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Convenient synthesis and host–guest compounds of 9,9′(10*H*,10′*H*)-spirobiacridines

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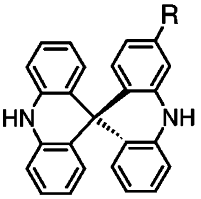
Abstract—9,9′(10*H*,10′*H*)-Spirobiacridine and its 2-methoxy derivative were prepared from the corresponding diphenylamines and acridone in three steps. A nearly D_{2d} molecular skeleton of the spiro compounds was confirmed by X-ray crystallographic analysis. The spirobiacridines can work as a new class of host compounds owing to their ability to form nearly rectangular hydrophobic cages in the crystal. © 2002 Elsevier Science Ltd. All rights reserved.

Spiro-compounds involving orthogonally fused π-conjugated moieties are supposed to have potential utility for molecular electronic devices,[1] and spirobifluorene[2] and spiro-fused thiophene systems[3] are proposed for action as a transistor source-drain channel. The orthogonal arrangement of two π-conjugated portions also attracts much attention in magnetochemistry[4] as well as physical organic chemistry, especially in connection with spiro-conjugation.[5,6] We have developed a convenient synthetic route to 9,9′(10*H*,10′*H*)-spirobiacridine (**1**) and its 2-methoxy derivative (**2**). Weber and coworkers proposed that crystals of spiro-compounds gave a high percentage of free volume into which small guest molecules might be enclosed, owing to their bulky and rigid molecular geometry.[7] However, there are quite a few reports on clathration using spiro-compounds.[7–9] In the course of our study on the crystal structure analysis of **1** and **2**, we have found that **2** afforded a variety of solvated crystalline compounds.



1 (R = H)
2 (R = OCH_3)

Compound **1** was prepared in three steps from the starting materials, diphenylamine (**3**) and acridone (**4**), as follows:

(i) The NH group in **3** was easily protected with a *t*-butoxycarbonyl group (BOC), giving BOC-**3** (for the structural formula, see Scheme 1). The BOC group facilitates directed *ortho*-metallation in BOC-**3**.[10]
(ii) The NH group in **4** was protected with a conventional 2-methoxyethoxymethyl group (MEM) by use of NaH followed by MEM-Cl in *N*,*N*-dimethylformamide to give MEM-**4**[11] (for the structural formula, see Scheme 1).
(iii) A one-pot procedure was developed for addition reaction of MEM-**4** with an *ortho*-lithiated compound from BOC-**3** and the acid-catalyzed intramolecular Friedel–Crafts reaction of the resultant carbinol[12] followed by acid-catalyzed cleavage of the BOC and MEM groups, giving the final product (**1**) (Scheme 1).

The following procedure is typical for the third step described above. To a tetrahydrofuran (THF) solution (10 mL) containing BOC-**3** (1.27 g, 4.71 mmol) and *N*,*N*,*N*′,*N*′-tetramethylethylenediamine (TEMDA; 0.80 mL, 5.3 mmol), a hexane solution of *t*-BuLi (1.48 mol/L, 3.50 mL, 5.2 mmol) was added with a syringe at −78°C. After being stirred for 2 h, a THF solution (25 mL) of MEM-**4** (1.41 g, 4.98 mmol) was added to the mixture at −78°C. The reaction vessel was gradually warmed to room temperature over 2 h. The solution was acidified with diluted HCl (0.5 mol/L, 5.0 mL) and stirred at room temperature overnight. The reaction mixture was further acidified with diluted HCl (0.5 mol/L, 10 mL) and again stirred for 1 day. After aqueous K_2CO_3 was added until the mixture was neutralized, CH_2Cl_2 was added. The organic layer was

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Keywords: spiro compounds; lithiation; acridines; X-ray crystal structures; host compounds.

