Tetrahedron 64 (2008) 6488–6493

Contents lists available at ScienceDirect

Tetrahedron

journal homepage: www.elsevier.com/locate/tet

Design of steroid-based imidazolium receptors for fluoride ion recognition

Mamta Chahar, Pramod S. Pandey *

Department of Chemistry, Indian Institute of Technology Delhi, Hauz Khas, New Delhi 110016, India

ARTICLE INFO

Article history:
Received 26 October 2007
Received in revised form 2 April 2008
Accepted 17 April 2008
Available online 22 April 2008

Keywords:
Deoxycholic acid
Fluoride recognition
Imidazolium receptors
Benzimidazolium receptors
Hydrogen bond

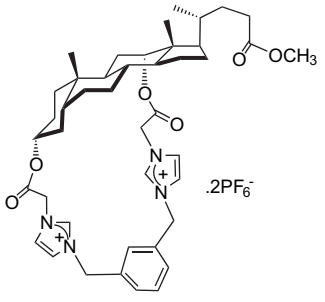
ABSTRACT

New deoxycholic acid-based cyclic receptors bearing imidazolium and benzimidazolium moieties bridged with *o*-xylelene and 1,8-dimethylenenaphthalene groups have been synthesized. Anion binding studies using ^{1}H NMR revealed that receptors having naphthalenic group as spacer exhibit very high selectivity for fluoride ion over other anions while receptors with *o*-xylelene group show a preference for the chloride ion.

1. Introduction

Anion recognition has attracted considerable interest in recent years in the area of supramolecular chemistry.[1] Among anions, the fluoride ion has received special attention as it is an essential ingredient in many drugs and a useful component of drinking water. It also plays a significant role in dental care and treatment of osteoporosis. An excess of fluoride, however, causes collagen breakdown, bone disorder (fluorosis), and also affects immune system and thyroid activity.[2] Hence, the design of sensors/receptors to detect fluoride ion in low concentration with high selectivity has always been an important area of analytical and supramolecular chemistry. This has led to the design of many receptors with amide, pyrrole, urea and benzimidazole groups, which bind the fluoride ion through N–H···F^- hydrogen-bond interaction.[3] Some 1,3-disubstituted imidazolium receptors developed by Kim and co-workers also show strong affinity for fluoride ion involving hydrogen-bonding interaction between imidazolium moieties and fluoride ion through (C–H)$^+$···F^- hydrogen bonds.[4]

Recently, the steroidal framework of bile acids has attracted much attention as a building block for the design of receptors for anion recognition.[5] Among them the molecular tweezers of Kim and co-workers based on hyodeoxycholic acid containing urea moieties as pendant show high selectivity towards fluoride ion over other anions.[3k] Maitra and co-workers have synthesized a cyclodimer derived from cholic acid, which binds fluoride ion with 1:2 stoichiometry.[6] Previously, we have reported a bile acid-based macrocyclic bisimidazolium receptor **1** with a *m*-xylene moiety as spacer, which binds anions through strong hydrogen-bond interactions involving the C(2)–H atoms of the imidazolium rings and inwardly directed methylene protons of acetyl units, and showed a moderate selectivity for fluoride ion over other halide ions (Fig. 1).[7] This prompted us to target tuning the cavity size of the receptor by varying the spacer group to get better fluoride-selective geometry. Thus, we synthesized deoxycholic acid-based imidazolium and benzimidazolium receptors bridged with *o*-xylelene and 1,8-dimethylenenaphthalene groups and assessed their binding capability for fluoride ion.

