Receptors for Oxo Acids: Effects of Intra-Ion-Pair Hydrogen Bonding on Acid-Base Equilibria

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Received July 9, 1993•

Receptor molecules 1-3 containing a quinoline unit and hydroxyl groups were synthesized, and their properties in salt formation with oxo acids such as *p*-toluenesulfonic acid (TsOH) and methyl phenylphosphonate (MPP) were studied by using ^{1}H NMR spectroscopy. In $CDCl_3$ solution the salt formation of the receptors with TsOH or MPP is enhanced by hydrogen bonds between the hydroxyl groups and the counteranion. The salt-formation enhancement of 1 over 2 suggests the presence of multiple interactions. The X-ray structure of 1·MPP·(acetone)$_2$ confirms that three hydrogen-bonding interactions stabilize the salt. In the salt formation of 5-(dimethylamino)quinoline derivative 3, the hydroxyl groups also affect the relative basicity of the basic nitrogens in 3. The results described here emphasize that acid-base equilibria in apolar solvents are significantly affected by intra-ion-pair hydrogen bonding (i.e., hydrogen bonding within a contact ion pair).

Introduction

Hydrogen bonding to a counteranion within a salt plays an important role in the chemistry of artificial receptors for anionic substrates such as phosphates,[2] carboxylates,[3] and sulfonates.[4] In the course of our research on molecular recognition,[5] we have been interested in the hydrogen-bonding effects on the salt formation in equilibrium with an acid and a base and have developed basic "receptors" for oxo acids on the basis of the following concept (eqs 1, 2). In an apolar solvent such as chloroform, an acid (HA) and a base (B:) are usually in equilibrium with a contact ion pair[6] in which a hydrogen bond is formed between the cation (B^+H) and the anion (A^-) (eq 1). If a base has

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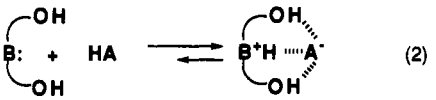

(2)

functional groups (e.g., hydroxyl groups) capable of hydrogen bonding to a counteranion, the equilibrium will shift to the salt stabilized by additional hydrogen bonding (eq 2). This additional hydrogen bonding, "intra-ion-pair hydrogen bonding",[7] will not only enhance the salt formation enthalpically but also enforce a rigid structure on the salt. The research on these hydrogen-bonding effects will contribute to the design of artificial anion receptors as well as to the understanding of acid-base equilibria in solvents of low polarity.[8]

Recently we have reported the effects of intra-ion-pair hydrogen bonding on the salt formation between quinoline-type synthetic receptor molecules and some oxo acids.[9] Here we present the details and some additional data for the salt formation induced and stabilized by hydrogen bonding.

Results and Discussion

In the following sections, we describe (1) the design of receptor molecules (1-3) and the synthesis of them and reference compounds (4-6), (2) ^{1}H NMR studies of the salt formation between 1, 2, or 4 and some oxo acids in chloroform-*d* solution and in DMSO-d_6 solution, together with the X-ray analysis of the salt containing 1 and methyl

• Abstract published in *Advance ACS Abstracts,* October 15, 1993.

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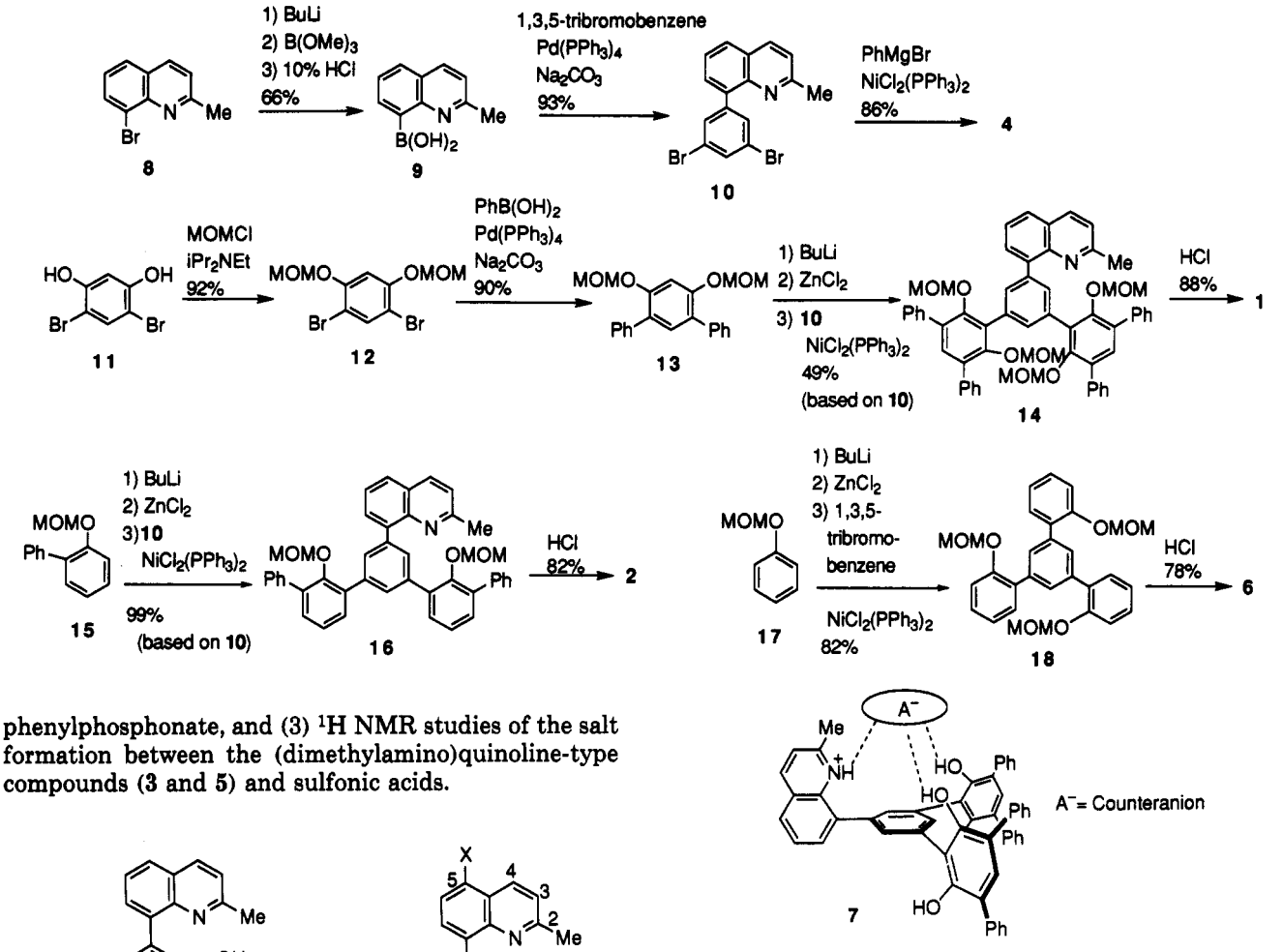
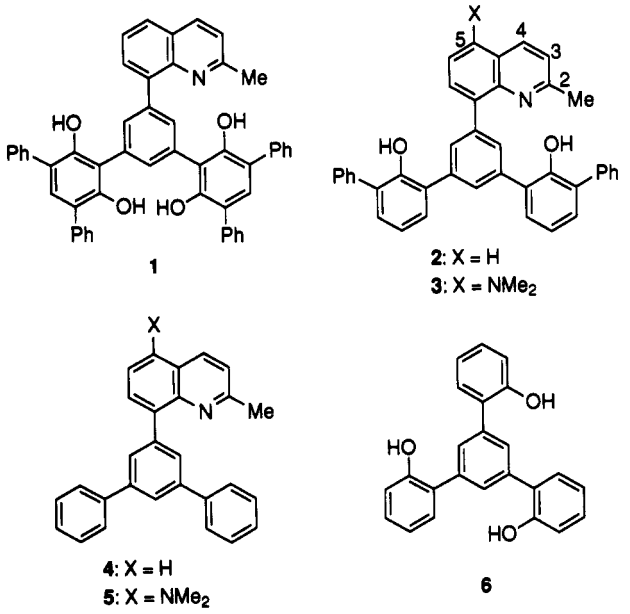
Scheme I



phenylphosphonate, and (3) ^{1}H NMR studies of the salt formation between the (dimethylamino)quinoline-type compounds (**3** and **5**) and sulfonic acids.



I. Design and Synthesis. To realize the salt-formation enhancement as shown in eq 2, we designed quinoline-containing receptor molecules such as **1–3**. Each of them has a basic quinoline-ring nitrogen and hydroxyl groups. On the basis of CPK modeling, we expected a salt with a structure like **7** which is stabilized by three hydrogen-bonding interactions (one $N^+H\cdots A^-$ and two $OH\cdots A^-$) between the protonated receptor and its counteranion. To determine the role of $OH\cdots A^-$ bonds in salt formation, reference compounds **4** and **5**, having no hydroxyl groups, and compoumd **6**, lacking a basic nitrogen, were designed and synthesized.

Scheme I shows the synthetic routes of **1**, **2**, **4**, and **6**. Boronic acid **9**, prepared from 8-bromoquinaldine (**8**),[10] was treated with 1,3,5-tribromobenzene in the presence of a palladium catalyst[11] to give dibromide **10**, the key compound of the syntheses of **1**, **2**, and **4**. The nickel-catalyzed coupling reaction[12] of **10** with phenylmagnesium bromide afforded **4**. Compound **13**, which was prepared from 4,6-dibromoresorcinol (**11**)[13] in two steps, was lithiated, transmetalated, and subjected to the coupling reaction[14] with dibromide **10** to give **14**. Deprotection of the MOM groups yielded receptor molecule **1**. Receptor **2** was also obtained from dibromide **10** and compound **15**.[15] Another reference compound **6** was prepared in a similar way.

