Conformational analysis of a fluorescent rotor, 6-(2,2-dicyanovinyl)-1-(2-hydroxyethyl)-1,2,3,4-tetrahydroquinoline

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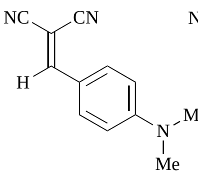
Two stable conformations of a fluorescent rotor have been estimated by a variable temperature ^{1}H NMR study, including NOE measurement. The height of energy barrier between them is also assessed and confirmed by MO calculation and X-ray crystal structure.

Fluorescent rotor is a dye whose fluorescent intensity depends on apparent viscosity around its molecules. Dyes like **1**, **2** and **3**[1,2] have been used to analyze micellar- or micro-



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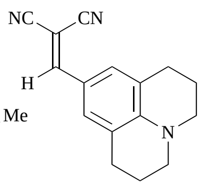

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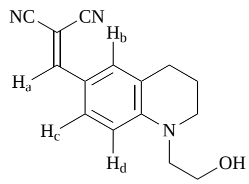

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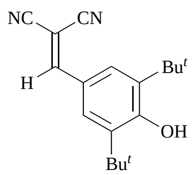

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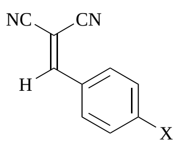


5a X = H
5b X = OH
5c X = NH_2

environments.[3,4] They are also employed to monitor the polymerization processes of synthetic monomers[1] and the association of compounds of biological interest[5–7] by observing the fluorescent intensity of a rotor included in the system. These rotors are commonly composed of two double bond systems, which are connected by a single bond with relatively low rotational free energy barriers and can conjugate to each other when a required conformation is attained. High solution viscosity, which is attained by the addition of viscous solvent or at low temperature, or forced attachment of the molecule to another molecule (usually of high molecular weight) hinders the rotation and increases the population of the more stable fluorescent rotational isomers, those with larger π-electron overlapping throughout the conjugated systems.[8,9] Those rotational isomers having lower energy levels are responsible for observed fluorescence and, therefore, the most fluorescent molecular species is considered to be a planar π-electron overlapping conformation of the rotor.

Yoshikawa and his colleagues[10] reported an NMR study on rotational isomers of the phosphorylation uncoupler SF 6847 **4**, the oxygen analog of the dyes, and a calculation of free energy diagrams around the single bond connecting two double bond systems of a model **5b** and its anion by semi-empirical (CNDO/2) and *ab initio* (STO/3G) molecular orbital (MO) calculations. They concluded from NMR observations that not the planar conformation but an unexpected orthogonal or twisted structure was the lowest energy conformation, although X-ray crystallography had showed a planar structure for the compound.[11] The conclusion was also supported by MO calculations which afforded a twisted structure with a dihedral angle $\theta = 40–60°$ (depending on the method of calculation) as favored. On the other hand, Safarzadeh-Amiri investigated two rotors, **1** and **2** by dynamic ^{1}H NMR analysis.[2] On each rotor, he observed coalescence temperatures and splitting of proton signals below these temperatures, calculated kinetic and thermodynamic parameters for rotation of the conjugated systems, and proposed the planar conformation as the most stable isomer. In order to solve this apparent contradiction, we attempted the present study and would like to report the rotational isomerism of **3**, focusing on conformational analysis by dynamic NMR and NOE, X-ray crystallography and MO calculations of simplified model compounds. The inherent non-equivalency of the aromatic protons of **3** seems to give more information in NMR studies.

Results and discussion

NMR measurements

^{1}H NMR spectra of **3** at various temperatures are shown in Fig. 1. The signal coalescence temperatures (T_c) were 213 K for H_b and H_c, and 200 K for H_d, respectively. Each proton signal observed at the temperatures lower than the T_c split into two sets of equal intensity, indicating that the rotor **3** existed as an equimolar mixture of two rotational isomers. Assuming periplanar **3a** and **3b** as the stable rotamers, the sets of signals can be rationally assigned as depicted in Fig. 1 and in Scheme 1, when the deshielding effect of dicyanovinyl group is taken into account.

