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CHEMILUMINESCENT 5-ARYLAMINO-1,2,4-TRIOXANES

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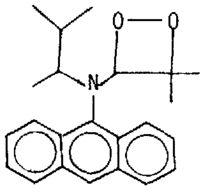
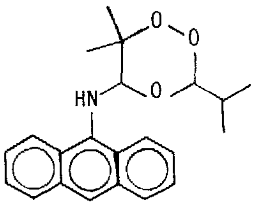
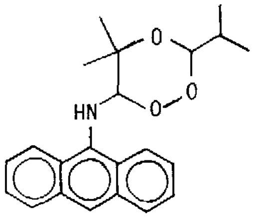
Recently Akutagawa et al.[1] claimed to have synthesized a stable aminodioxetane (I), for which structure Ia was assigned. In view of other works[2] on aminodioxetanes, however, it is hardly acceptable that such an aminodioxetane is stable at room temperature. From the spectral data described in their paper,[1] alternate structures, Ib, Ic and Id, cannot be eliminated. Among them Ib is most probable from the reaction scheme shown below. In this paper we propose that Ib is indeed the correct structure. In their recent paper[3] McCapra et al. also presumed Ib for correct structure of the compound from indirect evidence.



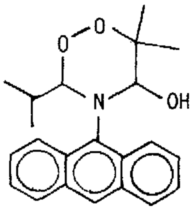
Ia



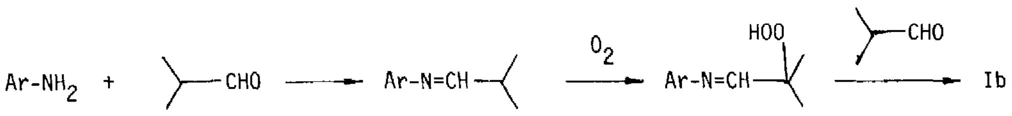
Ib
(correct structure)



Ic



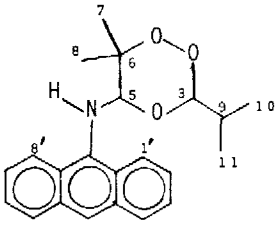
Id



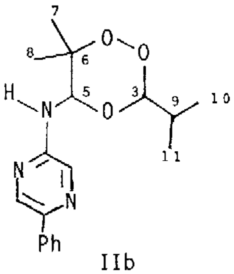
Compound I [pale yellow prisms, m.p. 122-124°, M^+ 351.1858, calc. 351.1834] was prepared according to the method of Akutagawa et al.[1] with slight modifications. Compound II [white powder, m.p. 100-110°, M^+ 329.1722, calc. 329.1739] was also prepared similarly from 2-amino-5-phenylpyrazine and isobutyraldehyde.[4]

Structure Ia is excluded since NMR spectrum of I (Table 1) clearly shows the presence of $\text{H-}\overset{|}{\underset{|}{\text{C}}}\text{-X-H}$ [(X)-H = exchangeable proton with D_2O] and $\text{H-}\overset{|}{\underset{|}{\text{C}}}\text{-CH(CH}_3)_2$. The large J value (12 Hz) of the $\text{H-}\overset{|}{\underset{|}{\text{C}}}\text{-X-H}$ system indicates that the protons are attached to a rigid system in which their dihedral angle is ca 180°. Molecular models show that the dihedral angle in Ib and Ic could be ca 180°, whereas free rotation of the OH group in Id is not completely restricted. ^{13}C NMR spectrum of I is also in favor of Ib and Ic, rather than Id; thus, the signal at 106.8 ppm (doublet in off-resonance decoupling spectrum) can be assigned to $\text{-O-}\overset{\text{H}}{\underset{|}{\text{C}}}\text{-O-}$ and not $\text{-N-}\overset{\text{H}}{\underset{|}{\text{C}}}\text{-O-}$.[5]

Table 1. Proton and Carbon-13 NMR Spectra of I and II
(in $CDCl_3$;δ in ppm, J in Hz)



Ib



IIb

H(X)	4.36 (d, J=12)	4.90 (d, J=12)
H(3)	4.80 (d, J=4.8)	5.18 (d, J=4.5)
H(5)	4.78 (d, J=12)	5.42 (d, J=12)
H(7,8)	1.68(s), 1.80(s)	1.22(s), 1.56(s)
H(9)	1.56-1.82 (m)	1.60-2.10 (m)
H(10,11)	0.76 (d, J=6.8)	0.98 (d, J=6.4)
H(Ar)	7.32-8.44	7.50-8.54
^{13}C(3)	106.8 (d)	107.3 (d)
^{13}C(5)	91.9 (d)	83.2 (d)
^{13}C(6)	81.0 (s)	79.8 (s)

Observed NOE[6] between the protons at 1',8'-positions of anthracene nucleus (irradiated) and H(X) and H(5) are 18% and 10%, respectively,but no NOE is observed between the aromatic protons and H(3), indicating the preference of structure Ib and Ic over Id. Comparison of NMR spectra of I and II shows that H(7,8) signals in I is more deshielded than the corresponding signal in II, whereas a reverse order is observed in case of H(10,11) signals. These effects are best explained with structure Ib and IIb; i.e., molecular models show that Ib has a rigid conformation and H(7,8) and H(10,11) are in deshielding and shielding regions, respectively, of the anthracene nucleus.