(Dimethylamino)quinoline analogs **3** and **5** were synthesized as shown in Scheme II. Nitration of **8** occurred at 5 position of the quinoline ring,[16] and then the resulting compound **19** afforded dibromide **21** by the reaction with

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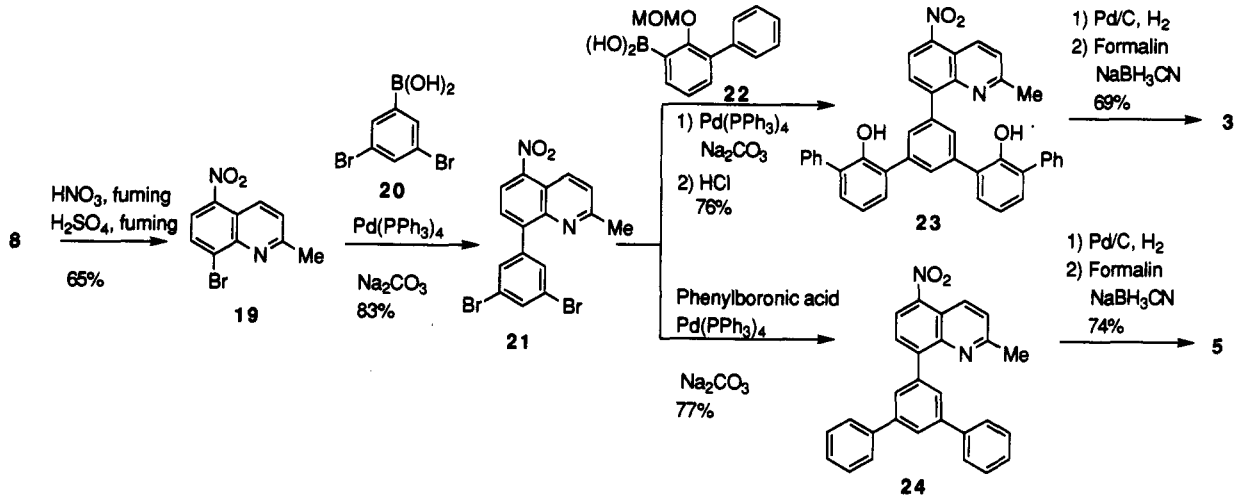
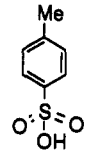
Scheme II

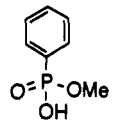


boronic acid **20**.[17] The palladium-catalyzed reaction between **21** and boronic acid **22**[15] gave **23**, which was converted to **3** by reduction and subsequent reductive dimethylation. Compound **5** was obtained by similar reactions.

II. Salt Formation of 1, 2, and 4. ^{1}H NMR studies (270 MHz) were carried out at 30 °C unless otherwise stated. Tetramethylsilane (TMS) was used as an internal standard. We used *p*-toluenesulfonic acid (TsOH) and methyl phenylphosphonate (MPP)[18] as oxo-acid substrates. Their salts with the bases are soluble in chloroform.



TsOH



MPP

(a) Salt Formation with TsOH in $CDCl_3$. Addition of 1 equiv of TsOH to a $CDCl_3$ solution of **1** caused ^{1}H NMR signal changes (Figure 1). For example, the 2-Me signal of **1** showed a salt-formation-induced shift values {$\Delta\delta$ = δ(observed) − δ(free base)} of 0.33 ppm (Figure 1a vs 1c). The Me signals of **2** and reference compound **4** also showed $\Delta\delta$ of 0.33 (not shown) and 0.59 (Figure 1b vs 1d), respectively, upon addition of 1 equiv of TsOH. These shifts indicate that the salt formation between the quinoline analogs and TsOH occurred in solution.

On the other hand, the selective salt formation for the receptors over the reference was observed in competitive salt-formation experiments. In a solution of a 1:1:1 mixture of **1**, **4**, and TsOH, the Me signal of **1** moved downfield ($\Delta\delta$ = 0.33), whereas that of **4** showed no shift (Figure 1e). Similarly, a 1:1:1 mixture of **2**, **4**, and TsOH also gave a downfield shift ($\Delta\delta$ = 0.33) of the Me signal of **2** and no shift of that of **4** (not shown). These results clearly show that the salt **1**·TsOH or **2**·TsOH is more thermodynamically stable than the salt **4**·TsOH. Addition of 1 equiv of another reference compound **6** to a 1:1 solution of **1** and TsOH did not affect the salt formation between **1** and TsOH (Figure 1f).

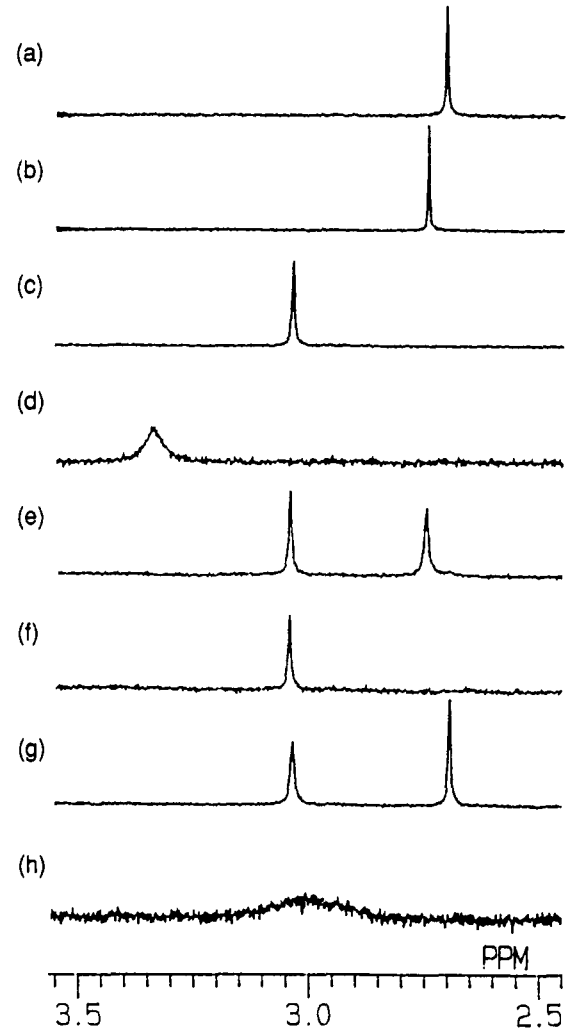


Figure 1. ^{1}H NMR spectra in $CDCl_3$ at 30 °C (each 0.75 mM): (a) **1**; (b) **4**; (c) **1** + TsOH (1:1); (d) **4** + TsOH (1:1); (e) **1** + **4** + TsOH (1:1:1); (f) **1** + **6** + TsOH (1:1:1); (g) **1** + TsOH (2:1); (h) **4** + TsOH (2:1).

For a 2:1 mixture of **1** and TsOH, two Me signals were observed in a 1:1 intensity ratio (Figure 1g); they correspond to the signal of free **1** (Figure 1a) and that of salt-formed **1** (Figure 1c). This result indicates that the exchange process between free **1** and salt-formed **1** is slow on the NMR time scale, and that TsOH molecules added to the solution form the salt with **1** almost completely. For

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a 2:1 mixture of 4 and TsOH (Figure 1h), however, only one broad Me signal was observed due to the relatively fast exchange between free 4 (Figure 1b) and salt-formed 4 (Figure 1d).

Table I shows the chemical shift values of the sulfonate moieties of the salts. These values depend on the coexisting countercations. This result indicates that the sulfonate anions and the countercations are so closely spaced together as to induce chemical shift changes. Taking into account of this result, we assume that the salts exist as contact ion pairs in chloroform due to low polarity of the solvent.[19] Consequently, the selectivity of the salt formation for the receptors over 4 seems to be caused by interactions within the contact ion pairs. Although there is the possibility that energy differences of the ground state conformations of these bases are attributed to the selectivity, this possibility is unsuitable for the explanation of the complete selectivity stated above. Later, we show direct evidence for the interactions, hydrogen bonding between the hydroxyl groups of the receptors and a sulfonate anion.

(b) Salt Formation with MPP in $CDCl_3$. Addition of 1 equiv of MPP to a $CDCl_3$ solution of 1 caused a downfield shift of the Me signal on the quinoline ring ($\Delta\delta$ = 0.19) due to partial salt formation. In the case of 4 in place of 1, however, no chemical shift changes occurred. For a 1:1:1 mixture of 1, 4, and MPP, the Me signal of 1 moved downfield ($\Delta\delta$ = 0.18), but the signals of 4 showed no shift. These results indicate that the salt 1·MPP is much more stable than the salt 4·MPP.

For a mixture of MPP and more than 1 equiv of 1, only one Me signal of the latter was observed at 30 °C due to the fast exchange between free 1 and salt-formed 1. At −60 °C (Figure 2), however, this exchange became slower on the NMR time scale. For example, in a 1:MPP ratio of 4 (Figure 2d), the two Me signals from 1 were observed in a 3:1 intensity ratio, corresponding to the signal of free 1 (Figure 2b) and that of salt-formed 1 (Figure 2c). The absence of the signals of free 1 in a 1:MPP ratio of 1 (Figure 2c) shows that complete salt formation occurred. On the other hand, no salt formation between 4 and MPP was observed even at −60 °C (Figure 2f), indicating that salt 4·MPP is too unstable to exist in chloroform. These experiments lead us to the conclusion that the hydroxyl groups of 1 are indispensable to the salt formaton with MPP.

