

## Guanidinium Ion as a Guest During and After Formation of 27-Crown-9 Polyether Hosts

By KHORSHED MADAN and DONALD J. CRAM\*

(Department of Chemistry, University of California at Los Angeles, Los Angeles, California 90024)

**Summary** Macrocyclic ethers containing nine oxygen atoms complex guanidinium tetraphenylborate or hexafluorophosphate, and formation of the cycles is aided by guanidinium as compared to tetramethylguanidinium ion.

COREY-PAULING-KOLTUN (CPK) molecular models of guanidinium ion complexed by six hydrogen bonds to 27-crown-9 as a host produces a wreath-like structure with a nearly perfect, complementary host-guest relationship. Consequently, guanidinium ion was examined for its ability to act as a template in the formation of benzo-27-crown-9 polyethers (*e.g.* **1**), and to complex the ethers once formed (*e.g.* **2**).

Octaethyleneglycol<sup>1</sup> ditosylate† (oil; 1 mmol) in tetrahydrofuran (THF) (10 ml) was added to a solution of catechol (1 mmol) in THF (32.5 ml) and KOBu<sup>t</sup> (2.2 mmol) in Bu<sup>t</sup>OH (2.5 ml) stirred under dry nitrogen, and the mixture was heated at reflux for 24 h. A further 1.1 mmol of base was added, and after 12 h of additional reflux, (**3**)‡ (m.p. 69–70 °C) was isolated by extraction, chromatography, distillation, and crystallization. The yield (59%) in this run (i) and in those of runs (ii) and (iii) was obtained by g.l.c. on a 1ft by 3/8 in SE-30 on Chromosorb W column at 275 °C (helium as carrier gas) with binaphtho-17-crown-5<sup>2</sup> as internal standard.§ In run (ii), 7.2 mmol of guanidine and 2.3 mmol of ditosylate produced 23% of (**3**). In run (iii) 8.8 mmol of tetramethylguanidine and 2.0 mmol of ditosylate gave 2% of (**3**) after 85 h at reflux. These

results indicate the following order of ability, K<sup>+</sup> > guanidinium ion > tetramethylguanidinium ion in bringing together the reacting ends of the intermediate that leads to (**3**). The templating properties of K<sup>+</sup> for preparing crown ethers is well established,<sup>3</sup> and the X-ray structure<sup>4</sup> of the KI complex of dibenzo-30-crown-10 indicates the cycle wraps about K<sup>+</sup> in a tennis-ball-seam arrangement. Structure (**1**) as an important intermediate offers an attractive explanation for the factor of ten higher yield obtained with guanidine as compared with tetramethylguanidine as base.

TABLE. Dependence of yields of cyclic ethers on base in reaction of catechol with diethyleneglycol ditosylate

| Run   | Base                                    | Yields (%) of crown ethers§ |     |      |
|-------|---|-----------------------------|-----|------|
|       |   | (4)                         | (5) | (6)  |
| (iv)  | KOBu <sup>t</sup> .. ..                 | 5                           | 44  | 20   |
| (v)   | HN=C(NH <sub>2</sub> ) <sub>2</sub> ..  | 4                           | 25  | 11.3 |
| (vi)  | HN=C(NMe <sub>2</sub> ) <sub>2</sub> .. | 11                          | 6   | 0    |
| (vii) | Bu <sup>n</sup> <sub>4</sub> NOH .. ..  | 15                          | 23  | 5.5  |

In similar experiments, catechol and diethyleneglycol ditosylate were converted into mixtures of (**4**),<sup>3</sup> (**5**),<sup>3</sup> and (**6**)‡ (m.p. 94–95 °C), whose yields§ were determined by g.l.c.¶ (see Table). From (**7**)<sup>3</sup> and (**8**)<sup>3</sup> under the conditions of run (iv) (**6**) was isolated in 24% yield, whereas under those of run (v), the isolated yield was 15%. Runs (iv)–(vii) demonstrate the order K<sup>+</sup> > guanidinium ion > Bu<sup>n</sup><sub>4</sub>N<sup>+</sup> > tetramethylguanidinium ion in assembling the six molecules that produce (**6**), and the four molecules that

† Carbon and hydrogen analyses were within 0.30% of theory.

‡ The mass spectrum contained the molecular ion, and the <sup>1</sup>H n.m.r. spectrum in CDCl<sub>3</sub> was as expected.

§ Yields are based on catechol, and the reactions were run until none remained (t.l.c.).

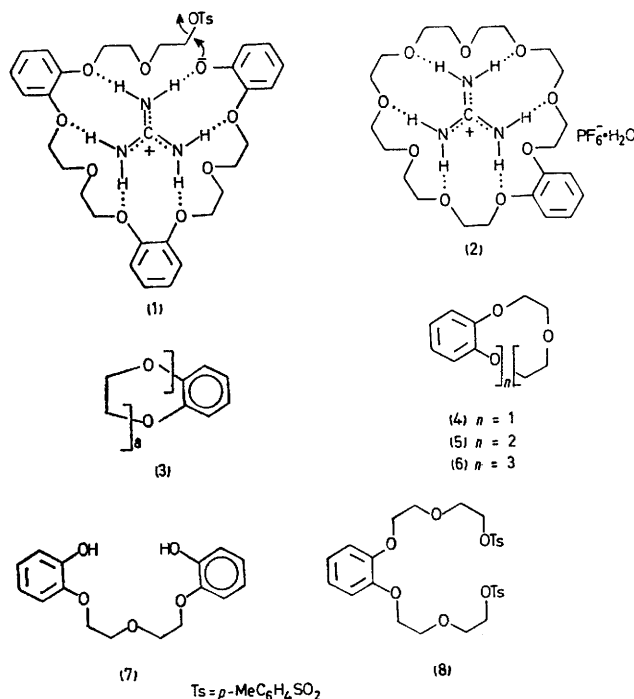
¶ To catechol (18.7 mmol) in THF (25 ml) and Bu<sup>t</sup>OH (25 ml) was added the appropriate base (13 mmol) in Bu<sup>t</sup>OH (50 ml). To the solution stirred at reflux under dry nitrogen was added ditosylate (9.4 mmol) in THF (50 ml). After 5 and after 12 h at reflux, similar additions of base and ditosylate to the solution were made. In runs (iv), (v), and (vii), after an additional 5 h of reflux, another equal addition of base was made, and the products were extracted after *ca.* 30 h reaction. In run (vi), three more additions of base (total of 77 mmol) and one of ditosylate (total of 32 mmol) were made, and the total reaction time was 104 h. Yields of products of runs (iv)–(vii) were analysed by g.l.c. (same column as for runs (i)–(iii)). For (**4**), benzophenone was the internal standard (140 °C column temperature), for (**5**), binaphtho-17-crown-5 (265 °C), and for (**6**), binaphtho-20-crown-6 (300 °C) was used (ref. 2).