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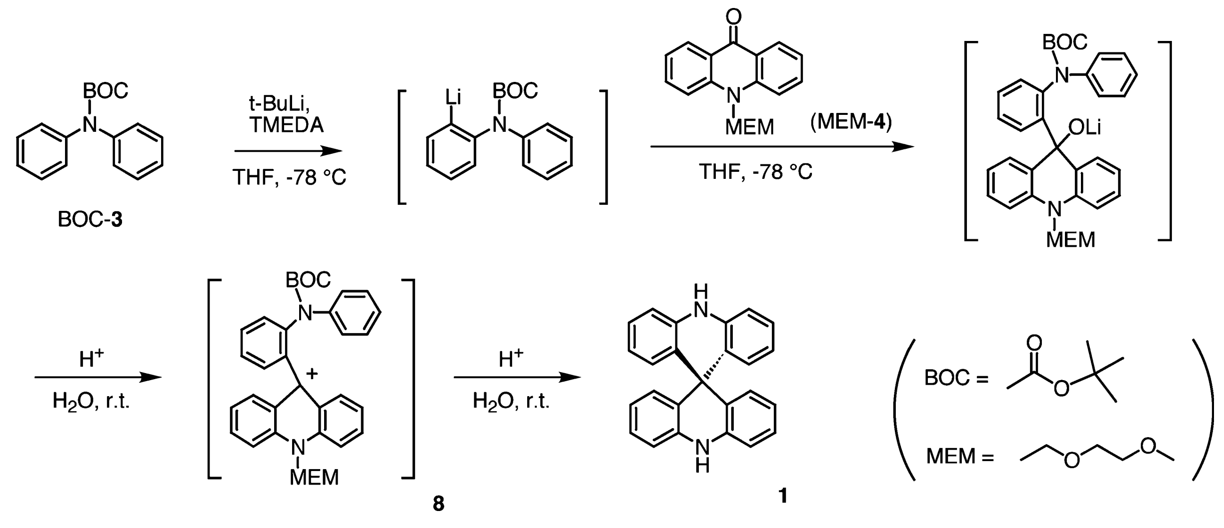
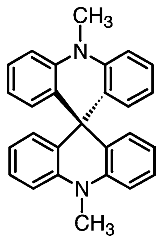


Scheme 1. Synthetic route to spirobiacridine.

separated, washed with water, dried over $MgSO_4$, and concentrated under reduced pressure. The residue was purified by passing a short column (silica gel, eluted with 1:1 hexane/CH_2Cl_2) and recrystallization from hexane/CH_2Cl_2 gave pure **1** (mp>300°C)[13] (0.847 g, 2.45 mmol). The isolated yield was 52% from BOC-**3**.

Daltrozzo and co-workers reported the synthesis of **1** in 7% yield from the same starting materials **3** and **4** under harsh conditions (260°C in an autoclave).[13] The present method considerably improves the yield, and the reaction can be easily conducted under ambient pressure in ordinary apparatus. They also reported the synthesis of **5** from **6** by applying the Grignard reaction with *N*-methylacridone.[14] However, *o*-halogenated diphenylamines are required and the synthetic labor increases accordingly, compared with the present preparation.



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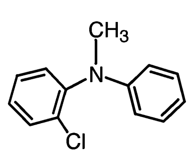
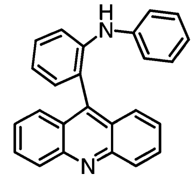


6

Note that only 9-(2-phenylaminophenyl)acridine (**7**)[15] was obtained as the final product when we used BOC-**4** in place of MEM-**4**. A trityl-type cation (**8**) is assumed to be a key intermediate. This finding suggests that aromatization of **8** competes with the desired Friedel–Crafts reaction. The retardation of the N-C(MEM) cleavage compared to the N-C(BOC) cleavage plays a crucial role in this reaction.



