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Receptors for Carboxylates Derived from 2-Furoic and Fusaric Acids

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Abstract: New cleft type hydrogen bonding receptors have been prepared with a view to complexing carboxylates derived from 2-furoic and fusaric acids. An H-bond between these hosts and the heteroatom in the ring of the guest has been established. © 1997 Elsevier Science Ltd.

Anions play a very important role in biological and chemical processes[1] and hence, the synthesis of molecular receptors designed to associate anionic guests by means of non-covalent bonds is receiving increasing attention.[2] We have previously described receptors with a symmetrically substituted dichromenone urea structure, able to recognize carboxylate anions by means of four H-bonds.[3] A new receptor **A**, with a structure very close to these, has been synthesized; **A** is very soluble in chloroform and its proposed complex with carboxylate function is shown in figure 1.

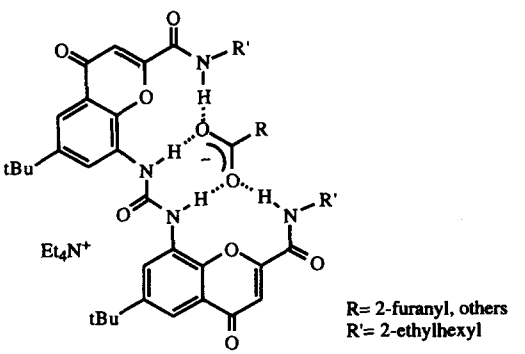
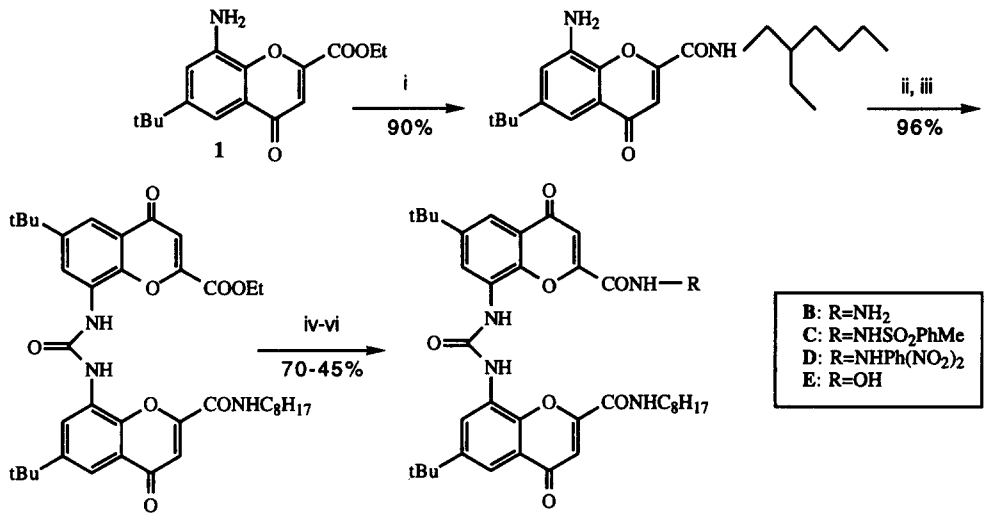


Figure 1: Proposed associate for receptor **A** with carboxylates.

We are interested in developing more specific receptors for complexing carboxylates derived from 2-furoic acid. As far as we know, there are no examples of these in the literature. The formation of an efficient linear 5th H-bond between the host and the oxygen in the furan ring could allow us to fix the position of the guest in the complex. This becomes very convenient for investigating certain types of catalytic activity with the receptors. With this aim, new non-symmetrically substituted receptors with a dichromenone urea structure were designed and built as binding partners for the carboxylate of 2-furoic acid. The convergent synthesis of these receptors, starting from the ethyl ester aminochromenone **1**[4] as the key building group, is shown in scheme 1.



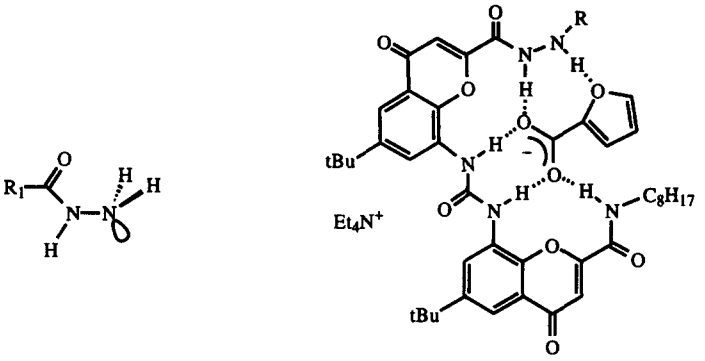
i= 2-ethylhexylamine; ii= $COCl_2$, toluene, THF; iii=**1**, THF; iv= KOH, EtOH; v=PCl_5, CH_2Cl_2; vi= (**B**): NH_2NH_2, CH_2Cl_2; (**C**): NH_2NHSO_2PhMe, CH_2Cl_2; (**D**): $NH_2NHPh(NO_2)_2$, CH_2Cl_2; (**E**): NH_3OHCl, pyridine, CH_2Cl_2

Scheme 1: Synthesis of receptors **B-E**.

The effect of the additional H-bond on the strength of the complex is measured by competitive titrations[5] with respect to receptor **A**, which lacks this H-bond.