give (5). The bimolecular reaction that produced (4) was favoured by the  $\text{Bu}^n\text{N}^+$  and tetramethylguanidinium ions more than by  $\text{K}^+$  or guanidinium ions. Again the ability of the guanidinium ion to favour the larger rings suggests the ion acts as a template during reaction, but again less effectively than  $\text{K}^+$ . Surprisingly the  $\text{Bu}^n\text{N}^+$  (point charge) gives much larger yields of the larger cycles than does the tetramethylguanidinium ion (dispersed charge). Cycles (3) and (6) are just large enough to encircle the nitrogen of  $\text{Bu}^n\text{N}^+$  (CPK models). Two butyl groups stick out from one side and two from the other side of the model complex. Use of  $\text{HCONMe}_2$  or  $\text{Me}_2\text{SO}$  as solvents with guanidine as base gave lower yields of (6) (7 and 3%, respectively) than  $\text{THF}-\text{Bu}^t\text{OH}$ . Treatment of 2,2'-dihydroxy-1,1'-binaphthyl with octaethyleneglycol ditosylate under the conditions of run (v) produced a 25% yield of binaphthyl-29-crown-9 (oil).††

Cycles (3), (5), and (6) in  $\text{CDCl}_3$  (0.12–0.06 M) solubilized by complexation ( $^1\text{H}$  n.m.r. spectral criteria) ca. 1 mol (per mol of host) of otherwise insoluble crystalline guanidinium tetraphenylborate (m.p. 170–172 °C).† The tosylate or thiocyanate salts failed to be solubilized. Extraction of a 0.5 M  $\text{LiPF}_6$  aqueous solution (pH adjusted to 5 with  $\text{LiOH}$ ), 0.5 M in guanidinium chloride, with a 0.08 M solution of (3) in  $\text{CDCl}_3$  gave an organic layer whose  $^1\text{H}$  n.m.r. spectrum indicated 0.84 mol of salt was extracted per mol of host. Concentration of the solution produced crystals, analysis† of which indicated them to be  $\text{C}_{22}\text{H}_{36}\text{O}_9 \cdot \text{CH}_6\text{N}_3\text{PF}_6 \cdot \text{H}_2\text{O}$  (dried 25 °C, desiccator), m.p. 130–140° (decomp.).

Probably the complex has structure (2). Extractions of 4 M  $\text{LiPF}_6$  aqueous solutions, 1.2 M in guanidinium chloride, with a 0.1 M solution of (5) or a 0.05 M solution of (6) in  $\text{CHCl}_3$  gave complexes that crystallized at the interface. Analyses (no chlorine present) indicated the complex of (5) to be  $(\text{C}_{20}\text{H}_{24}\text{O}_6)_2 \cdot (\text{CH}_6\text{N}_3\text{PF}_6)_3 \cdot (\text{H}_2\text{O})_3$  (dried at 78 °C, *in vacuo*), m.p. 150–200 °C (decomp.), and that of (6) to be  $(\text{C}_{30}\text{H}_{36}\text{O}_9)_2 \cdot (\text{CH}_6\text{N}_3\text{PF}_6)_3$  (dried at 25 °C, desiccator), m.p. 110 °C and upward (decomp.). Solutions of 5.5 M guanidinium thiocyanate in water when shaken with 0.08 M solutions of (3), (5), and (6) in  $\text{CDCl}_3$  extracted 0.97, <0.05 and <0.05 mol of salt respectively per mol of host ( $^1\text{H}$  n.m.r. spectral criteria). Thus (3) is the best host for the guanidinium ion, probably because of the number, location and basicity of its oxygens. Extraction of 0.57 M aqueous solutions of tetramethylguanidinium chloride, 0.57 M in  $\text{LiPF}_6$  at pH 5, with 0.08 M solutions in  $\text{CDCl}_3$  of (3), (5),

and (6) resulted in organic solutions whose molar ratios of salt to host ( $^1\text{H}$  n.m.r. spectral criteria) were 0.34, 0.19, and 0.12, respectively. Possibly the two hydrogen bond donating sites of the tetramethylguanidinium ion better complex the more rigidly arranged basic oxygen atoms (centred between benzene rings) of (5) and (6) than the less rigidly arranged basic oxygen atoms of (3).



The yields of hosts roughly correlate with the abilities of the hosts to complex the guanidinium salts. These results and others<sup>5</sup> indicate that CPK molecular model examination of complexes composed of organic hosts and guests provides a rational approach to designing host compounds to complex specific guests.

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