From the following observations, we conclude that the complex between 1 and MPP is not a hydrogen-bonded complex (B:···HA), but a salt (B^+···HA^-).[20] The hydrogen atom at 4 position of the quinoline ring in 1 showed $\Delta\delta$ of 0.69 at −60 °C upon addition of 1 equiv of MPP. This value is comparable with $\Delta\delta$ of 0.75 induced by addition of TsOH, which is a much stronger acid than MPP,[21] at the same temperature. Since it is likely that the complex between 1 and TsOH is a salt (not a hydrogen-bonded complex), the shift values indicate that 1 and MPP form a salt.

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(20) The position of the proton-tansfer equilibrium between a hydrogen-bonded complex and a salt in organic solvents cannot be deduced from only pK_a values in water. With decreasing solvent polarity the equilibrium is shifted in favor of the hydrogen-bonded complex.[6]

(21) p*Ka* of $PhSO_3H$, −6.5;[22] MPP, 2.97 (in water/dioxane 50/50).[18]

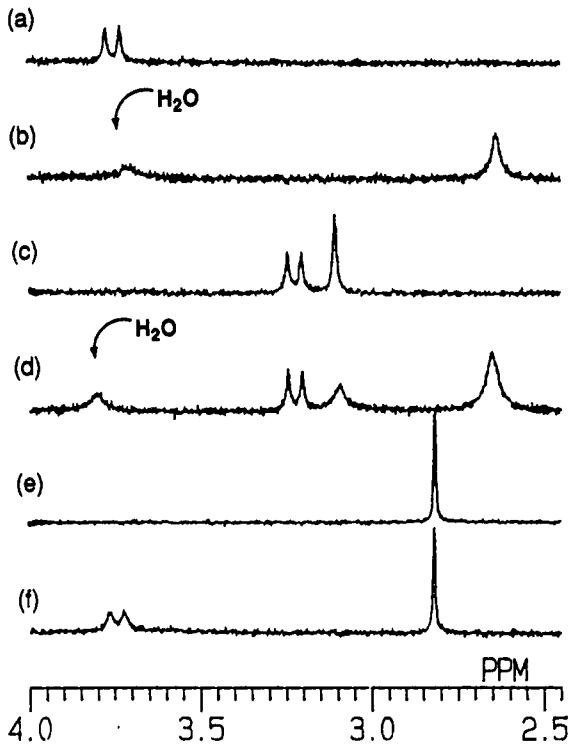


Figure 2. ^1H NMR spectra in $CDCl_3$ at −60 °C (each 0.75 mM): (a) MPP; (b) 1; (c) 1 + MPP (1:1); (d) 1 + MPP (4:1); (e) 4; (f) 4 + MPP (1:1). The signals of water were confirmed by chemical shift changes on addition of CD_3OD.

Table I. ^1H NMR Chemical Shift Values (ppm) of *p*-Toluenesulfonate Moieties in $CDCl_3$[a]

	δ (CH_3)[b]	δ (H_m)[c]	δ (H_o)[d]
TsOH + 1	2.31	7.07	*e*
TsOH + 2	2.27	6.99	*e*
TsOH + 4	2.12	6.67	*e*
$TsO^-{\cdot}^+NEt_4$[f]	2.33	7.13	*e*

[a] Each 0.75 mM. [b] δ (CH_3): the methyl signal of the sulfonate. [c] δ (H_m): the meta protons to the sulfonyl group. [d] δ (H_o): the ortho protons to the sulfonyl group. [e] Obscured by other signals. [f] Tetraethylammonium *p*-toluenesulfonate.

Table II. ^1H NMR Chemical Shift Values (ppm) of the OH groups[a]

receptor	acid	30 °C	−60 °C
1		5.86 (4H)	6.3 (br)
1	TsOH	*b*	5.73 (2H), 8.62 (2H)
1	MPP	*b*	5.80 (2H), 10.78 (2H)
2		6.15 (2H)	6.69 (2H)
2	TsOH	8.24 (2H)	8.53 (2H)

[a] In $CDCl_3$, 0.75 mM. [b] Not observed.

(c) OH Proton Signals of 1 and 2. Table II summarizes the chemical shift values of the phenolic hydroxyl protons of the receptors. The OH signal of 1, observed at 5.86 ppm, became too broad to be observed upon addition of the acid substrates at 30 °C. At −60 °C, however, the signal became observable and split into two signals: a higher field signal (δ 5.73 for TsOH, or 5.80 for MPP, each 2H) and a lower-field signal (8.62 for TsOH, or 10.78 for MPP, each 2H). The lower field signals, which are more substrate dependent than the higher field protons, are assignable to the OH protons that form hydrogen bonds with the counteranions. These results strongly suggest that the salts between 1 and the acid substrates are stabilized by *two additional hydrogen bonds between the counteranions and the two hydroxyl groups of 1* as shown

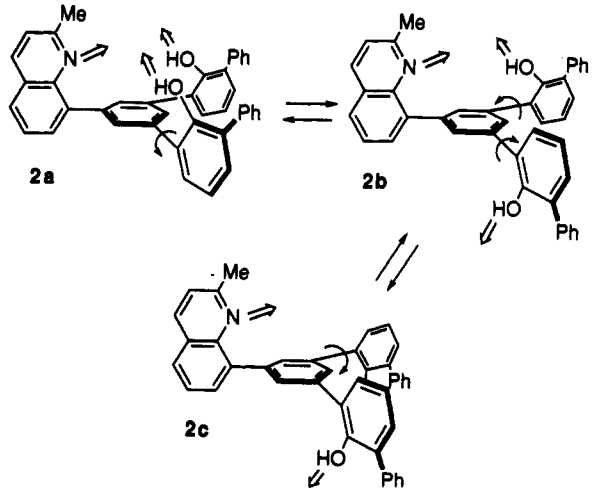
in 7. This conclusion is supported by the results that only the lower field signal (δ 8.53) was observed in the case of 2 with TsOH at −60 °C.

The receptor 2 with TsOH at 30 °C gave the signal at δ 8.24, but 1 with TsOH gave no observable OH signal due to extreme broadening which is explicable by the exchange process between the hydrogen-bonded OH groups and the non-hydrogen-bonded OH groups in the salt 1·TsOH via the rotation about the bonds connecting the resorcinol moieties with the central benzene ring.

(d) Comparison of 1 and 2. A salt-formation constant between 1 and MPP, K(1·MPP), was determined by ^{1}H NMR titration (in $CDCl_3$ at 30 °C) and found to be (7.1 ± 0.2) × 10^2 M^{-1}. K(2·MPP) was found to be (2.1 ± 0.1) × 10^2 M^{-1}. Thus, the ratio of these constants {K(1·MPP)/K(2·MPP)} is 3.4. To determine this kind of ratio for TsOH, we carried out a competitive salt-formation experiment[2k] using a 1:1:1 mixture of 1, 2, and TsOH, because the salt-formation constants are too large to be determined by titration. K(1·TsOH)/K(2·TsOH) was found to be 3.4.

The 3.4-fold enhancement of the salt formation for 1 over 2 is attributable to preorganization[23] in 1 for three hydrogen-bonding interactions like 7. There are three possible atropisomers for 2,[24] and only one isomer (**2a**) is suitable for three hydrogen-bonding interactions with a counteranion, whereas 1 is preorganized for this type of interactions.

One of the reviewers of this paper suggests that the 3.4-fold difference between 1 and 2 could be explained by the difference of the preferred low-energy conformations of these compounds. We have no information of the lowest energy conformations of the bases at the present time. Therefore, we cannot exclude the possibility suggested by the reviewer, although the preorganization seems to be the most plausible explanation.



(e) Salt Formation with TsOH in DMSO-d_6. Addition of 1 equiv of TsOH to separate DMSO-d_6 solutions of 1, 2, and 4 caused ^{1}H NMR spectral changes. For example, the Me signals of 1, 2, and 4 shifted downfield ($\Delta\delta$ = 0.06, 0.09, and 0.07, respectively). These shifts show that the proton transfer from the sulfonic acid to the basic quinoline nitrogens occurs to some extent.

Table III. ^{1}H NMR Chemical Shift Values (ppm) of *p*-Toluenesulfonate Moieties in DMSO-d_6[a]

	δ (CH_3)	δ (H_m)	δ (H_o)
TsOH + 1	2.29	7.11	7.48
TsOH + 2	2.29	7.11	*b*
TsOH + 4	2.29	7.11	*b*
$TsO^-{\cdot}^+NEt_4$	2.29	7.10	7.47
TsOH	2.29	7.11	7.47

[a] Each 5.0 mM. [b] Obscured by other signals.

In DMSO-d_6 solutions, unlike $CDCl_3$ solutions, the chemical shift values of the sulfonate moieties were independent from the coexisting countercations (Table III). Furthermore, the values were also identical with the case of TsOH alone. These results suggest the following: (1) in DMSO solution, TsOH is almost completely dissociated even in the absence of a base,[25] (2) the sulfonate anions exist as solvent-separated ion pairs or free ions (if the anions form contact ion pairs, the chemical shift values will depend on the countercations as in the case of $CDCl_3$ solutions).

To determine the proton affinity (basicity) of 1 and 4, we titrated these compounds with TsOH. According to the suggestions stated above, the ^{1}H NMR titration data give an association constant between a receptor and a proton. The constants were found to be (9.4 ± 0.5) × 10^1 M^{-1} for 1 and (9.5 ± 0.9) × 10^1 M^{-1} for 4. These almost identical constants indicate that the basicity of the nitrogen atom of 1 is equal to that of 4. Actually, a competitive salt-formation experiment of a 1:1:1 mixture of 1, 4, and TsOH gave the nearly equal $\Delta\delta$ of 0.05 for the Me signal of 1 and 0.06 for that of 4.

