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NITROGEN 14 NMR AND CORRELATIONS OF OXIDATION POTENTIALS OF DIBENZO[*a,d*]CYCL[2.2.3]AZINES WITH THE CORRESPONDING HOMOs : FURTHER EVIDENCE FOR PERIPHERAL CONJUGATE SYSTEM

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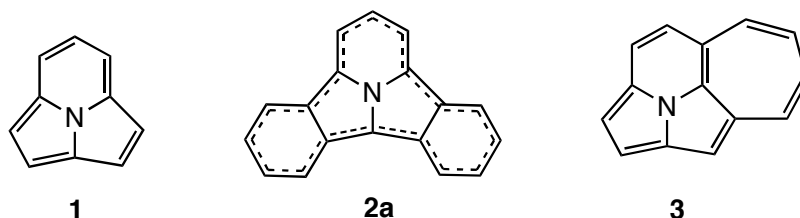
This paper is dedicated to the memory of Professor Ivar Ugi

Abstract – For the first time, ¹⁴N NMR spectra of a novel type of heterocycles, dibenzo[*a,d*]cycl[2.2.3]azines were described. The chemical shifts are almost independent of substituents at position 2. The correlations of oxidation potentials with HOMO energies of dibenzo[*a,d*]cycl[2.2.3]azines also offer very good correlation coefficients ($r^2 > 0.92$) regardless of calculation methods at various levels. Thus, it was concluded that the contribution of the unshared electron pairs of the central nitrogen to the peripheral conjugation in this system is almost negligible.

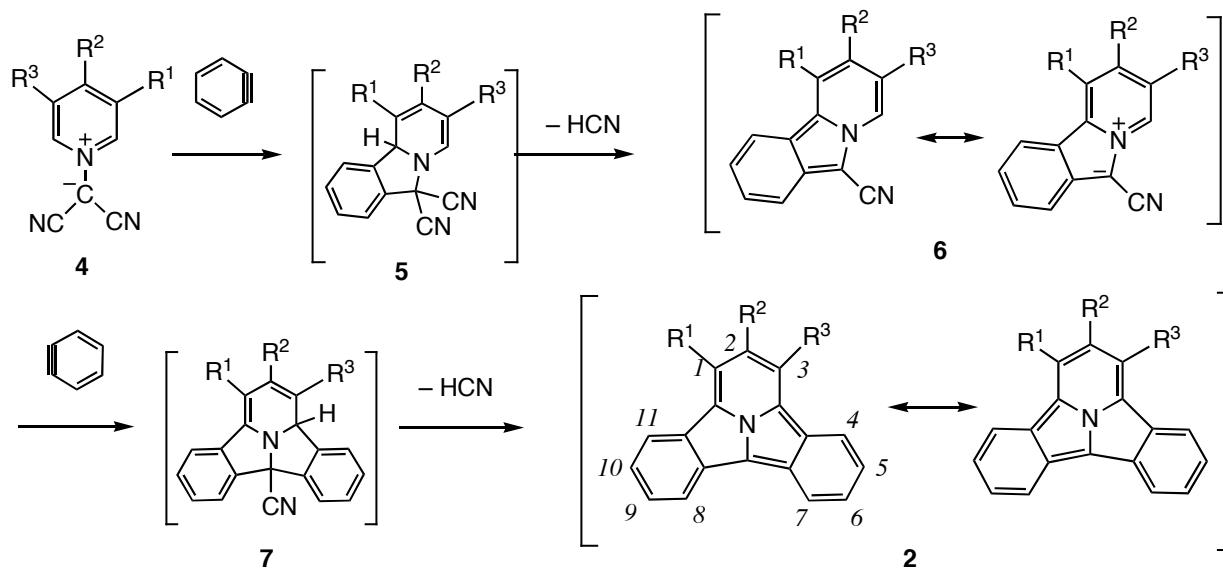
INTRODUCTION

Since Boekelheide *et al.* reported the first synthesis of cycl[2.2.3]azines,¹ the chemistry of cyclazines has attracted much attention in their synthetic and physicochemical aspects.² Specifically, peripheral conjugate heterocyclic systems such as bridged heteroannulenes and cyclazines are desired in order to obtain experimental evidence regarding the recognition of the net energy changes associated with π -electron delocalizations. Cycl[2.2.3]azine (**1**)³ is a typical example, giving a peripheral 10π electron conjugate system. However, little is known about a π -perimeter system larger than the parent cyclazine

