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Characterization of the Sulfonic Esters Adopting a Folded Conformation with Stacked Aromatic Moieties

Yoshimitsu NAGAO,* Shigeki SANO, Satoshi NAKAGAWA,
Miho TANAKA, Motoo SHIRO,*† and Tohru TAGA*††
Faculty of Pharmaceutical Sciences, The University of Tokushima, Sho-machi, Tokushima 770
†Rigaku Corporation, 3-9-12 Matsubara-cho, Akishima, Tokyo 196
††Faculty of Pharmaceutical Sciences, Kyoto University, Sakyo-ku, Kyoto 606

Systematic characterization of several molecules, adopting a folded conformation with stacked aromatic moieties, is investigated by utilizing X-ray crystallographic and ^{1}H NMR analyses. Bridging two aromatic moieties with a sulfonic ester bond proved to be a significant factor for adopting a folded conformation.

A stable conformation of some organic molecules cannot be rationalized in terms of the bulk-repulsive concept.[1] Recently, we are investigating synthetic design and conformational analysis of the molecules adopting an unusual stereochemistry.[2] It is familiar that a folded conformation of the bis-aromatic molecule can be adopted as a preferential one by formation of an intramolecular charge-transfer (CT) complex.[3] However, the molecular conformation may be, in some cases, governed by some unidentified weak interactions without clear CT complex formation.[4] We herein describe characterization of the simple molecules adopting rather a folded conformation (Fig. 1 **A**) than a stretched conformation (Fig. 1 **B**).

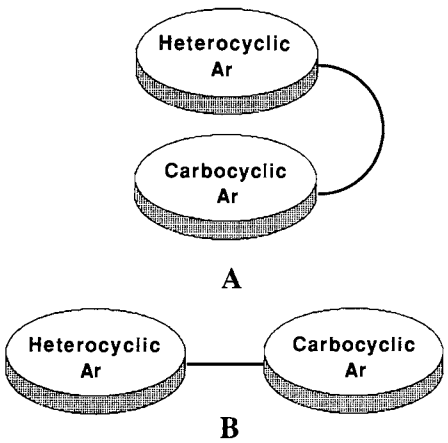
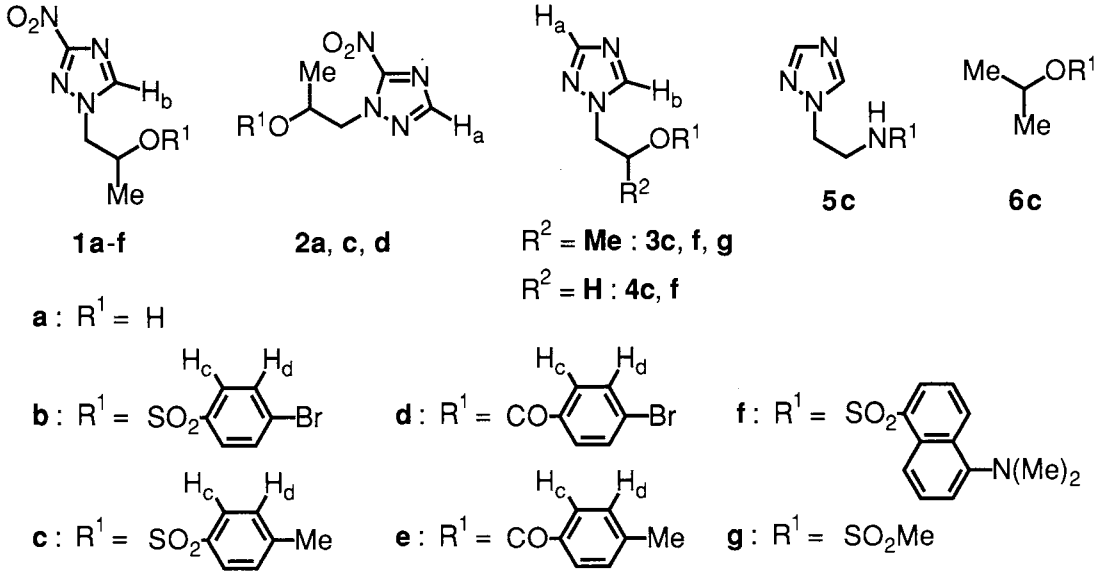


Fig. 1. Folded conformation **A** and stretched conformation **B**.