(f) X-ray Structure of Salt 1·MPP. Recrystallization of salt 1·MPP from acetone–hexane (7/4) gave yellow prisms as 1·MPP·(acetone)$_2$. X-ray analysis[26] of this crystal provides the evidence of intra-ion-pair hydrogen bonding. Figure 3 shows the structure of the salt, in which three hydrogen-bonding interactions are present.[27] One oxygen of MPP anion binds to the $^+$NH of the protonated 1 (N···O distance 2.745 Å) and one OH group (O···O 2.590 Å), and another oxygen of the anion binds to another OH group (O···O 2.557 Å). Two kinds of acetone molecules, hydrogen-bonded and non-hydrogen-bonded, are included. This structure of the salt, except for the presence of the acetone molecules, agrees with the results obtained in the ^{1}H NMR studies in $CDCl_3$.

III. Salt Formation of 3 and 5. The (dimethylamino)-quinoline-type compounds 3 and 5 have two kinds of basic nitrogens (i.e., ring nitrogen and 5-NMe_2). We studied the effects of intra-ion-pair hydrogen bonding on the relative basicity of the ring nitrogens and the NMe_2

(22) Cerfontain, H.; Koeberg-Telder, A.; Kruk, C. *Tetrahedron Lett.* **1975**, *42*, 3639.

(23) (a) Cram, D. J. *Angew. Chem., Int. Ed. Engl.* **1986**, *25*, 1039. (b) Zimmerman, S. C.; Mrksich, M.; Baloga, M. *J. Am. Chem. Soc.* **1989**, *111*, 8528. (c) Horiuchi, N.; Huff, J.; Rebek, J., Jr. *Tetrahedron Lett.* **1990**, *31*, 5121.

(24) The exchange process between the atropisomers is fast on the ^{1}H NMR time scale even at −60 °C.

(25) Sulfuric acid is completely dissociated in DMSO: Kolthoff, I. M.; Reddy, T. B. *Inorg. Chem.* **1962**, *1*, 189.

(26) 1·MPP(acetone)$_2$ crystallized in the monoclinic space group $P2_{1/a}$ (z = 4) with unit cell parameters a = 29.351(3) Å, b = 12.597(2) Å, c = 14.654(1) Å, β = 94.14(1)°, and D_{calcd} = 1.26 g/cm^3. A total of 6393 effective reflections ($|F_{obs}| \geq 2.67\delta|F_{obs}|$) were observed using graphite-monochromated Cu Kα radiation (2θ values in the range of 0–120°). The structure was solved by direct methods using the computer program SIR 85 and the difference Fourier method. The final R value is 0.082. The position of methyl group connected to phosphonate is disordered between two positions in the ratio of 1:1. Only one of the two positions is shown in Figure 3. For details, see supplementary material with ref 9a.

(27) Similar hydrogen-bonding arrangements are seen in the X-ray structure of ([$HOC_6H_4O(Ph)PO_2$][C_5H_5NH]·catechol): Poutasse, C. A.; Day, R. O.; Holmes, R. R. *J. Am. Chem. Soc.* **1984**, *106*, 3814.

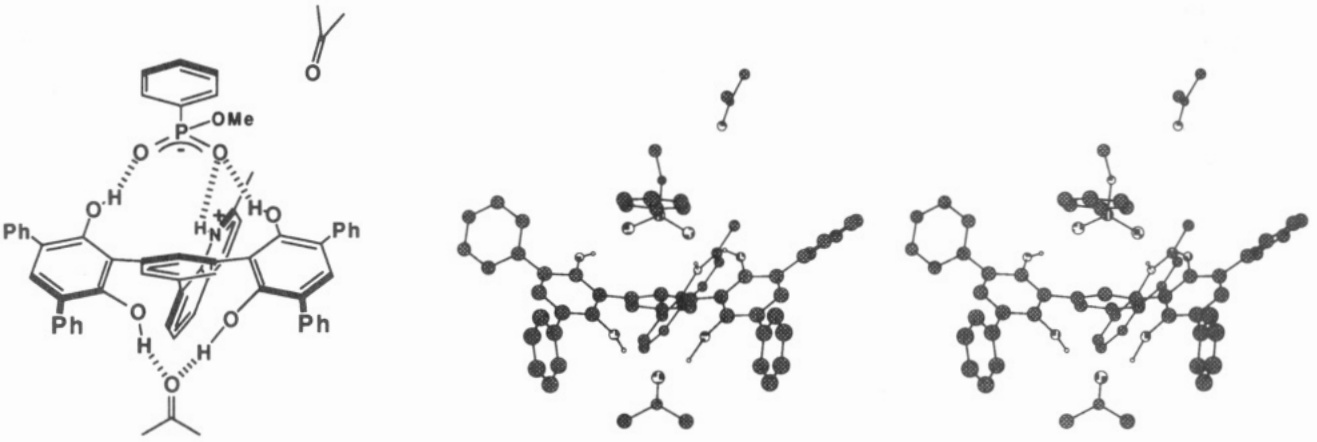


Figure 3. X-ray structure 1·MPP·(acetone)$_2$ (stereoview). The hydrogen atoms have been omitted for clarity with the exception of hydrogen-bonding atoms.

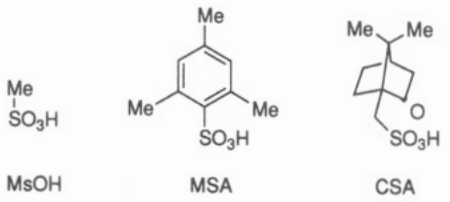
Table IV. ^{1}H NMR Chemical Shift Values, $\Delta\delta$, and the Ratios of RN and DM[a]

	δ 2-Me ($\Delta\delta$)	δ 5-NMe$_2$ ($\Delta\delta$)	RN/DM[b]
5	2.80	2.98	
5 + MsOH	3.31 (0.51)	3.05 (0.07)	6:4
	2.86 (0.06)	3.63 (0.65)	
5 + TsOH	3.37 (0.57)	3.04 (0.06)	5:5
	2.83 (0.03)	3.63 (0.65)	
5 + MSA	3.38 (0.58)	3.04 (0.06)	3:7
	2.83 (0.03)	3.64 (0.66)	
5 + CSA	3.30 (0.50)	3.04 (0.06)	1:9
	2.85 (0.05)	3.74 (0.76)	
		3.60 (0.62)	
3	2.68	2.97	
3 + TsOH	2.99 (0.31)	3.05 (0.08)	10:0
3 + CSA	3.22 (0.54)	3.04 (0.07)	10:0

[a] In $CDCl_3$ at −60 °C, each 0.75 mM. [b] Determined by integration of 5-NMe$_2$.

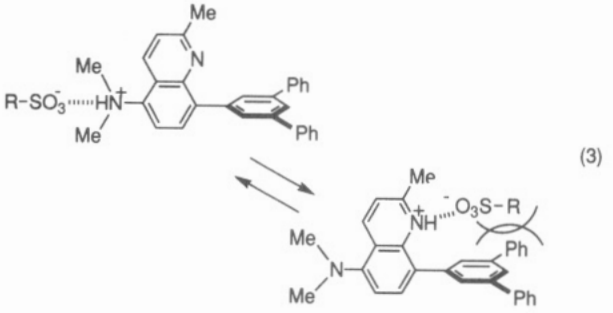
groups.[28] The relative basicity was estimated from the percentage of the protonation to each nitrogen by ^{1}H NMR spectroscopy at −60 °C.

First, we studied the salt formation between **5** and some sulfonic acids: TsOH, methanesulfonic acid (MsOH), mesitylenesulfonic acid (MSA), and D-(+)-camphorsulfonic acid (CSA). In a $CDCl_3$ solution of a 1:1 mixture of each base and acid, the signals of two species were observed. We conclude that one corresponds to the salt (RN) protonated at the ring nitrogen and the other corresponds to the salt (DM) protonated at the NMe$_2$ group. Their assignments were made on the basis of $\Delta\delta$ of 2-Me and 5-NMe$_2$ (Table IV); RN shows a large $\Delta\delta$ of 2-Me (0.50–0.58) and a small $\Delta\delta$ of 5-NMe$_2$ (0.06–0.07), and DM shows a small $\Delta\delta$ of 2-Me (0.03–0.06) and a large $\Delta\delta$ of 5-NMe$_2$ (0.62–0.76). When CSA was used, DM showed two diastereotopic Me groups for 5-NMe$_2$ due to the presence of the chiral sulfonate anion while RN showed only one Me signal for 5-NMe$_2$. At room temperature, the exchange between RN and DM became faster on the NMR time scale.



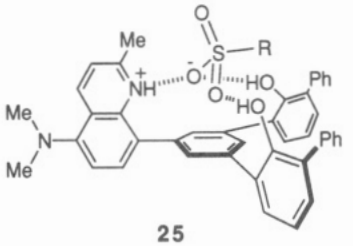
MsOH MSA CSA

Table IV also lists the ratios of RN and DM. In the salt formation of **5**, the ratios depend upon the sulfonic acids used; increasing the size of the sulfonates increases the proportion of DM. These results suggest that the steric repulsion between the 3,5-diphenylphenyl substituent and the sulfonates mainly affects the relative basicity of the nitrogens in these cases (eq 3).