(**1**) despite the potential aromaticity of the structure, though an example of a slightly more complex cycloheptadiene-fused cycl[2.2.3]azine system (**3**) has been known.⁴ One of the simplest possible compounds of 18π -perimeter would be dibenzo[*a,d*]cycl[2.2.3]azine (**2a**). We have previously reported a facile formation of several 2-substituted dibenzocycl[2.2.3]azines (DBC: **2a-f**).⁵ The reaction probably proceeds by a surprising sequence of reactions involving, (i) cycloaddition of pyridinium dicyanomethylides with benzyne, (ii) elimination of hydrogen cyanide to give 6-cyanobenz[*a*]indolizine **6**, (iii) cycloaddition of 6-cyanobenz[*a*]indolizine **6** with benzyne, and (iv) elimination of hydrogen cyanide.⁶ Consecutive studies of this potentially large peripheral systems by ESR either as radical cations



Scheme 1. Cyclo[2.2.3]azine (**1**) and dibenzo[*a,d*]cycl[2.2.3]azine (**2a**) and their analog **3**



a: $R^2 = \text{H}$; **b:** $R^2 = \text{Me}$; **c:** $R^2 = \text{Ph}$; **d:** $R^2 = \text{PhCO}$; **e:** $R^2 = \text{MeCO}_2$; **f:** $R^2 = \text{MeCO}$ ($R^1 = R^3 = \text{H}$ in these cases)

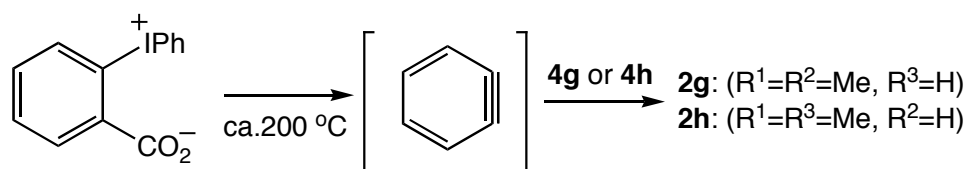
Scheme 2. Formation of dibenzo[*a,d*]cycl[2.2.3]azine **2** by a novel consecutive 1,3-dipolar cycloaddition to benzyne.

or radical anions revealed that, in contrast to **1**, the radical cation species were readily generated from **2a-f** upon oxidation with AgClO_4 . The effect of substitution on the spin densities in these radical cations were qualitatively discussed by simple HMO theory, suggesting the important role of the peripheral 18π conjugation and less contribution of the central nitrogen to the conjugation in this system.⁷ In order to

obtain further evidence for 18π peripheral nature of this system, we envisaged two experiments, e.g. nitrogen NMR spectral studies and correlations of oxidation potentials with calculated HOMO values. This is a subject of the present paper.

RESULTS AND DISCUSSION

Firstly, in addition to the previously described DBCs,⁵ the new disubstituted DBCs, namely 1,2-dimethyl- (**2g**: $R^1=R^2=Me$, $R^3=H$) and 1,3-dimethylDBC (**2h**: $R^1=R^3=Me$, $R^2=H$) were prepared in 12 % and 5 % yields, respectively, exactly in an analogous fashion to the reported method⁵ (Method A in ref. 5: from the corresponding pyridinium dicyanomethylides with benzyne generated from diphenyliodonium-2-carboxylate monohydrate at ca. 200 °C). In agreement with the previous results, the major products were 6-cyanobenzo[*a*]indolizines **6g** and **6h**.⁸ Among the two possible isomers, only **6g** was isolated in our hands.



Scheme 3 Preparation of disubstituted DBCs **2g** and **2h**

In the previous report, the evidence for 18π peripheral character of this system was mainly based upon the effect of substituents R^2 on the spin densities in their radical cations associated with simple Hückel MO. It occurred to us that if the contribution of lone pair electron of the central nitrogen to the peripheral conjugate system **2** were negligible, 1) ^{14}N NMR (and/or ^{15}N NMR) chemical shifts would be almost independent on substituents R^2 , and 2) almost equally good correlation between oxidation potentials and HOMO values would be obtained regardless of calculation methods at a variety of levels; this means that π electron conjugate peripheral delocalizations are important in this system.

