New ammonium carboxylate host compounds screened by combinatorial chemistry

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Seventeen new ammonium carboxylate host compounds were screened from a combinatorial library of one hundred ammonium carboxylates formed by mixing ten amines and ten carboxylic acids.

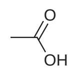
The combinatorial library approach has been widely used in the screening of drugs and biological receptors.[1] More recently, this method has been applied to searching for functional compounds in many fields, such as new synthetic reagents,[2,3] superconducting materials,[4] luminescent materials,[5] polymeric materials,[6] artificial molecular receptors,[7] and so on. However, there has been no application of combinatorial chemistry for screening lattice inclusion compounds.

Design of nanoporous materials using organic compounds is now one of the most interesting topics in organic solid-state chemistry.[8,9] However, it is difficult to design inclusion cavities *via* molecular structure. The most promising method for designing molecular cavities relies upon chemical modification of 'leading' compounds that have been found accidentally.[8] We report here seventeen new host compounds *via* application of combinatorial chemistry to finding lattice inclusion compounds.

Ten commercially available amines (**a–j**) and ten carboxylic acids (**1–10**) were used to form the combinatorial salt library. One hundred salts were prepared by mixing stock solutions of the two components in a 1:1 molar ratio. The resulting salt crystals were obtained by filtration or by removal of the solvents, and characterized by IR and ^{1}H NMR analysis. $\mathrm{Pr^iOH}$ was chosen as the trial guest due to the moderate solubility of the various salts in this solvent. All salts were subjected to recrystallization from $\mathrm{Pr^iOH}$, and the resulting crystals were characterized by ^{1}H NMR analysis and X-ray diffraction. Table 1 summarizes the clathrate formation results. Seventeen salts formed inclusion crystals with $\mathrm{Pr^iOH}$, fifty four salts yielded guest-free crystals only and twenty salts did not form crystalline materials at all. In some cases, single components crystallized from $\mathrm{Pr^iOH}$ solution. This result indicates that at least seventeen ammonium carboxylates have inclusion abilities. Testing other guest compounds will yield inclusion compounds with different compositions.

The salts of small carboxylic acids or small amines did not form inclusion compounds with $\mathrm{Pr^iOH}$. They formed guest-free crystals or failed to give crystalline materials. On the other hand, the salts of brucine (**j**) formed $\mathrm{Pr^iOH}$ clathrates. Its complex shell-like molecular structure with tertiary amino groups allows **j** to form molecular cavities in the crystalline state. The inclusion ability and the crystal structure of **3·j**, one of the seventeen host salts, were further investigated.

Complex **3·j** forms inclusion compounds with various organic solvents such as alcohols, ethers, ketones, aromatic esters and aromatic hydrocarbons. Table 2 summarizes the guest compounds and the host–guest ratios. Fig. 1 shows the crystal structure of **3·j** with $\mathrm{Pr^iOH}$ (1 : 1 : 1).§ The most striking structural feature is the one-dimensional corrugated monolayer structure of the conjugate anions of **3**, which has been observed in molecular complexes[10] or diastereomeric salts.[11] The conjugate cations of **j** bridge the monolayer *via* the salt bridge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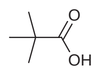
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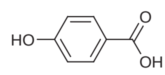
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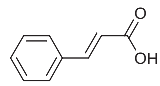
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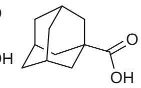
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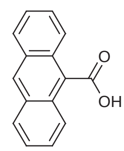
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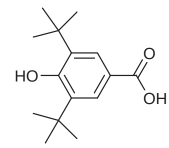
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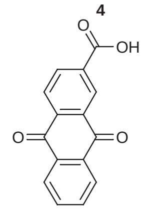
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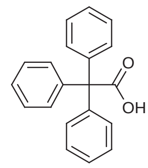
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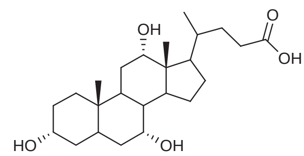
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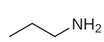
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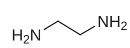
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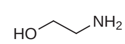
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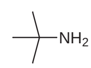
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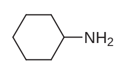
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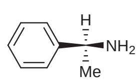
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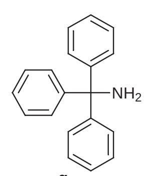
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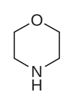
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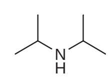
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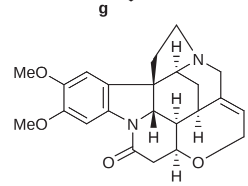
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Table 1 Formation of inclusion crystals of one hundred salts with $\mathrm{Pr^iOH}$[a]