(3)

In the case of **3** in place of **5**, however, only RN was observed (Table IV). On the basis of the X-ray structure of 1·MPP·(acetone)$_2$ (Figure 3), we conclude that the ion-pair structure **25**, which is stabilized by three hydrogen bonds, causes the preference for the ring N protonation. The presence of intra-ion-pair hydrogen bonding is supported by the chemical shift changes of the phenolic OH protons. The OH signal of **3** showed $\Delta\delta$ of 1.88 in the presence of TsOH. Furthermore, two diastereotopic OH signals ($\Delta\delta$ = 1.81 and 1.84) were observed in the presence of CSA.



25

The competitive salt formation of a 1:1:1 mixture of **3**, **5**, and TsOH in $CDCl_3$ afforded salt **3**·TsOH and free **5**.

(28) The effect of solvation on the relative basicity of the ring nitrogen and the NH$_2$ group in 4-amino-5-methylacridine has been reported: (a) Craig, D. P. *J. Chem. Soc.* **1946**, 534. (b) Menger, F. M.; Singh, T. D. *J. Org. Chem.* **1980**, *45*, 183.

No salt derived from 5 was observed in agreement with the experiment of the quinoline-type compounds 1 and 4 with TsOH. Another competition experiment of 2, 3, and TsOH gave the ratio of the salt-formation constants[2k] {K(3·TsOH)/K(2·TsOH)} of 4.8. This difference between 2 and 3 may be attributed to the electron-donating NMe_2 substituent in 3.

Conclusion

The salt between synthetic receptors and some acid substrates is stabilized by intra-ion-pair hydrogen bonding evidenced by ^1H NMR studies and an X-ray analysis. Thus, these hydrogen-bonding interactions significantly affect the relative basicity of 1, 2, and 4 as well as the relative basicity of two nitrogens in 3.

We have recently reported the control of relative basicity by other intra-ion-pair interactions, such as π-stacking interactions.[9b] These studies, including the results described here, can contribute to the understanding of acid–base equilibria in solvents of low polarity as well as to the development of artificial receptors for anionic substrates.

Experimental Section

General. THF and Et_2O were freshly distilled from sodium–benzophenone ketyl under Ar. Melting points are uncorrected. For the salt-formation experiments, $CDCl_3$ (99.8 atom % D) was treated with Al_2O_3, filtered, and then dried over MS4A for at least 3 h. DMSO-d_6 (99.9 atom % D) was dried over MS4A. These deuterated solvents were used within a day after drying.

2-Methyl-8-quinolineboronic Acid (9). A solution of 8-bromo-2-methylquinoline (8, 2.10 g, 9.46 mmol) in THF (8 mL) was cooled to −74 °C under Ar, and n-BuLi (1.55 N in hexane, 6.7 mL, 10.4 mmol) was added dropwise during 5 min. After 30 min, $B(OMe)_3$ (2.3 mL, 20.3 mmol) was added, and the mixture was stirred at −74 °C for 20 min and then at rt for 10 min. Water (20 mL) and 10% HCl (100 mL) were added, and the aqueous layer was washed with Et_2O and neutralized with $NaHCO_3$ (24.4 g). The resulting white precipitate was dried to give a pale yellow powder (1.58 g), which was recrystallized from benzene–hexane (3/1) to give 9 (1.16 g, 66%) as colorless fine prisms: mp 197–199 °C; ^1H NMR ($CDCl_3$, TMS, 270 MHz) δ 2.78 (3H, s), 7.32 (1H, d, J = 8.6 Hz), 7.57 (1H, t, J = 7.9 Hz), 7.89 (1H, dd, J = 7.9, 1.3 Hz), 8.13 (1H, d, J = 8.6 Hz), 8.36 (1H, d, J = 5.6 Hz), 8.82 (2H, br); ^{13}C NMR ($CDCl_3$, TMS, 67.8 MHz) δ 25.2, 121.6, 126.0, 130.5, 137.7, 137.9, 151.7, 157.8 (two carbon signals are superimposed); IR (KBr) 3340, 1610, 1600, 1575, 1500, 1470, 1390, 1310 cm^{-1}; MS m/z 187 and 186 (M^+). Anal. Calcd for $C_{10}H_{10}BNO_2$: C, 64.23; H, 5.39; N, 7.49. Found: C, 64.30; H, 5.36; N, 7.28.

8-(3,5-Dibromophenyl)-2-methylquinoline (10). $Pd(PPh_3)_4$ (0.42 g, 0.36 mmol) and 2 M aqueous Na_2CO_3 (34 mL) were added to a solution of 9 (6.29 g, 33.6 mmol) and 1,3,5-tribromobenzene (29.28 g, 93.0 mmol) in toluene (120 mL) and EtOH (20 mL). The mixture was heated at reflux for 18 h and then cooled to rt. Benzene (100 mL) was added, and the organic layer was washed with brine, dried over K_2CO_3, and evaporated to give a pale brown solid. To remove part of the excess tribromobenzene, the brown solid was recrystallized from benzene. Tribromobenzene (4.30 g) was obtained, and the mother liquor was evaporated and purified by silica gel column chromatography (benzene–hexane) to give a white solid (11.78 g), which was recrystallized from hexane to give 10 (11.08 g, 88%) as colorless needles: mp 121–123 °C; ^1H NMR ($CDCl_3$, TMS, 270 MHz) δ 2.71 (3H, s), 7.32 (1H, d, J = 8.3 Hz), 7.53 (1H, t, J = 7.6 Hz), 7.68 (1H, dd, J = 7.6, 1.7 Hz), 7.69 (1H, t, J = 1.7 Hz), 7.81 (1H, dd, J = 7.9, 1.3 Hz), 7.87 (2H, d, J = 1.7 Hz), 8.08 (1H, d, J = 8.3 Hz); ^{13}C NMR ($CDCl_3$, TMS, 67.8 MHz) δ 25.7, 122.1, 122.2, 125.3, 126.9, 128.4, 130.2, 132.4, 132.7, 136.3, 136.8, 142.9, 145.0, 159.3; IR (KBr) 1610, 1595, 1580, 1545, 1495 cm^{-1}; MS m/z 377 (M^+), 298 and 296 (M^+ − Br). Anal. Calcd for $C_{16}H_{11}Br_2N$: C, 50.97; H, 2.94; N, 3.71. Found: C, 51.19; H, 2.93; N, 3.74.

8-(3,5-Diphenylphenyl)-2-methylquinoline (4). A suspension of 10 (1.01 g, 2.68 mmol) and $NiCl_2(PPh_3)_2$ (0.14 g, 0.21 mmol) in Et_2O (30 mL) was cooled in an ice bath under Ar. PhMgBr (2.12 N in Et_2O, 3 mL, 6.36 mmol) was added during 5 min, and the reaction mixture was heated at reflux for 14 h. Saturated aqueous $NaHCO_3$ (20 mL) was added slowly at rt, and benzene (50 mL) was added. This was filtered to remove undissolved materials. The organic layer was washed with brine, dried over K_2CO_3, and evaporated to give a yellow oil (1.61 g), which was purified by silica gel column chromatography (AcOEt–hexane) to give 4 (0.86 g, 86%) as a white amorphous solid: ^1H NMR ($CDCl_3$, TMS, 270 MHz) δ 2.75 (3H, s), 7.33 (1H, d, J = 8.3 Hz), 7.36 (2H, t, J = 7.3 Hz), 7.47 (4H, t, J = 7.3 Hz), 7.57 (1H, t, J = 7.3 Hz), 7.75 (4H, d, J = 7.3 Hz), 7.81 (1H, d, J = 8.3 Hz), 7.84 (1H, t, J = 1.7 Hz), 7.85 (1H, d, J = 7.3 Hz), 8.04 (2H, d, J = 1.7 Hz), 8.11 (1H, d, J = 8.3 Hz); ^{13}C NMR ($CDCl_3$, TMS, 67.8 MHz) δ 25.9, 121.8, 125.0, 125.4, 127.0, 127.2, 127.4, 127.5, 128.7, 129.1, 130.3, 136.3, 139.5, 140.2, 141.1, 141.5, 145.4, 158.8; IR (KBr) 1595, 1500 cm^{-1}; MS m/z 371 (M^+), 294 (M^+ − Ph). Anal. Calcd for $C_{28}H_{21}N$: C, 90.53; H, 5.70; N, 3.77. Found: C, 90.34; H, 5.73; N, 4.05.

1,3-Dibromo-4,6-bis(methoxymethoxy)benzene (12). A solution of 4,6-dibromoresorcinol (11, 27.0 g, 0.101 mol) and iPr_2NEt (90 mL, 0.517 mol) in CH_2Cl_2 (150 mL) was cooled in an ice bath. MOMCl (23 mL, 0.303 mol) was added, and the mixture was stirred at 0 °C for 1 h and at rt for 1 h. The reaction mixture was evaporated to half-volume. This was diluted with Et_2O (300 mL), washed with 10% HCl, water, 10% NaOH, and brine, dried over $MgSO_4$, and evaporated to give a white solid (34.6 g). The product was recrystallized from hexane to give 12 (33.0 g, 92%) as colorless prisms: mp 67 °C; ^1H NMR ($CDCl_3$, TMS, 270 MHz) δ 3.52 (6H, s), 5.22 (4H, s), 7.03 (1H, s), 7.69 (1H, s); ^{13}C NMR ($CDCl_3$, TMS, 67.8 MHz) δ 56.5, 95.4, 105.0, 105.4, 135.9, 153.8; IR (KBr) 1580, 1480, 1275, 1210, 1205, 1175, 1150, 1090, 1060 cm^{-1}; MS m/z 356 and 354 (M^+). Anal. Calcd for $C_{10}H_{12}Br_2O_4$: C, 33.74; H, 3.40. Found: C, 33.78; H, 3.37.