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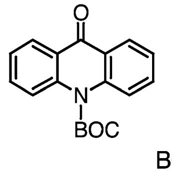
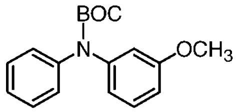


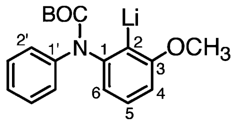
BOC-**4**

A methoxy-substituted derivative could also be prepared in a similar manner to that of **1**. After a BOC group was introduced to 3-methoxydiphenylamine (**9**), the resultant BOC-**9** was coupled with MEM-**4** to give a new compound 2-methoxyspirobiacirdine (**2**), which was purified by means of HPLC (Japan Analytical Industry, JAIGEL 1H+1H, eluted with $CHCl_3$). The isolated yield was 23% from BOC-**9**. The spectroscopic data of **2** satisfy the molecular structure,[16] which was finally confirmed by X-ray crystallographic analysis (see below).

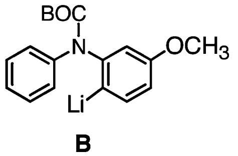


BOC-**9**

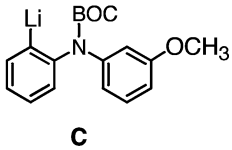
We have to state possible positions of directed lithiation in BOC-**9**, since **2** was obtained as an unexpected major isomer. Detailed analyses of ^1H NMR and mass spectra for the deuterated products after D_2O-quenching experiments reveal that the lithiation preferentially takes place at the 2 position (**A**); deuterated BOC-**9** showed a considerably lowered signal at 6.78 ppm ascribable to the proton of the 2 position and practically no ^1H–^1H coupling related to H2 in the 1D and 2D ^1H NMR measurements. This finding is explained by the stabilization with both neighboring BOC and CH_3O groups in **A**. However, the structure of main product **2** indicates that the 6 and 2′ positions are lithiated (**B** and **C**, respectively). There seems to be an equilibrium among **A**–**C**, and **A** hardly reacts with MEM-**4** because of the steric congestion while **B** and **C** are consumed and supplied from **A** via the equilibrium.



A



B



C

We confirmed the molecular structures of **1** and **2** by means of X-ray crystallographic analysis.[17] Two acridine planes in **1** are perpendicular to each other as demonstrated by the dihedral angle between the two averaged planes of 90.53(3)° (each least-square averaged plane was defined with the C and N atoms in a diphenylamine moiety). No appreciable pyramidalization is found at the nitrogen atoms. The molecule has a pseudo-D_{2d} structure although two acridine moieties are crystallographically independent. As Fig. 1 shows, **2** has essentially the same structure as that of **1** except for the additional methoxy group. The orthogonal arrangement between two acridine planes was indicated similarly by the dihedral angle of 90.20(3)° between them.

The spirobiacridines can work as a new class of a host compound. The rigid molecular structure of **2** is likely to form nearly rectangular hydrophobic cages in the crystal, where the solvent molecules can be incorporated. In fact, solvated crystals were obtained by crystallization in all cases investigated here. Binary compounds **2**·$(CH_2Cl_2)_2$ and **2**·$(CHCl_3)_2$ and a ternary compound **2**·CH_2Cl_2·C_6H_6 (Fig. 2) were obtained from the corresponding solutions, whose compositions were determined by X-ray crystallographic analysis.[17] A few appreciable van der Waals contacts could be found between the guest molecules and **2**. The nearest interatomic distance is 3.366(3) Å [Cl(1)···C(16)] between **2** and CH_2Cl_2, which is shorter than the sum of the van der Waals radii.[18] For the crystals of **2**·$(CH_2Cl_2)_2$ and **2**·$(CHCl_3)_2$, the chlorine atoms of the solvent molecules have contact likewise with the skeletal carbon atoms in **2**; the shortest Cl···C distances are 3.482(2) and 3.260(6) Å for **2**·$(CH_2Cl_2)_2$ and **2**·$(CHCl_3)_2$, respectively.