The free energy of activation for the interchange between the two isomers was calculated from eqn. (1) as 41 kJ mol^{-1} (a

$$\Delta G^{\ddagger} = -RT\,\ln(\pi h \Delta\nu / 2^{\frac{1}{2}} kT) = 19.14 T_c (9.97 + \log T_c/\Delta\nu)\ (\text{J mol}^{-1}) \quad (1)$$

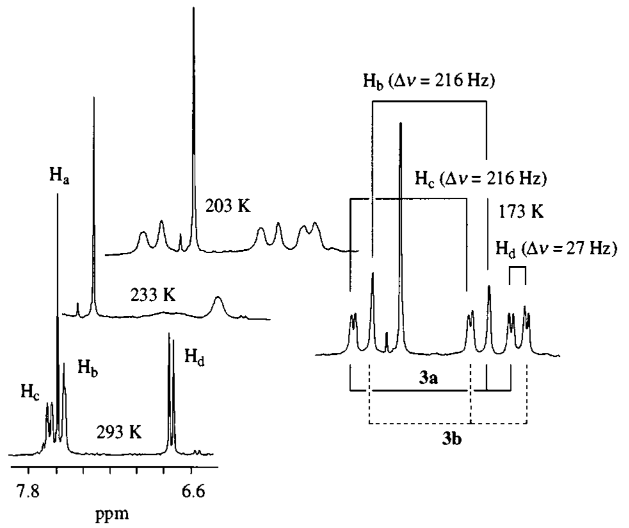
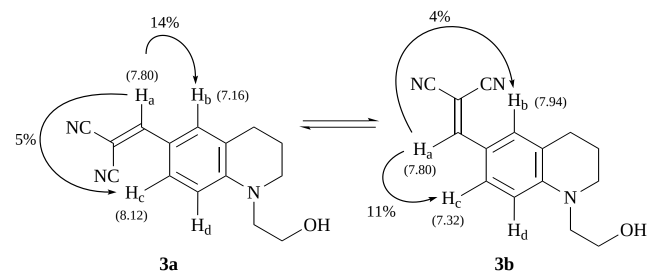


Fig. 1 Aromatic region of ^{1}H NMR of **3** at various temperatures



Scheme 1 NOEs and δ in blanket at 168 K

mean of 40.6 kJ mol^{-1} from H_b and H_c and 41.5 kJ mol^{-1} from H_d), which was close to the values of 40 and 39 kJ mol^{-1} reported for **1** and **2**, respectively.[2] The $\Delta\nu$ (signal separations in Hz between the two isomers) are 216 Hz for H_b and H_c and 27 Hz for H_d, respectively.

A difference NOE experiment was carried out under irradiation of H_a in the same temperature range as the preceding ^{1}H NMR measurements. While all the NOEs of H_b and H_c were small (4–5%) and remained apparently constant above the T_c, the NOEs of the higher field H_b and H_c increased sharply below the T_c to 14 and 11%, respectively, at 168 K (Scheme 1). These results indicate that H_a is located close to H_b in **3a** and to H_c in **3b**, and would seem to support the proposal that the periplanar conformation of **3a** and **3b** is the more stable one. It can be also concluded from the above observations that a conformer having a dihedral angle of *ca.* 90° between the dicyanovinyl group and the aromatic ring is, at least, more unstable than **3a** and **3b** even if it is not the transition state of the conformational change between **3a** and **3b**.