In the course of development of new radiosensitizers to hypoxic cancer cells, we have synthesized various N1- and N2-derivatives of 3-nitro-1,2,4-triazole (3-NTR).[5] In order to confirm the regiochemistry of alkylation at the N1 or N2 position of 3-NTR, crystalline compounds **1b** and **1d** were submitted to X-ray crystallographic analysis.[6] Interestingly, the crystal structure of sulfonic ester **1b** was shown to be a folded conformation with stacked aromatic moieties (**A** in Fig. 2). However, the



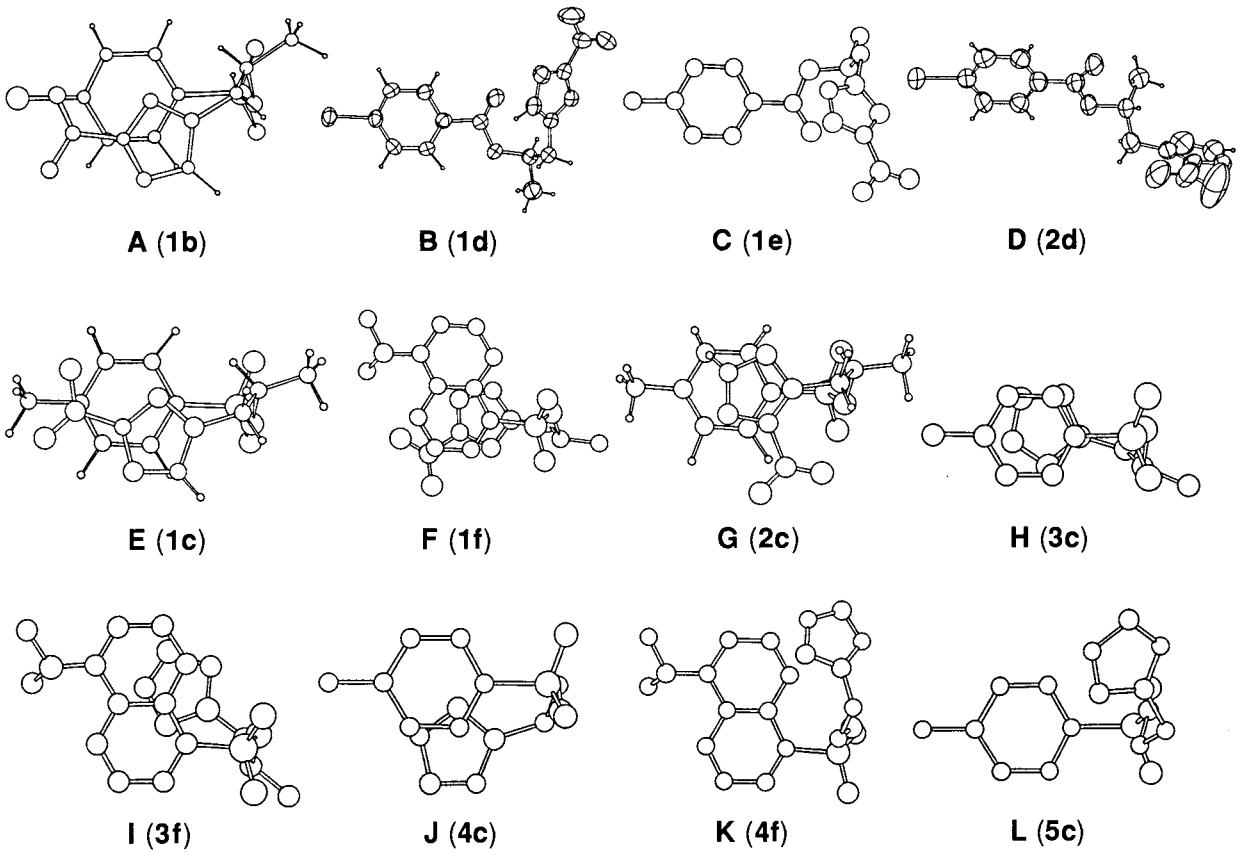


Fig. 2. Perspective top views of the crystal structures of compounds **1b-f**, **2c,d**, **3c,f**, **4c,f**, and **5c**.