Receptor **B**, bearing a hydrazide group, was prepared and proved to be sparingly soluble in chloroform. Competitive titration of **B** relative to **A** with the tetraethylammonium salt of the 2-furoic acid as guest afforded poor results (table 1). This is probably because the most stable conformation of hydrazides in solution is the one shown in figure 2,[6] which hinders cooperativity between this binding site in the receptors and the oxygen atom ring in the guest. Figure 2 also shows the proposed complex between **B** and that guest.

In order to increase the strength of the 5th H-bond, monosubstituted hydrazines with more acidic hydrogens were used to synthesize receptors **C** and **D**, the former as a tosylhydrazide derivative and the latter with a 2,4-dinitrophenylhydrazide group.[7] Preparation of these receptors was easily carried out, as shown in scheme 1. These new hosts promised higher association constants relative to **A**, but in both cases the results obtained previously were only slightly improved (table 1).



B: R=H; **C**: R=SO_2PhMe; **D**: R=$Ph(NO_2)_2$

Figure 2: Most stable conformation of hydrazides in solution. Proposed complexes between receptors **B**, **C**, and **D** and the tetraehtylammonium salt of 2-furoic acid.

A good solution was found with receptor **E**,[8] in which the high acidity of the hydrogen in its hydroxamic acid moiety[9] is able to improve by more than 30-fold the relative value of the association constants of this receptor with respect to **A** using the tetraethylammonium salt of 2-furoic acid as guest. This very good result was corroborated taking a more basic guest; namely, the tetraethylammonium salt of fusaric acid (5-butylpicolinic acid). In this case, the association led to a 600-fold increase in the constant over receptor **A** (table 1). Figure 3 shows the proposed complexes between the new receptor and both carboxylates derived from 2-furoic and fusaric acids.

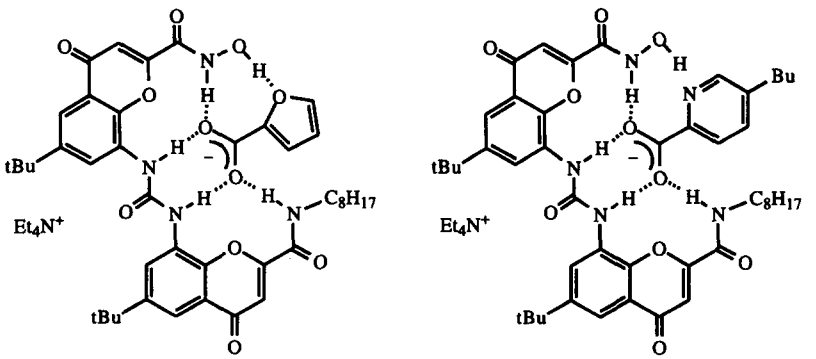


Figure 3: Proposed complexes between receptor **E** and the tetraethylammonium salts of 2-furoic acid and fusaric acid.

Table 1: Relationships between the association constants for receptors **B-E** relative to **A**, and the tetraethyl ammonium salts of 2-furoic and fusaric acids.

Receptor	Guest	K_{rel}	Solvent
B	2-furoic	3	$CDCl_3$/acetone-d_6 95:5
C	2-furoic	4	$CDCl_3$/acetone-d_6 95:5
D	2-furoic	5	$CDCl_3$/acetone-d_6 95:5
E	2-furoic	36	$CDCl_3$/methanol-d_4 99:1
E	fusaric	648	$CDCl_3$/methanol-d_4 99:1

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References and notes.

1. Beer, P. D., *J. Chem. Soc., Chem. Commun.* **1996**, 689.
2. Calnan, B. J.; Tidor, B.; Biancalana, S.; Hudson, D. and Frankel, A. D., *Science* **1991**, *252*, 1167.
3. Raposo, C.; Crego, M.; Mussons, M. L.; Caballero, M. C. and Morán, J. R., *Tetahedron Lett.* **1994**, *35*, 3409.
4. Raposo, C.; Pérez, N.; Almaraz, M.; Mussons, M. L.; Caballero, M. C. and Morán, J. R., *Tetrahedron Lett.* **1995**, *36*, 3255.
5. Competitive NMR titrations were carried out with 10^{-2} M solutions of both hosts in the solvent indicated. Increasing amounts of the corresponding guest were added until saturation was achieved. The proton shifts of both receptors were plotted against each other, and the ratios of the association constants were calculated making use of a Monte Carlo nonlinear curve-fitting method.
6. Lumbroso, H. and Barassin, J., *Bull. Soc. Chim. France* **1964**, 3190.
7. Cohen, S. G. and Nicholson, J., *J. Org. Chem.* **1965**, *30*, 1162.
8. Receptor **E**: mp=150°C; ^{1}H NMR (DMSO-d_6) δ=11.7 (1H, s, OH), 9.84 (1H, s, NH), 9.29 (2H, s, NHCONH), 8.70 (1H, d, *J* =2.2 Hz), 8.64 (1H, t, *J* =5.4 Hz, $NHCH_2$), 8.48 (1H, d, *J* =1.6 Hz), 7.71 (1H, d, *J* =2.2 Hz), 7.64 (1H, d, *J* =1.6 Hz), 6.87 (1H, s), 6.83 (1H, s), 3.24 (2H, m), 1.5-1.1 (9H, m), 1.35 (9H, s), 1.33 (9H, s), 0.9-0.6 (6H, m) ppm; MS (*m/z*) 675 $(M+H)^+$.
   All the new compounds show spectroscopic and analytical data in accordance with the proposed structures.
9. Bauer, L. and Exner, O., *Angew. Chem. Int. Ed. Engl.* **1974**, *13*, 376.

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