4′,6′-Bis(methoxymethoxy)-m-terphenyl (13). $Pd(PPh_3)_4$ (0.16 g, 0.14 mmol) and 2 M aqueous Na_2CO_3 (8.3 mL) were added to a solution of 12 (1.36 g, 3.82 mmol) and phenylboronic acid (1.02 g, 8.37 mmol) in toluene (6 mL) and EtOH (1 mL). The mixture was heated at reflux for 23 h under Ar and then cooled to rt. Benzene (10 mL) was added, and the organic layer was washed with water and brine, dried over $MgSO_4$, and evaporated to give a brown oil (1.85 g). The product was purified by silica gel column chromatography (AcOEt–hexane) to give 13 (1.21 g, 90%) as colorless prisms: mp 61–64 °C; ^1H NMR ($CDCl_3$, TMS, 270 MHz) δ 3.41 (6H, s), 5.15 (4H, s), 7.13 (1H, s), 7.28–7.34 (3H, m), 7.37–7.43 (4H, m), 7.52–7.55 (4H, m); ^{13}C NMR ($CDCl_3$, TMS, 67.8 MHz) δ 56.2, 95.4, 104.2, 126.0, 126.7, 128.0, 129.5, 132.8, 138.1, 154.2; IR (KBr) 1605, 1510, 1480, 1215, 1200, 1150, 1080, 1030 cm^{-1}; MS m/z 350 (M^+). Anal. Calcd for $C_{22}H_{22}O_4$: C, 75.41; H, 6.33. Found: C, 75.53; H, 6.37.

8-[3,5-Bis[2,6-bis(methoxymethoxy)-3,5-diphenylphenyl]-phenyl]-2-methylquinoline (14). A solution of 13 (16.45 g, 47.0 mmol) in Et_2O (100 mL) was cooled in an ice bath under Ar. n-BuLi (1.58 N in hexane, 33 mL, 52.1 mmol) was added dropwise during 10 min. The mixture was stirred at 0 °C for 1 h and then at rt for 1 h. The resulting red clear solution was added dropwise to a solution of $ZnCl_2$ (7.23 g, 53.1 mmol) in THF (100 mL) during 6 min at 0 °C and stirred at rt for 1 h. This mixture (yellow suspension) was added to a suspension of 10 (7.01 g, 18.6 mmol) and $NiCl_2(PPh_3)_2$ (1.89 g, 2.89 mmol) during 18 min, and then the whole was heated at reflux for 17 h. After cooling to rt, the reaction mixture was partitioned between benzene (500 mL) and saturated aqueous $NaHCO_3$ and filtered to remove undissolved materials. The organic layer was washed with brine, dried over K_2CO_3, and evaporated to give a pale-yellow amorphous solid (26.09 g), which was purified by silica gel column chromatography (AcOEt–hexane) to give 14 (8.41 g, 49%) as a white solid: mp 209 °C (CH_2Cl_2–hexane (1/4)); ^1H NMR ($CDCl_3$, TMS, 270 MHz) δ 2.60 (3H, s), 2.68 (12H, s), 4.49 (8H, s), 7.26 (1H, d, J = 8.3 Hz), 7.30 (4H, t, J = 7.3 Hz), 7.39 (2H, s), 7.40 (8H, t, J = 7.3 Hz), 7.53 (1H, t, J = 7.6 Hz), 7.61 (8H, d, J = 7.9 Hz), 7.75 (1H, d, J = 6.9 Hz), 7.78 (1H, d, J = 7.6 Hz), 7.91 (1H, t, J = 1.7 Hz), 7.99 (2H, d, J = 1.7 Hz), 8.06 (1H, d, J = 8.6 Hz); ^{13}C NMR ($CDCl_3$, TMS, 67.8 MHz) δ 25.3, 56.9, 99.0, 121.8, 125.3, 126.9,

127.3, 128.1, 129.9, 130.4, 131.7, 132.8, 132.8, 132.9, 133.6, 136.0, 138.9, 139.7, 139.9, 152.1, 158.5 (three carbon signals are under other signals); IR (KBr) 1590, 1450, 1430, 1150 cm^{-1}. Anal. Calcd for $C_{60}H_{53}NO_8$: C, 78.67; H, 5.83; N, 1.53. Found: C, 78.42; H, 5.88; N, 1.60.

8-[3,5-Bis(2,6-dihydroxy-3,5-diphenylphenyl)phenyl]-2-methylquinoline (1). A solution of HCl in MeOH (35%, 50 mL) was added to a solution of 14 (7.61 g, 8.31 mmol) in CH_2Cl_2 (100 mL). After being stirred at rt for 3 h, the reaction mixture was evaporated to give a yellow solid. To this were added CH_2Cl_2 (400 mL), saturated aqueous $NaHCO_3$ (100 mL), and water (100 mL), and the whole was stirred for 15 min. The aqueous layer was extracted with CH_2Cl_2 (100 mL). The combined organic extracts were washed with brine, dried over $MgSO_4$, and evaporated to give a pale-green solid (6.08 g), which was recrystallized from $CHCl_3$–hexane (1/2) to give 1 (5.38 g, 88%) as a white powder: mp 197.5–200 °C; ^1H NMR ($CDCl_3$, TMS, 270 MHz) δ 2.71 (3H, s), 5.86 (4H, s), 7.30–7.36 (5H, m), 7.44 (8H, t, J = 7.3 Hz), 7.55 (1H, t, J = 7.3 Hz), 7.59 (8H, d, J = 7.3 Hz), 7.81 (1H, d, J = 7.3 Hz), 7.82 (1H, t, J = 1.7 Hz), 7.88 (1H, d, J = 7.3 Hz), 8.01 (2H, d, J = 1.7 Hz), 8.09 (1H, d, J = 8.6 Hz); ^{13}C NMR ($CDCl_3$, TMS, 67.8 MHz) δ 25.1, 115.6, 121.2, 122.4, 125.5, 127.0, 127.9, 128.6, 129.1, 129.3, 129.8, 131.6, 133.2, 133.3, 133.4, 136.9, 137.8, 138.7, 142.0, 145.4, 150.2, 159.4; IR (KBr) 3510, 1600, 1465, 1165, 1150 cm^{-1}; MS m/z 739 (M^+). Anal. Calcd for $C_{52}H_{37}NO_4$: C, 84.42; H, 5.04; N, 1.89. Found: C, 84.15; H, 4.94; N, 2.19.

8-[3,5-Bis[2-(methoxymethoxy)-3-phenylphenyl]phenyl]-2-methylquinoline (16). A solution of 15 (3.07 g, 14.3 mmol) in THF (15 mL) was cooled in an ice bath under Ar. n-BuLi (1.58 N in hexane, 10 mL, 15.8 mmol) was added dropwise during 4 min. The reaction mixture was stirred at 0 °C for 30 min and then at rt for 1 h. The resulting pale-brown suspension was added to a solution of $ZnCl_2$ (2.16 g, 15.9 mmol) in THF (20 mL) at 0 °C, and the whole was stirred at rt for 1 h. The resulting pale yellow suspension was added to a suspension of 10 (2.16 g, 5.73 mmol) and $NiCl_2(PPh_3)_2$ (0.33 g, 0.50 mmol) in THF (80 mL), and the whole was heated at reflux for 23 h. Saturated aqueous $NaHCO_3$ (20 mL) and benzene (40 mL) were added at rt and filtered to remove undissolved materials. The organic layer was washed with brine, dried over K_2CO_3, and evaporated to give an orange oil (6.27 g), which was purified by silica gel column chromatography (AcOEt–hexane) to give 16 (3.65 g, 99%) as a white powder: mp 156–158 °C (CH_2Cl_2–hexane (1/4)); ^1H NMR ($CDCl_3$, TMS, 270 MHz) δ 2.68 (3H, s), 2.72 (6H, s), 4.52 (4H, s), 7.25–7.38 (7H, m), 7.43 (4H, t, J = 7.3 Hz), 7.50 (2H, dd, J = 7.6, 2.0 Hz), 7.57 (1H, d, J = 7.6 Hz), 7.63 (4H, d, J = 7.3 Hz), 7.80 (1H, d, J = 6.6 Hz), 7.90 (1H, t, J = 1.7 Hz), 7.98 (2H, d, J = 1.7 Hz), 8.09 (1H, d, J = 8.3 Hz); ^{13}C NMR ($CDCl_3$, TMS, 67.8 MHz) δ 27.0, 58.1, 100.6, 123.3, 126.0, 126.8, 128.4, 128.6, 128.8, 129.6, 131.1, 131.3, 131.6, 132.1, 132.5, 137.7, 137.8, 137.9, 139.7, 140.6, 141.2, 141.3, 147.0, 153.5, 160.1 (one carbon signal is superimposed); IR (KBr) 1155, 1070 cm^{-1}; MS m/z 644 (M^+ + 1), 638 ($M^+ - CH_3$). Anal. Calcd for $C_{44}H_{37}NO_4$: C, 82.09; H, 5.79; N, 2.18. Found: C, 81.82; H, 5.83; N, 2.44.