MO calculation and X-ray crystal structure

In order to assess the energy profile of the rotation of dicyanovinyl group, we performed PM3 calculation as to simplified rotor models **5a**–**c** (Fig. 2). The most stable conformations calculated were those having dihedral angles 36–45° and 135–140° which were nearly consistent with that of Yoshikawa.[10] However, the calculated energy barriers (3.0–4.5 kJ mol^{-1}) are significantly smaller than those obtained by NMR measurement (41 kJ mol^{-1}) although this stable twist structure could explain the NOE observations. This discrepancy led us to carry out *ab initio* calculations (RHF/3-21G) of **5a**–**c** (Fig. 3). Although the calculated energy barrier (25 kJ mol^{-1}) was smaller than that found by NMR analysis, results in the feature of the energy diagram were consistent with NMR analyses. The planar conformation was the most stable and the twisted one having a dihedral angle of 90° was the most unstable. The height of

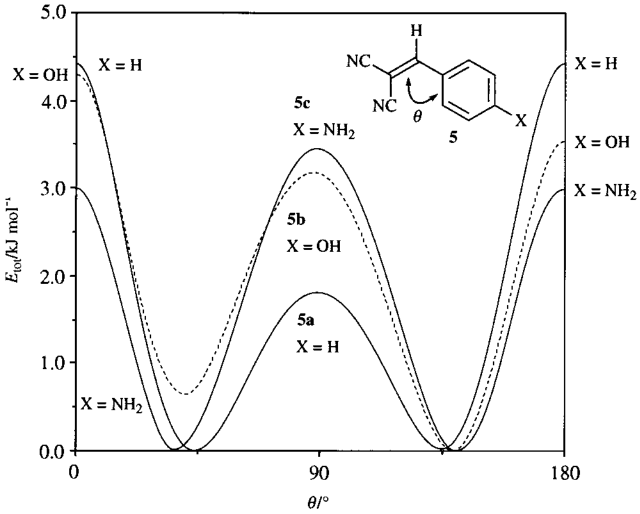


Fig. 2 PM3 calculation of changes in the total energy with the dihedral angle between the dicyanovinyl and the aromatic ring of **5**. The reaction coordinate method employed a constrained rotation of the torsion in 5° angle increments from 0 to 180°. At each step, the remaining degrees of freedom were optimized. Unconstrained optimizations were carried out to obtain the fully minimized structures.

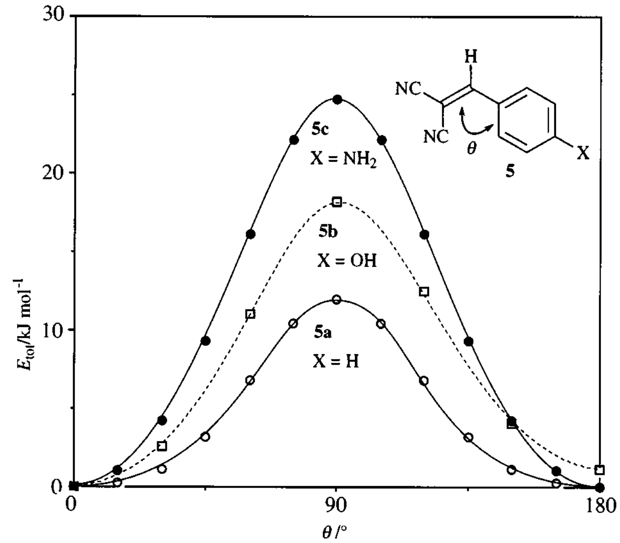


Fig. 3 RHF calculation of changes of the total energy with the dihedral angle between the dicyanovinyl and the aromatic ring of **5**

Table 1 Calculated relative energies (in kJ mol^{-1}) of **6** with 6-31G//3-21G

	Ground state **6b** ($\theta = 179.5°$)	Transition state ($\theta = -90.3°$)	Ground state **6a** ($\theta = -0.5°$)
3-21G	0.0	+26.1	+0.6
6-31G//3-21G	0.0	+30.5	+0.5

energy barrier increased with the electron donating property of *para*-substituents.