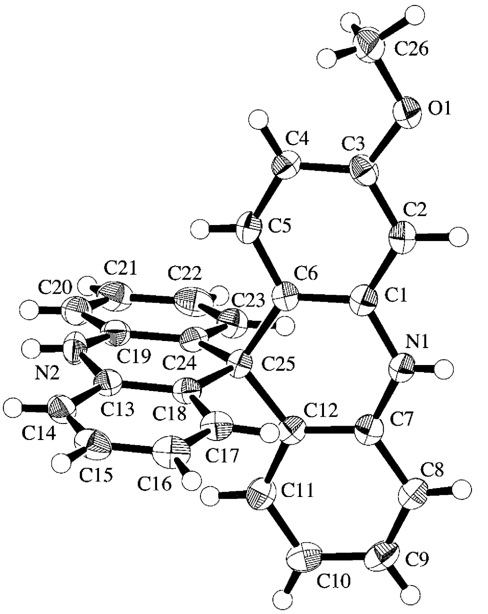


Figure 1. Molecular structure of **2** in the crystal of **2**·$(CH_2Cl_2)_2$ with thermal ellipsoids at the 50% level. Selected bond lengths (Å) and angles (°): C6–C25 1.532(3), C12–C25 1.535(3), C18–C25 1.532(3), C24–C25 1.530(3), C6–C25–C12 110.7(2), C18–C25–C24 110.8(2).

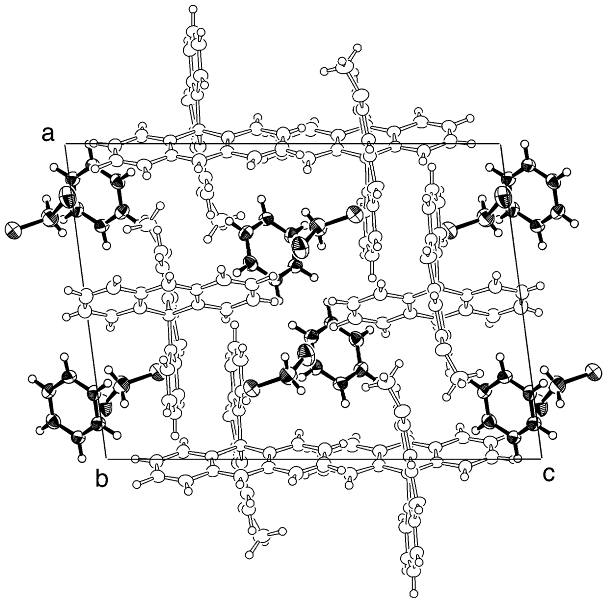


Figure 2. Crystal structure of **2**·CH_2Cl_2·C_6H_6 with thermal ellipsoids at the 50% level. The guest molecules CH_2Cl_2 and C_6H_6 are shaded.

Although **2** has two NH groups, there are no hydrogen bonds in the above solvated crystals, which is in sharp contrast to the hydrogen-bonded host–guest compounds involving 9,9′-spirobifluorene-2,2′-dicarboxylic acid[7] for example. The host–guest interactions in the solvated crystalline compounds of **2** originate in hydrophobic interaction and van der Waals contacts.

In summary, we have reported here a convenient synthesis of **1** and **2** from the corresponding diphenylamines and acridone in three steps. Novel host–guest compounds have been characterized. Conducting and/or magnetic materials derived from spiro-conjugation systems are of great interest as described above, and the present work suggests that these physical properties based on intermolecular interactions may be tuned and controlled by formation of host–guest complexes. Synthesis of nitroxide radicals from **1** and **2** according to established methods[19] is now underway.[20]