8-[3,5-Bis(2-hydroxy-3-phenylphenyl)phenyl]-2-methylquinoline (2). A solution of HCl in MeOH (33%, 20 mL) was added to a solution of 16 (3.21 g, 4.99 mmol) in CH_2Cl_2 (20 mL). After being stirred at rt for 1 h, the reaction mixture was evaporated. CH_2Cl_2 (30 mL) and saturated aqueous $NaHCO_3$ (30 mL) were added to the residue, and the aqueous layer was extracted with CH_2Cl_2 (10 mL × 2). The combined organic extracts were washed with brine, dried over $MgSO_4$, and evaporated to give a white solid (3.06 g), which was recrystallized from CH_2Cl_2–hexane (1/4) to give 2 (2.26 g, 82%) as a white powder: mp 221–222 °C; ^1H NMR ($CDCl_3$, TMS, 270 MHz) δ 2.72 (3H, s), 6.13 (2H, s), 7.08 (2H, t, J = 7.6 Hz), 7.32 (2H, dd J = 7.6 and 2.0 Hz), 7.34–7.49 (5H, m), 7.47 (4H, t, J = 7.3 Hz), 7.55 (1H, t, J = 7.6 Hz), 7.61 (4H, d, J = 6.9 Hz), 7.79–7.82 (2H, m), 7.86 (1H, dd, J = 6.9 and 1.3 Hz), 7.99 (2H, d, J = 1.6 Hz), 8.10 (1H, d, J = 8.6 Hz); ^{13}C NMR ($CDCl_3$, TMS, 67.8 MHz) δ 25.5, 120.6, 122.2, 125.4, 127.0, 127.4, 127.8, 128.4, 128.6, 128.9, 129.2, 129.5, 129.7, 130.0, 130.2, 130.7, 136.5, 137.7, 137.9, 138.7, 140.3, 145.3, 149.8, 159.4; IR (KBr) 3520, 1590, 1500, 1215 cm^{-1}; MS m/z 555 (M^+). Anal. Calcd for $C_{40}H_{29}NO_2$: C, 86.46; H, 5.26; N, 2.52. Found: C, 86.22; H, 5.21; N, 2.77.

1,3,5-Tris[2-(methoxymethoxy)phenyl]benzene (18). n-BuLi (1.64 N in hexane, 44 mL 72.2 mmol) was added dropwise to a solution of (methoxymethoxy)benzene (17, 10.01 g, 72.5 mmol) in Et_2O (100 mL) during 7 min at rt. The mixture was stirred for 2 h. The resulting pale-yellow suspension was added dropwise to a solution of $ZnCl_2$ (9.90 g, 72.6 mmol) in THF (40 mL) during 7 min and stirred for 1 h. This mixture was added to a suspension of 1,3,5-tribromobenzene (5.09 g, 16.2 mmol) and $NiCl_2(PPh_3)_2$ (0.87 g, 1.33 mmol) during 15 min, and then the whole was heated at reflux overnight. After cooling to rt, the reaction mixture was partitioned between benzene (200 mL) and 10% NaOH (100 mL). The aqueous layer was extracted with benzene, and the combined organic extracts were washed with brine, dried over $MgSO_4$, and evaporated to give a colorless solid and an orange oil (11.76 g), which was purified by recrystallization from benzene–hexane (1/4) to give 18 (4.55 g) as colorless plates. The mother liquor was evaporated, and the residue was purified by silica gel column chromatography (AcOEt–hexane) to give 18 (1.91 g, total 82%): mp 112 °C; ^1H NMR ($CDCl_3$, TMS, 270 MHz) δ 3.39 (9H, s), 5.15 (6H, s), 7.11 (3H, t, J = 7.3 Hz), 7.22–7.34 (6H, m), 7.43 (3H, dd, J = 7.6, 1.7 Hz), 7.69 (3H, s); ^{13}C NMR ($CDCl_3$, TMS, 67.8 MHz) δ 56.0, 95.3, 116.1, 122.4, 128.6, 129.4, 131.1, 132.1, 137.8, 154.4; IR (KBr) 1590, 1485, 1235, 1190, 1145, 1115, 1070 cm^{-1}; MS m/z 486 (M^+). Anal. Calcd for $C_{30}H_{30}O_6$: C, 74.06; H, 6.21. Found: C, 74.36; H, 6.26.

1,3,5-Tris(2-hydroxyphenyl)benzene (6). A solution of 18 (4.13 g, 8.49 mmol) in 30% HCl–MeOH (10 mL) and THF (10 mL) was stirred for 10 min. The solution was evaporated to give a white solid (3.09 g), which was recrystallized from benzene–hexane (2/1) to give 6 (2.35 g, 78%) as colorless fine needles: mp 188–189 °C; ^1H NMR ($CDCl_3$, TMS, 400 MHz) δ 5.46 (3H, brs), 6.96 (3H, dd, J = 8.1, 1.1 Hz), 7.01 (3H, td, J = 7.7, 1.1 Hz), 7.26 (3H, td, J = 8.1, 1.8 Hz), 7.33 (3H, dd, J = 7.7, 1.8 Hz), 7.64 (3H, s); ^{13}C NMR ($CDCl_3$, TMS, 100 MHz) δ 116.2, 121.2, 127.5, 129.0, 129.4, 130.4, 138.8, 152.5; IR (KBr) 3320, 1590, 1485, 1450, 1280, 1215, 1175, 1100 cm^{-1}; MS m/z 354 (M^+). Anal. Calcd for $C_{24}H_{18}O_3$: C, 81.34; H, 5.12. Found: C, 81.28; H, 5.17.

8-Bromo-2-methyl-5-nitroquinoline (19). In an ice bath, fuming HNO_3 (d 1.50, 20 mL) was added dropwise to a solution of 8 (12.54 g, 56.5 mmol) in fuming H_2SO_4 (30%, 30 mL) during 10 min. The reaction mixture was allowed to stand for 1.5 h. With stirring, 10% NaOH (500 mL) was added dropwise during 40 min, and then NaOH pellets were added until pH > 11. The resulting precipitate was filtered off, washed with water, and dried *in vacuo* to give a pale-orange powder (16.32 g), which was recrystallized from MeOH to give 19 (9.86 g, 65%) as pale orange needles: mp 97–99 °C; ^1H NMR ($CDCl_3$, TMS, 270 MHz) δ 2.86 (3H, s), 7.57 (1H, d, J = 8.9 Hz), 8.12 (1H, d, J = 8.3 Hz), 8.16 (1H, d, J = 8.3 Hz), 8.90 (1H, d, J = 8.9 Hz); ^{13}C NMR ($CDCl_3$, TMS, 67.8 MHz) δ 25.5, 120.4, 123.6, 125.7, 131.2, 132.3, 132.7, 144.8, 145.0, 161.8; IR (KBr) 1600, 1510, 1350 cm^{-1}; MS m/z 268 and 266 (M^+), 222 and 220 ($M^+ - NO_2$). Anal. Calcd for $C_{10}H_7BrN_2O_2$: C, 44.97; H, 2.64; N, 10.49. Found: C, 44.77; H, 2.60; N, 10.19.

8-(3,5-Dibromophenyl)-2-methyl-5-nitroquinoline (21). $Pd(PPh_3)_4$ (65 mg, 0.056 mmol) and 2 M aqueous Na_2CO_3 (1.3 mL) were added to a solution of 19 (421 mg, 1.58 mmol) and 20 (368 mg, 1.32 mmol) in toluene (10 mL) and EtOH (1 mL) under Ar. The mixture was heated at reflux for 14 h and then cooled to rt. Benzene (30 mL) and water (10 mL) were added, and the organic layer was washed with water and then brine, dried over K_2CO_3, and evaporated to give a pale-yellow solid (0.71 g), which was purified by silica gel column chromatography (benzene–hexane) to give 21 (464 mg, 83%) as a pale-yellow solid: mp 208–210 °C (CH_3CN–CH_2Cl_2 (6/1)); ^1H NMR ($CDCl_3$, TMS, 270 MHz) δ 2.74 (3H, s), 7.55 (1H, d, J = 8.9 Hz), 7.76 (1H, d, J = 7.9 Hz), 7.76 (1H, t, J = 2.0 Hz), 7.81 (2H, d, J = 2.0 Hz), 8.33 (1H, d, J = 7.9 Hz), 8.92 (1H, d, J = 8.9 Hz); ^{13}C NMR ($CDCl_3$, TMS, 67.8 MHz) δ 25.4, 119.9, 122.3, 123.0, 124.8, 128.1, 131.9, 132.6, 133.5, 141.3, 143.5, 145.1, 145.3, 160.7; IR (KBr) 1600, 1580, 1545, 1500, 1340 cm^{-1}; MS m/z 422 (M^+), 343 and 341 ($M^+ - Br$) 297 and 295 ($M^+ - Br - NO_2$). Anal. Calcd for $C_{16}H_{10}Br_2N_2O_2$: C, 45.53; H, 2.39; N, 6.64. Found: C, 45.52; H, 2.35; N, 6.38.

