_6$ for 1 h to afford the 1 : 1 molybdenum complex (12) in 74% yield.† The 4J coupling constant between H(5) and H(7) of (12) was found to be -0.2 Hz by a simulation method, which indicates that the torsional angle C(5)–C(6)–C(7)–C(8) is $45 \pm 5^\circ$.⁸ This value is also supported by X-ray crystallographic study of (12),‡ which gives a value of 51° for the torsional angle C(5)–C(6)–C(7)–C(8) (Figure 1). Noteworthy is that in the ^1H NMR spectrum (C_6D_6) of (12), the proton absorptions [except H(2) and H(11)] are shifted to high field as compared to those of (2), presumably either owing to the flattening of the molecule towards a distorted $4n\pi$ conjugated system⁹ upon metal co-ordination, or more appropriately owing to the charge transfer involving low lying metal to ligand transfer (MLCT) excited states.

In an attempt to resolve (2) into its corresponding enantiomers, the chiral palladium complex (*R,R*)-(13)¹⁰ was allowed to react with (2) in methanol at -3°C . The complexes formed were converted to the perchlorate (14)† in almost quantitative yield by adding sodium perchlorate to the reaction mixture. Interestingly, the resolution reaction between (2) and (*R,R*)-(13) is believed to provide preferentially only one diastereoisomerically pure palladium complex with (*R,R,R*) stereochemistry, whose assignments are attested by comparison with a related complex¹¹ as well as by one-dimensional and two-dimensional NMR methods.

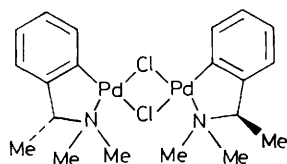
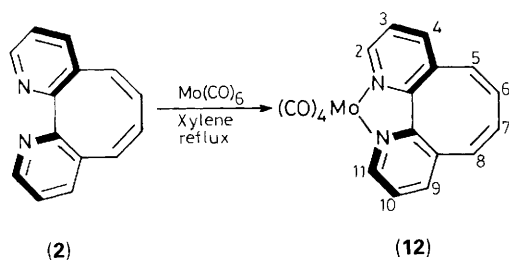
As can be substantiated by the 2D COSY and NOESY study of (14), all the four N–Me groups are correlated, which is indicative that complex (14) is a pure diastereoisomer. The complexity of the ^1H NMR spectrum nevertheless shows that



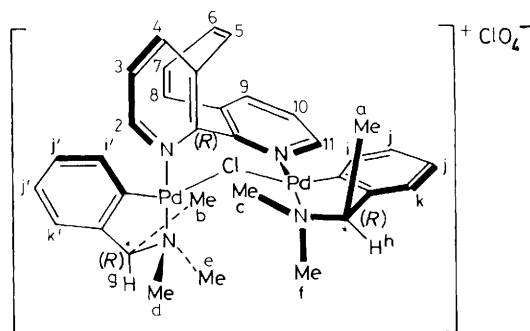
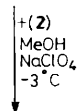
Scheme 1. Reagents and conditions: i, NH_4OAc , Et_3N , 120°C ; ii, PhCHO , Ac_2O , reflux; iii, O_3 , CH_2Cl_2 , -40°C then Me_2S ; iv, $\text{CH}_2=\text{CHCH}_2\text{ONH}_2\cdot\text{HCl}$ (8), NaOAc , Na_2CO_3 , EtOH , reflux; v, 180°C ; vi, NBS , CCl_4 , reflux; vii, KOH , EtOH , reflux.

‡ Crystal data for (12) (Nicolet R3m/V diffractometer using graphite-monochromatized $\text{Mo-K}\alpha$ radiation, $\lambda = 0.71073$ Å): $\text{C}_{18}\text{H}_{10}\text{N}_2\text{MoO}_4$, $M = 414.23$, monoclinic, space group $P2_1/c$, $a = 11.671(3)$, $b = 10.228(2)$, $c = 14.423(2)$ Å, $\beta = 95.42(2)^\circ$, $U = 1714.0(6)$ Å³, ρ_{measd} (floatation in $\text{CCl}_4/\text{BrCH}_2\text{CH}_2\text{Br}$) = 1.593 , $Z = 4$, $\rho_{\text{calcd}} = 1.605$ g cm^{-3} , $\mu = 7.69$ cm^{-1} , crystal size $0.32 \times 0.24 \times 0.19$ mm, mean $\mu_r = 0.09$, transmission factors $0.756 - 0.799$, $2\theta_{\text{max}} = 55^\circ$, ω - 2θ variable-scan technique, 3959 unique reflections. All non-hydrogen atoms were refined anisotropically, and all H atoms were included in structure-factor calculations. Final R_w based on 2701 observed data [$|F_o| > 6\sigma(|F_o|)$] and 226 parameters is 0.062. Atomic co-ordinates, bond lengths and angles, and thermal parameters have been deposited at the Cambridge Crystallographic Data Centre. See Notice to Authors, Issue No. 1.

(14) is a sterically-congested molecule without C_2 symmetry. Indeed, computer simulation of the alkenic H(5,6,7,8) absorptions of (14) confirms that they constitute a complex four spin ABCD system,† which again indirectly supports our argument that (14) is a single diastereoisomer. Compelling evidence for the (*R,R,R*) stereochemistry of (14) was obtained by observing in its 2D NOESY data a strong correlation between H(2) and Me_a . Examination of the one-dimensional ^1H NMR spectrum of (14) also reveals that Me_a is shielded by one of the pyridine rings due to the (*R*) stereochemical configuration of ligand (2). Furthermore, the fact that repeated recrystallization of (14) did not result in a change in its melting point or ^1H NMR spectrum also convincingly



(R,R)-(13)



(R,R,R)-(14)

demonstrates that the complex is a pure diastereoisomer, *i.e.* (R,R,R)-(14).

On the other hand, (S,S)-(13) as expected reacted with (2) to furnish (S,S,S)-(14) which exhibits identical ¹H NMR spectra as (R,R,R)-(14). However, our efforts to thoroughly investigate the chemistry of (R,R,R)-(14) and (S,S,S)-(14) and to generate enantiomerically pure (R)-(2) and (S)-(2) from (R,R,R)-(14) and (S,S,S)-(14), respectively have been severely hindered by the limited quantities of (2) and (14) at this stage. We also hope that ¹³C NMR spectrometry and X-ray crystallographic analysis can be carried out in due course when (14) is available in sizeable amounts either on repeated runs or by modified preparations.

In conclusion, we have prepared a new C₂ ligand (2) and have shown that it is able to form molybdenum and palladium complexes with potential theoretical and practical significance.

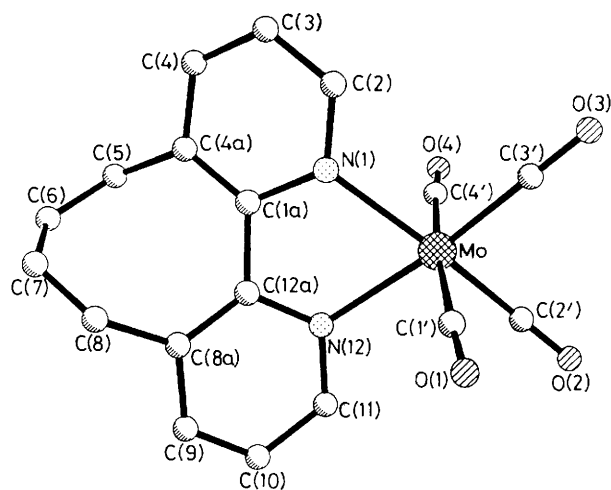


Figure 1

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