Secondly, neither the attempts to obtain ^{15}N nor ^{14}N NMR of the DBCs were successful presumably because of a facile formation of a trace of radical cations; indeed their 1H and ^{13}C NMR often become broad. To overcome this problem, addition of a small amount of $Cr(acac)_2$ as a paramagnetic relaxation reagent often have been proved to be useful.¹⁰⁻¹² However, our attempts to obtain ^{15}N NMR spectra failed presumably because of its low natural abundance and therefore low sensitivity of ^{15}N nucleus and because of the large relaxation time of the central nitrogen atom. Thus, ^{14}N NMR were recorded in $CDCl_3$ with a small amount of $Cr(acac)_2$ using nitromethane as an external standard.¹¹ The results are summarized in Table 1. As expected, the chemical shifts are almost constant regardless of substituents at position 2. Only 2-phenylDBC (**2c**) showed a slight deviation.

Table 1 ^{14}N NMR chemical shifts of DBCs **2a-f**^a

2	2a	2b	2c	2d	2e	2f
δ	67.62	67.65	66.98	67.65	67.66	67.67

a) Chemical shifts are expressed in ppm up field from nitromethane as external standard.

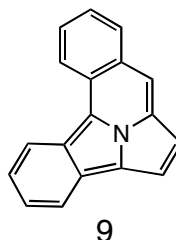
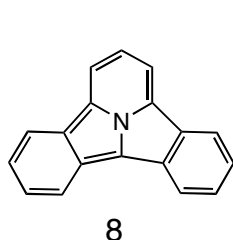
The oxidation potentials of **2g** and **2h** were estimated in an exactly similar fashion as previously reported,⁷ the values being 0.650 and 0.710 V, respectively. The results of oxidation potentials and HOMO energies of **2a-h** are summarized in Table 2 along with the correlation coefficients r^2 . It has proved that very good correlations between the oxidation potentials and HOMO energies were obtained regardless of calculation methods at various levels. It is particularly noted that even the Extended Hückel (EH) method whose approximation is based upon π electron conjugate system afforded a best correlation.

Table2. Oxidation potentials (V) and HOMO energies (eV) of **2a-2h** and correlation coefficient (r^2)^a

2	Oxidation Potential (V)	EH	MNDOd	AM1	PM3	PM5	3-21G*	6-31G*	6-31G**	B3LYP (6-31G*)
2a	0.700	-11.195	-7.495	-7.524	-7.761	-7.486	-6.350	-6.190	-6.190	-4.800
2b	0.680	-11.157	-7.488	-7.458	-7.694	-7.419	-6.230	-6.070	-6.070	-4.700
2c	0.640	-11.144	-7.437	-7.457	-7.685	-7.413	-6.280	-6.100	-6.100	-4.750
2d	0.850	-11.290	-7.648	-7.718	-7.957	-7.663	-6.600	-6.440	-6.440	-5.060
2e	0.865	-11.277	-7.749	-7.798	-8.004	-7.790	-6.620	-6.450	-6.450	-5.050
2f	0.870	-11.300	-7.710	-7.750	-7.970	-7.765	-6.620	-6.470	-6.470	-5.090
2g	0.650	-11.144	-7.482	-7.425	-7.663	-7.374	-6.190	-6.040	-6.040	-4.650
2h	0.710	-11.181	-7.492	-7.466	-7.705	-7.405	-6.270	-6.120	-6.120	-4.710
r^2		0.978	0.945	0.954	0.965	0.931	0.941	0.959	0.959	0.925

a) The *ab initio* calculations were performed using RHF method.

In conclusion, our investigations indicate that the contribution of the unshared electron pairs of the central nitrogen to the conjugation in this system is almost negligible, and therefore the dibenzo[*a,d*]cycl[2.2.3]azine system is considered a peripheral 18π system (**2**, Scheme 2), or otherwise at least 14π system when the contribution of the resonance structure (**8**) is important. A similar point has been noted by Tominaga concerning the dibenzocycl[2.2.3]azine (**9**).^{13, 14}



(Tominaga's dibenzocycl[2.2.3]azine)