carboxylic ester **1d** was shown to be a conformation (**B** in Fig. 2) quite different from that of **1b**. Thus, carboxylic esters **1e** and **2d** and sulfonic esters **1c,f**, and **2c**, prepared from 3-NTR derivatives **1a** and **2a** under the usual manner,[5] were submitted to X-ray crystallographic analysis.[6] Their perspective top views are represented in Fig. 2 (**C-G**). It is obvious that the sulfonic ester compounds adopt each corresponding folded conformation with the nitrotriazole ring stacked with *p*-substituted benzene moieties regardless of the different substitution mode (N1 or N2) on the nitrotriazole ring (**E** and **G** in Fig. 2). On the other hand, carboxylic esters **1e** and **2d** were shown to be a non-stacked conformation (**C**) or a typical stretched one (**D**) as shown in Fig. 2. A sulfonic ester **1f** bearing a dimethylamino-substituted naphthalene ring also adopts a similar folded conformation (**F**). Even without nitro group of the triazole moiety, sulfonic esters **3c** and **3f** adopt each corresponding beautiful folded conformation **H** and **I**.[6] However, a methyl group of the triazole side chain seems to be fairly significant for stacking of the aromatic moieties based on the comparisons of **J** (**4c**) with **H** (**3c**) and of **K** (**4f**) with **I** (**3f**), respectively, as shown in Fig. 2.[6] Steric repulsion between the methyl group and the aromatic rings may predominate an aromatic rings-stacked conformation. Bridging between two aromatic moieties with a sulfonic amide bond (**5c**)[6] seems to be unfavorable for the stacking (compare **L** with **J** in Fig. 2).

Table 1. ^{1}H NMR (200 MHz) Spectral data of compounds **1c,e, 3c,f,g**, and **6c**

Compd	^{1}H Chemical shift (δ ppm)[a]				Conform[b] (Crystalline)
	Ha	Hb	Hc	Hd	
1e	—	8.18	7.84	7.25	S
1c	—	8.08	7.54	7.25	F
3c	7.74	8.04	7.61	7.29	F
6c	—	—	7.74	7.33	
3g	7.99	8.17	—	—	
6c + 3g	7.99	8.18	7.79	7.33	
3f	7.61	7.84	—	—	F

a) Determined in $CDCl_3$. b) S: Stretched conformation, F: Folded conformation.

Compounds **1c**, **3c**, and **3f** may adopt a folded conformation with stacked aromatic moieties even in $CDCl_3$ solution similar to that in the crystal. Namely, considerable upfield shifts of H_b, H_c, H_d and/or H_a peaks in the ^{1}H NMR (200 MHz) charts of compounds **1c**, **3c**, and **3f** were evidently recognized when compared with those of the non-stacked compounds **1e**, **3g**, and **6c** (Table 1). Thus, such a phenomenon as observed in **1c**, **3c**, and **3f** should be rationalized in terms of the

diamagnetic effect due to stacking of the aromatic moieties. Possibility of intermolecular stacking between aromatic molecules can be denied by the fact that chemical shifts of H_{a-d} of an equimolar mixture of **3g** and **6c** are same as those of each **3g** or **6c**. There is no evidence at all for CT complex formation between aromatic moieties in the UV spectra of the compounds adopting a preferential folded conformation. The distance between the closest carbon atoms of two aromatic moieties in the crystalline molecules **1c** and **2c** is 3.44 Å and 3.53 Å, respectively. Some aspect for adopting a folded conformation in the sulfonic esters would be explained in terms of sum of the weak force like electrostatic and van der Waals attraction between two aromatic moieties under the free rotatory system such as a sulfonic ester bond. The results described above may be suggestive for stacking between an anticancer planar molecule and nucleic bases and for molecular recognition between a planar surface of the substrate and aromatic moieties of an enzyme (protein).

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6) The detailed crystallographic data for compounds **1b-f**, **2c,d**, **3c,f**, **4c,f**, and **5c** should be available in correspondence with the authors (YN, MS, and TT).

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