8-[3,5-Bis(2-hydroxy-3-phenylphenyl)phenyl]-2-methyl-5-nitroquinoline (23). $Pd(PPh_3)_4$ (0.13 g, 0.112 mmol) and 2 M aqueous Na_2CO_3 (24 mL) were added to a solution of 22 (6.04

g, 23.4 mmol) and **21** (3.95 g, 9.36 mmol) in toluene (120 mL) and EtOH (10 mL) under Ar. The mixture was heated at reflux for 17 h and then cooled to rt. Benzene (100 mL) and water (50 mL) were added, the organic layer was washed with brine, dried over K_2CO_3, and evaporated to give a pale-brown amorphous solid (7.91 g), which was dissolved in THF (20 mL), and concd HCl (20 mL) was added with cooling in an ice bath. After 30 min, the reaction mixture was partitioned between AcOEt (200 mL) and water (200 mL). The organic layer was washed with water (until the aqueous layer became neutral) and brine, dried over $MgSO_4$, and evaporated to give a yellow amorphous solid (7.23 g), which was purified by silica gel column chromatography (Et_2O–benzene–hexane) and then by recrystallization from benzene–hexane (8/5) to give **23** (4.29 g, 76%) as yellow fine needles: mp 151–156 °C; ^1H NMR ($CDCl_3$, TMS, 270 MHz) δ 2.76 (3H, s), 5.99 (2H, brs), 7.09 (2H, t, J = 7.6 Hz), 7.32 (2H, dd, J = 8.2, 1.7 Hz), 7.36–7.60 (5H, m), 7.47 (4H, t, J = 7.3 Hz), 7.58 (4H, d, J = 7.3 Hz), 7.89 (1H, s), 7.92 (1H, d, J = 8.3 Hz), 8.36 (1H, d, J = 8.3 Hz), 8.97 (1H, d, J = 8.9 Hz); ^{13}C NMR ($CDCl_3$, TMS, 67.8 MHz) δ 25.4, 120.2, 120.8, 123.4, 124.8, 127.6, 128.1, 128.2, 128.8, 129.0, 129.4, 129.8, 130.3, 130.4, 130.9, 132.1, 137.6, 137.9, 138.7, 144.9, 145.4, 145.9, 149.7, 160.7; IR (KBr) 3400, 1600, 1515, 1500, 1330, 1215, 1165 cm^{-1}; MS m/z 600 (M^+). Anal. Calcd for $C_{40}H_{28}N_2O_4$: C, 79.98; H, 4.70; N, 4.66. Found: C, 79.69; H, 4.71; N, 4.48.

5-(Dimethylamino)-8-[3,5-Bis(2-hydroxy-3-phenylphenyl)-phenyl]-2-methylquinoline (3). A suspension of Pd/C (10%, 0.54 g) in EtOH (10 mL) was added to a suspension of **23** (4.29 g, 7.14 mmol) in AcOEt (50 mL) and EtOH (50 mL), and the mixture was stirred under H_2. After 2 h, the suspension was filtered and evaporated to give an orange solid (4.76 g). This was dissolved in CH_3CN (100 mL), and formalin (37%, 6 mL) and $NaBH_3CN$ (1.48 g, 23.6 mmol) were added. AcOH (0.75 mL) was added dropwise during 4 min. After 2 h, AcOH (0.75 mL) was added and the reaction mixture was stirred for 30 min. This was partitioned between benzene (400 mL) and saturated $NaHCO_3$ (100 mL), and the organic layer was washed with water and brine, dried over $MgSO_4$, and evaporated to give an orange amorphous solid (4.83 g), which was purified by column chromatography (Al_2O_3, AcOEt–benzene) and then by recrystallization from CH_2Cl_2–MeOH (1/1) to give **3**·$(MeOH)_2$ (3.23 g, 69%) as fine yellow prisms: mp 120–180 °C. Anal. Calcd for $C_{42}H_{34}N_2O_2 \cdot C_2H_6O_2$: C, 79.73; H, 6.39; N, 4.23. Found: C, 79.92; H, 6.31; N, 4.50. MeOH molecules in the crystal of **3**·$(MeOH)_2$ were azeotropically removed with benzene to give **3** as a yellow powder: mp 120–130 °C; ^1H NMR ($CDCl_3$, TMS, 270 MHz) δ 2.69 (3H, s), 2.92 (6H, s), 6.11 (2H, s), 7.07 (2H, t, J = 7.6 Hz), 7.10 (1H, d, J = 7.9 Hz), 7.307.49 (7H, m), 7.46 (4H, t, J = 7.6 Hz), 7.61 (4H, d, J = 7.6 Hz), 7.74 (1H, s), 7.75 (1H, d, J = 8.9 Hz), 7.96 (2H, d, J = 1.7 Hz), 8.47 (1H, d, J = 8.9 Hz); ^{13}C NMR ($CDCl_3$, TMS, 67.8 MHz) δ 25.2, 45.2, 113.2, 120.5, 120.9, 122.2, 127.3, 128.5, 128.6, 128.8, 128.9, 129.5, 129.6, 129.8, 130.2, 130.7, 133.2, 133.2, 137.6, 138.0, 140.8, 146.5; IR (KBr) 3520, 1600, 1580, 1450, 1330, 1220, 1165, 1030 cm^{-1}; MS m/z 598 (M^+). Anal. Calcd for $C_{42}H_{34}N_2O_2$: C, 84.25; H, 5.72; N, 4.68. Found: C, 83.98; H, 5.69; N, 4.95.

8-(3,5-Diphenylphenyl)-2-methyl-5-nitroquinoline (24). $Pd(PPh_3)_4$ (0.08 g, 0.069 mmol) and 2 M aqueous Na_2CO_3 (6.5 mL) were added to a solution of **21** (1.00 g, 2.37 mmol) and phenylboronic acid (0.79 g, 6.48 mmol) in toluene (30 mL) and EtOH (3 mL) under Ar. The mixture was heated at reflux for 21 h and then cooled to rt. Benzene (30 mL) and water (20 mL) were added, and the organic layer was washed with brine, dried over K_2CO_3, and evaporated to give a pale-brown amorphous solid (1.02 g), which was purified by silica gel column chromatography (benzene–hexane) and then by recrystallization from AcOEt–EtOH (1/1) to give **24** (0.76 g, 77%) as fine yellow needles: mp 150–152 °C; ^1H NMR ($CDCl_3$, TMS, 270 MHz) δ 2.77 (3H, s), 7.39 (2H, t, J = 6.9 Hz), 7.49 (4H, t, J = 6.9 Hz), 7.55 (1H, d, J = 8.9 Hz), 7.73 (4H, d, J = 6.9 Hz), 7.90 (1H, t, J = 1.7 Hz), 7.91 (1H, d, J = 8.3 Hz), 7.97 (2H, d, J = 1.7 Hz), 8.38 (1H, d, J = 8.3 Hz), 8.98 (1H, d, J = 8.9 Hz); ^{13}C NMR ($CDCl_3$, TMS, 67.8 MHz) δ 25.7, 120.2, 123.4, 124.6, 126.2, 127.4, 127.5, 128.3, 128.9, 129.0, 130.0, 138.8, 141.1, 141.5, 144.7, 145.5, 146.6, 160.2; IR (KBr) 1590, 1510, 1500, 1355, 1335 cm^{-1}; MS m/z 416 (M^+). Anal. Calcd for $C_{28}H_{20}N_2O_2$: C, 80.75; H, 4.84; N, 6.73. Found: C, 80.48; H, 4.86; N, 6.74.

5-(Dimethylamino)-8-(3,5-diphenylphenyl)-2-methylquinoline (5). A suspension of Pd/C (10%, 58 mg) in EtOH (2 mL) was added to a suspension of **24** (585 mg, 1.40 mmol) in EtOH (15 mL), and the mixture was stirred under H_2. After 2 h, the suspension was filtered and evaporated to give a yellow amorphous solid (0.64 g). This was suspended in CH_3CN (15 mL), and formalin (37%, 1.1 mL) and $NaBH_3CN$ (273 mg, 4.34 mmol) were added. AcOH (0.14 mL) was added dropwise during 3 min. After 3 h, AcOH (0.14 mL) was added and the reaction mixture was stirred for 1 h. This was partitioned between benzene (50 mL) and 10% NaOH (15 mL), and the organic layer was washed with brine, dried over K_2CO_3, and evaporated to give a yellow amorphous solid (0.75 g), which was purified by column chromatography (Al_2O_3, benzene–hexane) to give **5** (429 mg, 74%) as a pale yellow amorphous solid: mp 64–79 °C; ^1H NMR ($CDCl_3$, TMS, 270 MHz) δ 2.73 (3H, s), 2.94 (6H, s), 7.13 (1H, d, J = 7.9 Hz), 7.31 (1H, d, J = 8.6 Hz), 7.36 (2H, tt, J = 7.6, 1.3 Hz), 7.47 (4H, tt, J = 7.6, 1.3 Hz), 7.75 (4H, dd, J = 7.6, 1.3 Hz), 7.80 (1H, t, J = 1.7 Hz), 8.01 (2H, d, J = 1.7 Hz), 8.50 (1H, d, J = 8.6 Hz); ^{13}C NMR ($CDCl_3$, TMS, 67.8 MHz) δ 25.7, 45.2, 113.3, 120.6, 122.1, 124.5, 127.1, 127.4, 128.7, 129.0, 130.1, 132.9, 134.0, 140.6, 141.1, 141.7, 146.5, 150.7, 158.3; IR (KBr) 1580, 1455, 1330 cm^{-1}; MS m/z 414 (M^+). Anal. Calcd for $C_{30}H_{26}N_2$: C, 86.92; H, 6.32; N, 6.76. Found: C, 86.77; H, 6.59; N, 6.58.

^1H NMR Titrations.[29] In the case of salt formaiton in DMSO-d_6, [receptor] = 5.0 mM, [TsOH] = 1.8–20 mM. For MPP in $CDCl_3$, [receptor] = 0.32–5.0 mM, [MPP] = 1.0 mM.

Typically, a 5.0 mM DMSO-d_6 solution of **1** was prepared, a 600-μL aliquot was transferred to an NMR tube, and a spectrum was recorded. Ten aliquots of a DMSO-d_6 solution of TsOH (55 mM) and **1** (5.0 mM) were added, and a spectrum was recorded after each addition. The chemical shift of the 2-Me signal was recorded after each addition. The salt-formation constant was calculated by a nonlinear least-squares fitting.

(29) Tjivikua, T.; Deslongchamps, G.; Rebek, J., Jr. *J. Am. Chem. Soc.* **1990**, *112*, 8408.