Chemiluminescence of I and II is observed in aprotic polar solvents in the presence of a base. Isolable products of this reaction are the corresponding amides. Chemiluminescence spectra are identical with fluorescence spectra of the amides in the same solvent [in diglyme-KOH, I: λ_{max} 538 nm; II: λ_{max} 428 nm]. When the quantum yield of luminol is taken as 0.036,[7] quantum yields of chemiluminescence of I and II are calculated as 0.13 and 0.005, respectively. That chemiluminescence light yield of a Cypridina luciferin analog (III) is comparable to II, indicates that yield of the excited product is similar between the following two reactions.

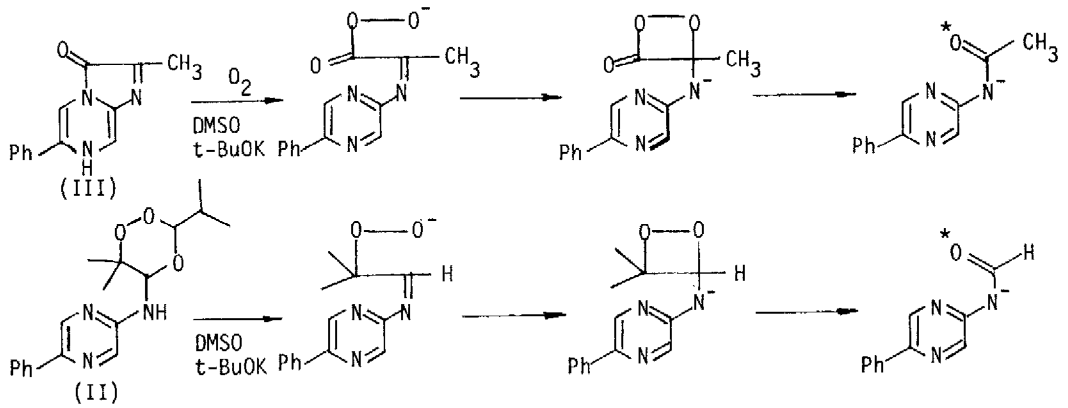


Table 2. Chemiluminescence of I and II

		I		II	
solvent	base	relative light yield	$t_{1/2}$	relative light yield	$t_{1/2}$
DMSO	0.85N t-BuOK (50 μl)	160	< 1 sec	3.2	2 sec
"	1N KOH (")	100	< 1	2.7	1.5
diglyme	0.85N t-BuOK (")	90	6	1.8	0.5
"	1N KOH (")	48	1200	0.9	12

Conditions: concentration of the substrates is 10^{-7} - 10^{-8} M and total volume is 3 ml.

Relative light yield of luminol in DMSO containing t-BuOK 46[7]

" (III) in DMSO containing t-BuOK 3.0

" (III) in diglyme containing Ac buffer 7.3[8]

REFERENCES AND FOOTNOTES

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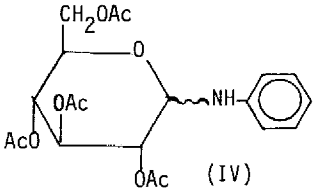
2) C. S. Foote, A. A. Dzakpasu and J. W.-P. Lin, Tetrahedron Letters, 1247 (1975); H. H. Wasserman and S. Terao, Tetrahedron Letters, 1735 (1975).

3) F. McCapra, Y. C. Chang and A. Burford, J.C.S. Chem. Commun., 608 (1976).

4) A solution of 2-amino-5-phenylpyrazine (150 mg) in isobutyraldehyde (7 ml) and ethyl ether (40 ml) was stirred with $CaCl_2$ tube at room temp. in a dark. After 2 weeks the solvent was evaporated at room temp. and the residue chromatographed on a silica gel column at 5° using CH_2Cl_2-n-hexane (1:1) as eluant. Pale yellow syrup (40 mg) thus obtained was triturated with n-hexane to give white powder, m.p. 100-110°; ν 3290 cm^{-1} (NH); λ_{max} 274, 336 nm.

5) No ^{13}C NMR signals of aliphatic carbon atoms were found in the fields lower than 85 ppm in NMR spectrum of IV.



(IV)

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7) J. Lee, A. S. Wesley, J. F. Ferguson, III, and H. H. Seliger, in F. H. Johnson and Y. Haneda Ed., Bioluminescence in Progress, Princeton Univ. Press, Princeton, N. J., 1966, p. 35; J. W. Hastings and G. T. Reynolds, ibid., p. 45.

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