As to a simplified model **6** bearing H atom in place of hydroxyethyl group, stable conformations and transition states were located by 3-21G base set, and those energies were refined by 6-31G base set (Table 1). The transition state structure was searched from the energy profile of Fig. 3 and refined using TS command. The most stable conformations are also almost planar, and the energies of the two planar conformers **6a**,**b** (Scheme 2) are almost the same, which are coincident with the NMR study. At the transition state, the dicyanovinyl group and the aromatic ring are almost perpendicular ($\theta = 90.3°$).

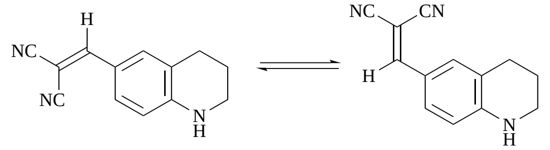
Table 2 Selected geometry parameters of the crystal structure of **3** and the calculated molecular structure of **6a**[a]

	X-ray	3-21G	PM3
Bond length/Å			
C(4)–C(5)	1.366	1.372	1.391
C(5)–C(6)	1.400	1.400	1.400
C(6)–C(7)	1.400	1.400	1.398
C(7)–C(8)	1.354	1.369	1.385
C(8)–C(9)	1.405	1.402	1.404
C(9)–C(4)	1.428	1.405	1.408
C(9)–N(1)	1.357	1.360	**1.428**
C(6)–C(10)	1.434	1.477	1.455
C(10)–C(11)	1.344	1.345	1.349
C(11)–C(12)	1.435	1.427	1.428
C(12)–N(2)	1.142	1.141	1.160
C(11)–C(13)	1.437	1.422	1.425
C(13)–N(3)	1.135	1.141	1.160
Bond angle/°			
C(4)–C(5)–C(6)	124.0	123.0	120.8
C(5)–C(6)–C(7)	116.2	117.2	119.4
C(6)–C(7)–C(8)	121.1	120.7	120.4
C(7)–C(8)–C(9)	122.8	121.5	120.2
C(8)–C(9)–C(4)	116.7	118.4	119.8
C(9)–C(4)–C(5)	119.0	119.1	119.4
C(4)–C(9)–N(1)	120.4	121.0	121.1
C(8)–C(9)–N(1)	122.9	120.6	119.0
C(9)–N(1)–C(1)	121.3	123.6	**116.5**
C(9)–N(1)–C(14)	121.4	118.3[b]	**112.1**[b]
C(1)–N(1)–C(14)	116.6	118.1[b]	**112.1**[b]
C(5)–C(6)–C(10)	117.6	117.2	118.3
C(7)–C(6)–C(10)	126.2	125.6	122.3
C(6)–C(10)–C(11)	131.1	131.8	126.4
C(10)–C(11)–C(12)	119.5	119.3	120.2
C(10)–C(11)–C(13)	125.9	125.2	125.3
C(12)–C(11)–C(13)	114.6	115.5	114.5
C(11)–C(12)–N(2)	179.1	180.0	180.0
C(11)–C(13)–N(3)	179.7	180.0	178.3
Dihedral angle/°			
C(4)–C(5)–C(6)–C(7)	3.4	0.4	1.0
C(5)–C(6)–C(7)–C(8)	−2.3	0.0	−0.3
C(6)–C(7)–C(8)–C(9)	−1.4	−0.3	0.0
C(7)–C(8)–C(9)–C(4)	4.2	0.0	−0.3
C(8)–C(9)–C(4)–C(5)	−3.1	0.3	0.9
C(9)–C(4)–C(5)–C(6)	−0.6	−0.5	−1.3
C(5)–C(4)–C(9)–N(1)	178.9	−179.2	−174.3
C(7)–C(8)–C(9)–N(1)	−177.9	180.0	175.1
C(4)–C(9)–N(1)–C(1)	−2.8	−1.1	**−19.5**
C(8)–C(9)–N(1)–C(1)	179.4	179.7	**165.3**
C(4)–C(9)–N(1)–C(14)	172.4	−178.7[b]	**−150.5**[b]
C(8)–C(9)–N(1)–C(14)	9.7	2.0[b]	**34.3**[b]
C(4)–C(5)–C(6)–C(10)	−177.4	−180.0	180.0
C(8)–C(7)–C(6)–C(10)	178.5	−180.0	−178.9
C(5)–C(6)–C(10)–C(11)	175.9	180.0	**141.5**
C(7)–C(6)–C(10)–C(11)	−4.9	−0.5	**−40.0**
C(6)–C(10)–C(11)–C(12)	−180.0	−180.0	179.3
C(6)–C(10)–C(11)–C(13)	0.0	0.0	−1.9

