Pergamon

Tetrahedron Letters, Vol. 35, No. 20, pp. 3409-3410, 1994
Elsevier Science Ltd
Printed in Great Britain
0040-4039/94 $6.00+0.00

0040-4039(94)E0543-7

Readily Available Chromenone Receptors for Carboxylates

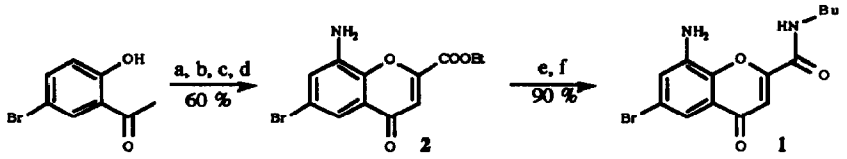
César Raposo, Mercedes Crego, Mª Luisa Mussons, Mª Cruz Caballero, J. R. Morán

Departamento de Química Orgánica, Universidad de Salamanca, Plaza de los Caidos 1-5, E-37008 Salamanca, Spain.

Abstract: *Several carboxylate group receptors able to bind syn and anti electron lone pairs have been prepared making use of an aminochromenone fragment. Symmetric ureas and sulfuryl amides permit the establishment of four linear hydrogen bonds with the carboxylate. The flat geometry of the sulfuryl amides complexes and the higher acidity of their hydrogens yield the best association constants.*

Several hydrogen bond carboxylate group receptors have recently been published[1]. Most such compounds, however, only make use of the syn lone pairs, and when anti lone pairs are used non linear hydrogen bonds are set[1].

An 8-amino-6-bromo-4-oxo-4*H*-chromene-2-carboxylic acid butylamide**1** fragment seems to be suitable in agreement with CPK models, for setting two linear hydrogen bonds simultaneously with the syn and anti non-bonding electrons of a carbonyl group. 8-amino-4-oxo-4*H*-chromene-2-carboxylic acid ethyl ester has already been described[2]; however, due to its ready availability we preferred the 6-bromo analog **2** (Scheme 1). Aminolysis of this compound with butylamine allows preparation of the desired fragment **1** in high yield.

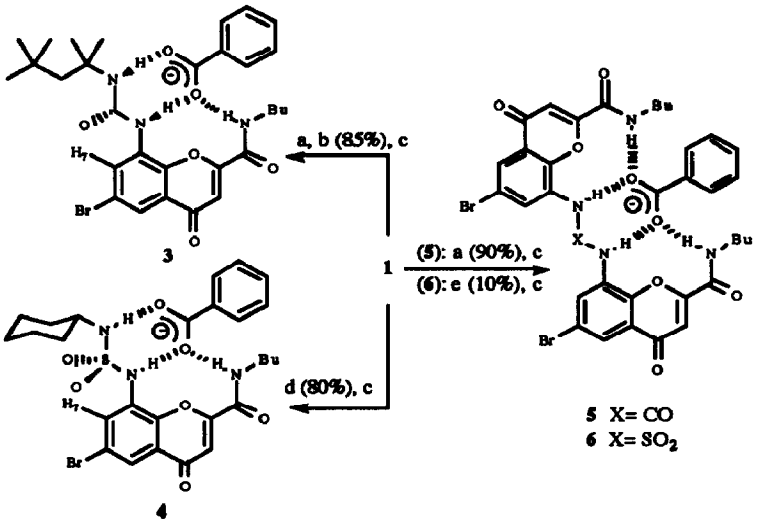


(a) HNO_3/ H_2SO_4; (b) Diethyl oxalate/ EtONa; (c) H_2SO_4; (d) $SnCl_2$/ HCl; (e) $BuNH_2$; (f) AcOH

Scheme 1

Ureas are known to be suitable to complex carboxylates through their syn lone pairs[3]. Combining the aminochromenone **1** with a urea function, it is possible to obtain receptor **3** (Scheme 2). The association constant of this receptor with tetraethylammonium benzoate[4] in DMSO (Ks=20 M^{-1}) is surprisingly small compared with other known urea associates[5]. CPK models reveal some steric interference between the benzoate aromatic ring and the receptor butyl substituent. Moreover, the urea function has to be twisted with respect to the chromenone ring due to the hindrance between the urea carbonyl and the chromenone H-7. This makes the cleft wider and prevents the formation of any linear hydrogen bonds. To overcome this drawback the sulfuryl amide **4** was prepared. The tetrahedral geometry of the sulfur atom allows the H-7 to be placed between the two sulfuryl oxygens, leaving the NH bond in the chromenone plane. The association constant of this receptor with tetraethylammonium benzoate in DMSO (Ks=3.3x10^2 M^{-1}) is, as expected, higher than for the preceding urea **3**. Probably, the better geometry combined with the higher acidity of the sulfuryl amide

hydrogen atoms accounts for its better binding properties. The high chloroform solubility of the sulfuryl amide **4** allows titration in this solvent. The association constant with tetraethylammonium benzoate is, however, over $K_s=10^5\ M^{-1}$ and cannot be easily measured.



(a) Phosgene; (b) *tert*-Octylamine; (c) Tetraethylammonium benzoate; (d) N-Cyclohexylsulfamoyl chloride/ Triethylamine; (e) Sulfuryl chloride/ Pyridine

Scheme 2

Receptor **5** combines two chromenone fragments with a urea function; it can set four linear hydrogen bonds with a carboxylate guest. Its association constant with the benzoate guest in DMSO ($K_s=1.5x10^4 M^{-1}$) is, as expected, higher than for the foregoing receptors.

Again, to prevent the twisted geometry of the urea receptors, the symmetric sulfuryl amide **6** was prepared. Despite the apparent stability of receptor **4**, compound **6** proved to be labile and was prepared only in a small 10% yield. From competitive titration in DMSO with the symmetric urea **5**, it is possible to evaluate its association constant as at least 10 times higher; therefore over $10^5\ M^{-1}$.

Acknowledgments: We thank the "Dirección General de Investigación Científica y Técnica" (DGICYT Grant PB 92-0286) for its support of this work. Two of us (M.C. and C.R.) also thank the MEC for a fellowship.

References and Notes

1. a) Schiessl, P.; Schmidtchen, F. P. *Tetrahedron Lett.* **1993**, *34*, 2449-2452. b) Hamann, B. C.; Branda, N. R.; Rebek, Jr. J. *Tetrahedron Lett.* **1993**, *34*, 6837-6840, and references cited therein.
2. Toda, M.; Arai, Y.; Miyamoto, T.; Eur. Pat. Appl. EP.173,516 **1986**, C.A. *105*, 172484, **1986**.
3. a) Smith, P. J.; Reddington, M. V.; Wilcox, C. S. *Tetrahedron Lett.* **1992**, *33*, 6085-6088. b) Etter, H. C.; Urbańczyk-Lipkowska, Z; Zia-Ebrahimi, M.; Panuto, T. W. *J. Am. Chem. Soc.* **1990**, *112*, 8415-8426.
4. Titrations were carried out at 20°C as proposed by P. Scmidtchen[1a], adding portions of a stock solution of the host to a guest solution, following the benzoate ortho proton signal by NMR, and making use of a software which accounts for the increasing dilution.
5. Fan, E.; Van Arman, S. A.; Kincaid, S.; Hamilton, A. D. *J. Am. Chem. Soc.* **1993**,*115*, 369-370

(*Received in UK* 23 *February* 1994; *accepted* 17 *March* 1994)