Acknowledgements

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15. Mp 122–123°C. ^{1}H NMR (270 MHz, $CDCl_3$): δ 5.1 (1H, bs), 6.85–6.94 (2H, m), 7.07–7.25 (4H, m), 7.41–7.55 (4H, m), 7.71–7.79 (4H, m), 8.22 (2H, d, $J=8.7$ Hz). ^{13}C NMR (125 MHz, $CDCl_3$): δ 116.1, 119.7, 120.3, 122.0, 123.8, 125.4, 126.2, 126.4, 129.2, 129.6, 129.8, 130.3, 131.8, 142.1, 142.2, 143.8, 149.0. MS (EI, 70 eV) m/z 346 (M^+), 269, 77.
16. ^{1}H NMR (500 MHz, $CDCl_3$): δ 3.73 (3H, s), 6.21 (2H, brs), 6.24 (1H, d, $J=2$ Hz), 6.28 (1H, dd, $J=2$, 9 Hz), 6.66–6.70 (6H, m), 6.84 (1H, d, $J=9$ Hz), 6.93–6.96 (3H, m), 6.98–7.01 (3H, m). ^{13}C NMR (125 MHz, $CDCl_3$): δ 46.6, 55.1, 97.8, 107.2, 113.11, 113.13, 120.8, 120.9, 123.8, 126.9, 130.7, 130.9, 132.2, 132.3, 133.3, 135.6, 135.7, 136.6, 158.5. Two signals accidentally overlap at 126.9 ppm, as suggested by the relative signal intensity. MS (EI, 70 eV) m/z 376 (M^+), 360, 345. The mp could not be determined because of liberation of crystal solvent molecules.
17. Data were collected on a Rigaku RAPID IP diffractometer using graphite-monochromated CuKα radiation ($\lambda=1.54184$ Å) at 100 K. All of the atoms including hydrogens could be found in difference Fourier maps. The atomic coordinates and thermal displacement parameters were refined anisotropically for non-hydrogen atoms and isotropically for hydrogen atoms using all the reflection data of $2\theta<136°$. Selected crystallographic data: **1**, $C_{25}H_{18}N_2$, monoclinic, $C2/c$, $a=17.576(1)$, $b=11.7483(8)$, $c=18.449(2)$ Å, $\beta=115.730$ (3)°, $V=3431.9(4)$ Å^3, $Z=8$, $D_{\text{calc}}=1.341$ g cm^{-3}, R $(I>2\sigma(I))=0.0550$, R_{w} (all data) $=0.1346$ for 3043 observed reflections. **2**·$(CH_2Cl_2)_2$, $C_{28}H_{24}Cl_4N_2O$, monoclinic, $P2_1/c$, $a=15.332(1)$, $b=9.9600(7)$, $c=16.605(1)$ Å, $\beta=95.671(2)°$, $V=2523.3(3)$ Å^3, $Z=4$, $D_{\text{calcd}}=1.438$ g cm^{-3}, R $(I>2\sigma(I))=0.0545$, R_{w} (all data) $=0.1437$ for 4590 observed reflections. **2**·$(CHCl_3)_2$, $C_{28}H_{22}Cl_6N_2O$, orthorhombic, $Pca2_1$, $a=19.8734(8)$, $b=13.1781(5)$, $c=10.5520(4)$ Å, $V=2763.5(3)$ Å^3, $Z=4$, $D_{\text{calc}}=1.479$ g cm^{-3}, R $(I>2\sigma(I))=0.0693$, R_{w} (all data) $=0.2093$ for 2650 observed reflections. **2**·CH_2Cl_2·C_6H_6, $C_{33}H_{26}Cl_2N_2O$, monoclinic, $P2_1/n$, $a=13.9196(6)$, $b=10.2311(5)$, $c=19.0260(9)$ Å, $V=2686.4(2)$ Å^3, $Z=4$, $D_{\text{calcd}}=1.329$ g cm^{-3}, R $(I>2\sigma(I))=0.0661$, R_{w} (all data) $=0.1720$ for 4706 observed reflections. One chlorine atom in **2**·$(CHCl_3)_2$ was analyzed to be disordered into two positions. Crystallographic data (excluding structure factors) for **1**, **2**·$(CH_2Cl_2)_2$, **2**·$(CHCl_3)_2$, and **2**·CH_2Cl_2·C_6H_6 have been deposited with the Cambridge Crystallographic Data Centre as supplementary publication nos. CCDC 184259–184262.
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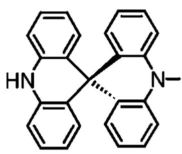
20. A nitroxide radical (**10**) prepared from **1** was found to possess ability to construct host–guest complexes. The crystal structure of **10** precipitated from CH_2Cl_2 was preliminarily characterized to be **10**·$(CH_2Cl_2)_2$ in a monoclinic $C2/c$ space group by means of X-ray crystallographic analysis.



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