[a] Values with pronounced difference between the observed and the calculated are given in bold. [b] C(14) is replaced with H atom in the molecular structure for the present calculation.

Although the energy barrier of the conformational change (30.5 kJ mol^{-1}) is still somewhat smaller than that found by the NMR study, the difference decreases with 6-31G base set.

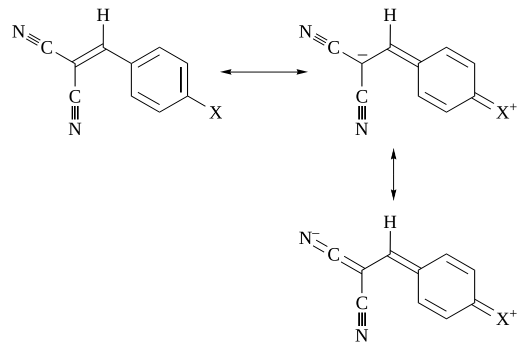
The X-ray crystal structure of **3** was fairly consistent with the structure of **6a** located by *ab initio* calculation (Table 2). On the other hand, pronounced differences between the calculated structure with PM3 and the experimental one are found in the dihedral angle [C(5)–C(6)–C(10)–C(11) or C(7)–C(6)–C(10)– C(11)] between the dicyanovinyl group and the aromatic ring. Another discrepancy is found in the structure around the nitrogen atom [N(1)] adjacent to the aromatic ring. The bond length of C(9)–N(1) with PM3 (1.428 Å) is longer than observed one (1.357 Å) while that with 3-21G (1.360 Å) agrees



6a (θ = −0.5°) **6b** (θ = −179.5°)

Scheme 2

well with the value observed. Moreover, the summation of the bond angles around N(1) with PM3 is 340.7° which indicates N(1) is pyramidal while it is planar in the X-ray structure (359.3°) and the 3-21G calculation (360.0°). This problem is also found in the dihedral angles around N(1); C(4)–C(9)–N(1)–C(1), C(8)–C(9)–N(1)–C(1), C(4)–C(9)–N(1)–C(14) and C(8)–C(9)–N(1)–C(14). The above facts strongly suggest that the semi-empirical calculation does not reproduce the proposed



Scheme 3

resonance[9,12] in Scheme 3 while the *ab initio* calculation does. This conclusion is supported by the periplanar orientation of the two groups and the planar structure of the nitrogen atom in the reported X-ray structures of the relating compounds; *N*,*N*-dimethyl-4-(1,2,2-tricyanovinyl)aniline,[13] *N*-phenyl-4-(1,2,2-tricyanovinyl)aniline[14] and 1-(2,2-dicyanovinyl)-2-(pyrrolidin-1-yl)benzene.[15]

In conclusion, the stable periplanar conformers of the fluorescent rotor **3** were confirmed by the present NMR experiments including NOE measurement, *ab initio* MO calculation and X-ray analysis. The dynamic NMR measurement assessed that the energy barrier to the rotation around the single bond between the dicyanovinyl and aromatic groups was 41 kJ mol^{-1}, and they were almost perpendicular to each other in the transition state. The conclusions were also confirmed by *ab initio* MO calculation.