EXPERIMENTAL

Mps were determined on a Yanagimoto micro melting point apparatus and are uncorrected. The ^1H NMR spectra were measured either on a JNM-ALPHA500 (500 MHz) or on a Bruker AV400M (400 MHz) instrument. ^{13}C NMR spectra were recorded either on a JNM-ALPHA500 or on a Bruker AV400M

spectrometer operating at 125.65 Hz and 100.57 Hz respectively. Chemical shifts are expressed in parts per million downfield from internal tetramethylsilane. ^{14}N NMR measurements were performed on a JNM-ALPHA500 operating at 36.12 Hz. Mass spectra were obtained on a JEOL JMS-DX303 spectrometer at 70 eV of ionization energy for EI-HRMS. The UV-visible spectra were taken on a Hitachi 220A spectrophotometer. CV measurements were carried out either using an ALS50W (ALS Co. Ltd.) or a CV1B (BAS Co. Ltd.) or an HECS331B (Huso Co. Ltd.). Platinum working electrode was used. Purified and dried acetonitrile and tetrapropylammonium perchlorate of special grade for polarography were used as a solvent and a supporting electrolyte, respectively. In order to avoid the ambiguity of the potential of the reference electrode in the CV measurements, a small amount of ferrocene was added and the position of the waves of the compounds under consideration was directly compared to that of ferrocenium/ferrocene peak (0.400 V vs. NHE) as an internal standard. A good reproducibility was observed between the results obtained by the different instruments, except for **2b**. The value of oxidation potentials using an ALS50W (ALS Co. Ltd.) was around 0.680 V which was adopted in this paper.

DBC **2a-f** were prepared by 1,3-dipolar cycloaddition of pyridinium dicyanomethylides with benzyne as reported before (Method A in ref. 5). Preparative medium-pressure liquid chromatography (MPLC) was carried out using a column (25 x 310 mm) prepacked with silica gel (Lobar, LiChroprep Si60, Merck). All the solvents used for the preparation of dibenzocycl[2.2.3]azines (**2**) were freshly distilled under nitrogen from appropriate drying agents.

1,2-Dimethyldibenzo[*a,d*]cycl[2.2.3]azine (2g): Yellowish-brown plates (from EtOAc-hexane), mp 178-179 °C; 14 %, ^1H NMR(400MHz, CDCl_3) δ 2.84(s, 3H), 3.13(s, 3H), 7.45(m, 2H), 7.70(dd, $J=7.8$ and 8.0 Hz, 2H), 8.30(s, 1H), 8.36(dd, $J=7.8$ and 8.0 Hz, 2H), 8.44(d, $J=8.0$ Hz, 1H), 8.61(d, $J=8.0$ Hz); ^{13}C NMR(100.55 Hz) δ 15.34, 20.62, 113.32, 113.96, 118.72, 118.77, 120.40, 120.44, 121.95, 123.28, 123.50, 123.74, 124.88, 125.07, 125.63, 126.37, 126.64, 127.14, 127.51, 127.64; IR(KBr) cm^{-1} 2921, 1614, 1508, 1343. MS m/z : 269. *Anal.* Calcd for $\text{C}_{20}\text{H}_{15}\text{N}$: C, 89.19; H, 5.61; N, 5.20. Found C, 89.11; H, 5.60; N, 5.09. Oxidation potential: 0.650 V

1,3-Dimethyldibenzo[*a,d*]cycl[2.2.3]azine (2h): Yellowish-brown powder (from EtOAc-hexane), mp 204-205 °C (from EtOAc-hexane); 8 %; ^1H NMR(400MHz, CDCl_3) δ 3.21(s, 6H), 7.41(brs, 1H), 7.48(brt, $J=7.8$ Hz, 2H), 7.71(t, $J=7.8$ Hz, 2H), 8.41(brd, $J=7.8$, 2H), 8.53(d, $J=7.8$ Hz); ^{13}C NMR(100.75Hz) δ 18.60, 118.91, 120.85, 122.15, 122.65, 123.20, 125.52, 125.98, 126.06, 126.98 (one signal is overlapped with another one); IR(KBr) cm^{-1} 2918, 1595, 1508, 1375. MS m/z : 269. *Anal.* Calcd for $\text{C}_{20}\text{H}_{15}\text{N}$: C, 89.17; H, 5.61; N, 5.20. Found : C, 89.42; H, 5.71; N, 5.17. Oxidation potential: 0.710 V.

Molecular orbital calculations were performed either using CAChe[®] (Version 7, Fujitsu Co. Ltd. : EH, MNDOd, AM1, PM3, and PM5) or Spartan[®]04 [Version 1.03, Wavefunction, Inc.: 3-21G*, 6-31G*,

6-31G**, and B3LYP(6-31G*)]. Correlations between oxidation potentials and HOMO values were obtained using Project Leader[®] (included in CAChe[®] package).

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