	1	**2**	**3**	**4**	**5**	**6**	**7**	**8**	**9**	**10**
a	nc	nc	gf	nc	gf	gf	INC	gf	gf	gf
b	gf	acid	INC	gf	acid	gf	nc	nc	gf	gf
c	nc	nc	gf	gf	gf	nc	nc	gf	INC	gf
d	gf	gf	gf	gf	acid	INC	gf	INC	gf	INC
e	gf	gf	gf	gf	nc	INC	gf	gf	nc	nc
f	gf	gf	gf	gf	gf	gf	nc	gf	gf	gf
g	amine	amine	INC	nc	amine	INC	amine	gf	INC	amine
h	gf	nc	gf	gf	gf	INC	gf	gf	gf	gf
i	nc	nc	gf	acid	gf	gf	gf	gf	gf	nc
j	nc	nc	INC	INC	INC	gf	INC	INC	gf	INC

[a] INC = inclusion crystal, gf = guest-free crystal, nc = no crystallization, acid = crystal of acid only, amine = crystal of amine only

Table 2 Guest molecules of **3·j** and molar ratios of **3**, **j** and guest molecules in the inclusion crystals[a]

Guest molecule	Molar ratio	Guest molecule	Molar ratio
MeOH	2:2:3	acetone	2:2:1
EtOH	1:1:1	butan-2-one	1:1:1
Pr^nOH	1:1:1	MeOAc	1:1:1
Pr^iOH	1:1:1	MeCN	2:2:1
Bu^nOH	1:1:1	toluene	2:1:1
Bu^sOH	1:1:1	PhEt	2:1:1
Bu^tOH	1:1:1	*o*-xylene	2:1:1
$C_5H_{11}OH$	1:1:1	*m*-xylene	2:1:1
$PrMeCHCH_2OH$	1:1:2	*p*-xylene	2:2:1
$Pr^i(CH_2)_3OH$	1:1:2	$PhPr^n$	4:2:1
$Bu^t(CH_2)_2OH$	1:1:3	CH_2Cl_2	1:2:4
$MeOCH_2CHMeOH$	1:1:1	$ClCH_2CH_2Cl$	2:2:1
THF	1:1:1		

[a] Molar ratios determined by ^1H NMR analysis.

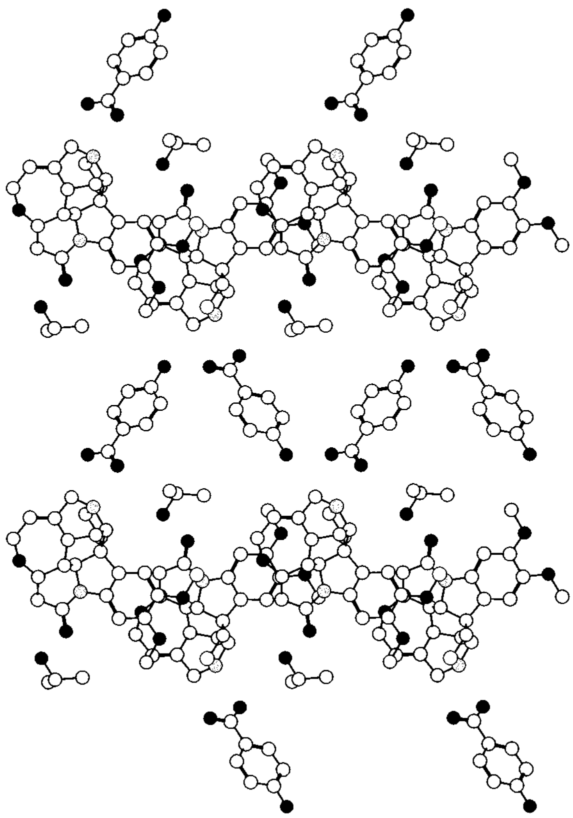

Fig. 1 X-Ray crystal structure of **3·j** with Pr^iOH (1 : 1 : 1)

and the hydrogen bond between them. The corrugated monolayer provides molecular channels that the guest alcohol is included in. The unique shell-like molecular shape of **j** yields the robust monolayer structure *via* van der Waals forces, and the monolayer motif enables **j** to form the Pr^iOH clathrates with various counter carboxylate anions.

In summary, we demonstrated the application of combinatorial chemistry to finding lattice inclusion compounds. Some ammonium carboxylates such as **3·j** form inclusion compounds with various organic compounds. Inclusion compounds of inorganic quaternary salts are already known.[12] However, ammonium carboxylates have been recognized as a source of host compounds.[13] Proper choice of amines and carboxylic acids provides us with various host compounds. Application to chiral recognition by enclathration of salt formation between chiral acid and achiral amines, achiral amine and chiral acid, or chiral acid and chiral amines, is now under investigation.

Notes and References

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§ *Crystal data* for **3·j**·Pr^iOH (1:1:1): $C_{23}H_{27}N_2O_4{\cdot}C_7H_5O_3{\cdot}C_3H_8O$ (592.69), orthorhombic, space group $P2_12_12_1$ (#19), a = 13.070(1), b = 18.901(2), c = 12.120(3) Å, V = 2994.2(6) Å^3, −55 °C, Z = 4, m = 0.94 cm^{-1}, 2140 independent reflections, R = 0.040. CCDC 182/931.

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