Experimental

Materials and measurements

Rotor **3** was prepared as described in the previous report.[6] ^{1}H NMR spectra were taken on a JEOL JNM EX-270 spectrometer (270 MHz for H), at temperature range from 293 to 168 K (the temperature 5 degrees higher than the freezing point of the solution) with 20 mg of **3** in 1.0 cm^3 of [$^2H_8$]tetrahydrofuran. Differential nuclear Overhauser effect (NOE) spectra were taken at the same temperature range by irradiating H_a-proton signal of **3**.

MO Calculations

MOPAC (PM3) calculations were carried out using CAChe system (CAChe Scientific, Inc.) and *ab initio* MO calculations were done with GAUSSIAN92 (RHF/3-21, RHF/6-31//3-21G).[16]

Single-crystal X-ray diffraction analysis of 3

Crystals of **3** for X-ray diffraction studies were prepared in a mixture of toluene and hexane. A red prismatic crystal having the approximate dimensions 0.10 × 0.10 × 0.30 mm^3 was

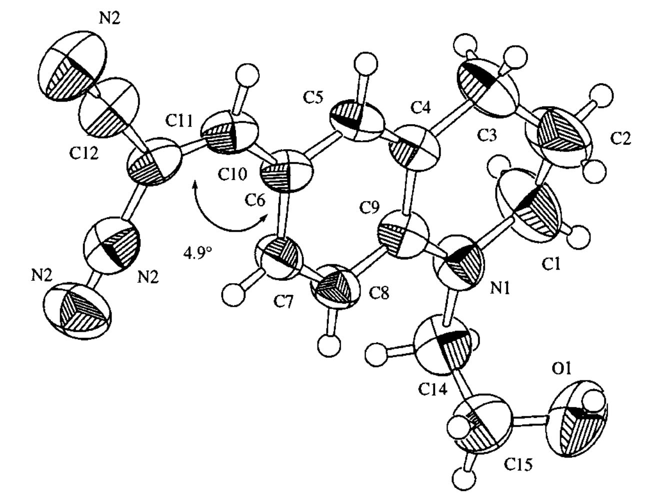


Fig. 4 X-ray crystal structure of **3**

mounted on a glass fibre. The intensity measurement was performed on a Rigaku AFC7R diffractometer using Ni-filtered Cu-Kα radiation from a rotating anode X-ray generator run at 40 kV, 300 mA. Cell constants and an orientation matrix for data collection, obtained by a least-squares refinement using set angles of 25 carefully centered reflections in the range $40.14 < 2\theta < 49.94°$, corresponded to a primitive monoclinic cell with dimensions: $a = 6.969(2)$, $b = 10.712(1)$, $c = 18.214(2)$ Å, $\beta = 99.63(2)°$ and $V = 1340.5(4)$ Å^3. For $Z = 4$ and $M = 253.30$, the calculated density is 1.25 g cm^{-3}. Systematic absences of h01: $1 \neq 2n$ and $0k0$: $k \neq 2n$ uniquely determine the space group to be $P2_1/c$ (#14). Data were collected at 20 ± 1 °C using ω–2θ scan technique to a maximum 2θ value of 120.1°. The width of $(1.26 + 0.30 \tan\theta)°$ was scanned for each reflection at a speed of 8.0° min^{-1} (in omega). Of 2321 collected reflections, 2125 were unique. The structure was determined by direct methods[17] and Fourier techniques.[18] Non-hydrogen atoms were refined anisotropically. Hydrogen atoms were refined isotropically. The final cycle of full-matrix least-squares refinement was based on 1122 observed reflections $[|F_o| > 3.0\sigma(|F_o|)]$ and 187 variable parameters and converged with $R = 0.060$ and $R_w = 0.064$. All calculations were performed using the teXsan[19] crystallographic software package.

Full crystallographic details, excluding structure factor tables, have been deposited at the Cambridge Crystallographic Data Centre (CCDC). For details of the deposition scheme, see 'Instructions for Authors', *J. Chem. Soc.*, *Perkin Trans. 2*, available *via* the RSC Web pages (http://chemistry.rsc.org/authors). Any request to the CCDC for this material should quote the full literature citation and the reference number 188/116.

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