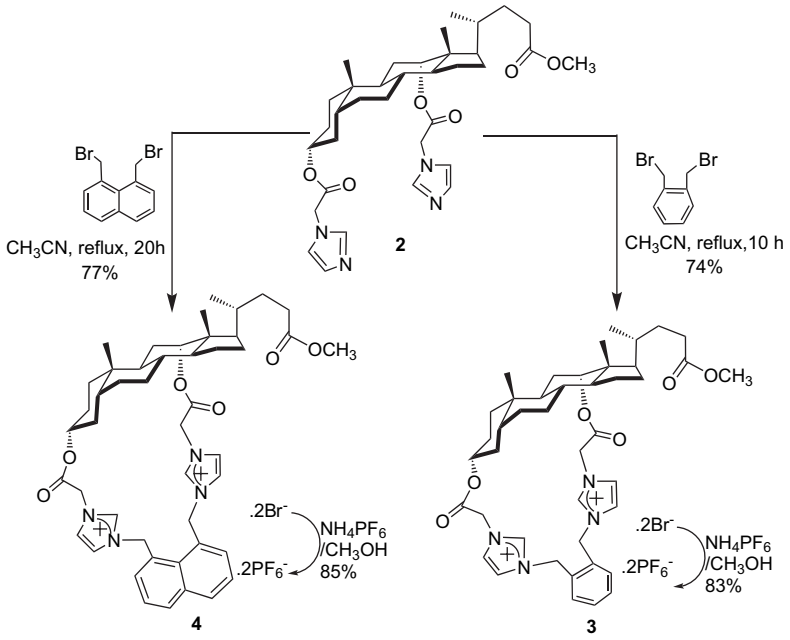


1

Figure 1. *m*-Xylene bridged bisimidazolium receptors.

* Corresponding author. Tel.: +91 11 26591506; fax: +91 11 26582037.
E-mail address: pramod@chemistry.iitd.ac.in (P.S. Pandey).

0040-4020/$ – see front matter © 2008 Elsevier Ltd. All rights reserved.
doi:10.1016/j.tet.2008.04.065



Scheme 1. Synthesis of imidazolium receptors.

2. Result and discussion

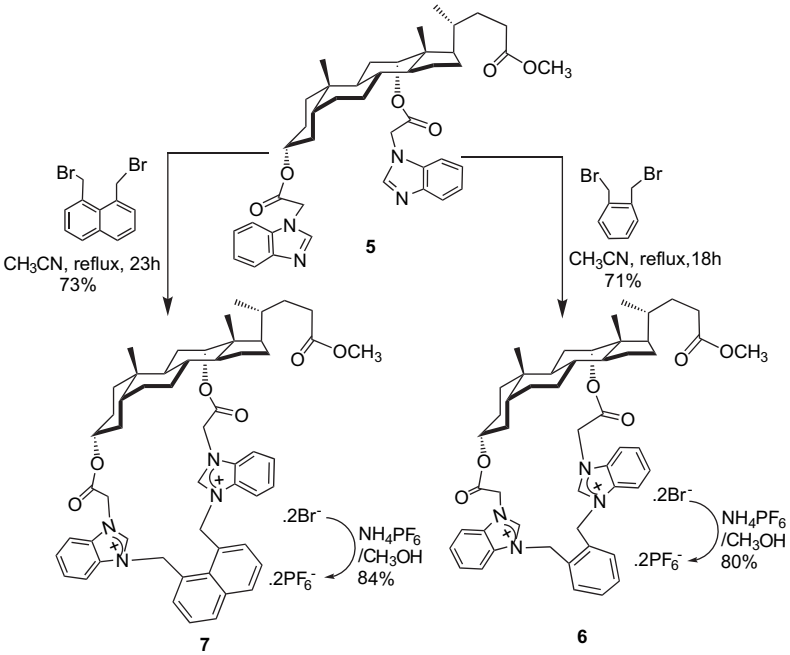
2.1. Synthesis

The deoxycholic acid-based receptors **3**, **4**, **6** and **7** were synthesized as shown in Schemes 1 and 2.

The steroidal bisimidazole derivative **2** was refluxed with *o*-xylelene bromide and 1,8-bis(bromomethyl)naphthalene in acetonitrile for 10 h and 20 h to give their corresponding dibromide salts **3** and **4**, respectively. These dibromide salts were subsequently anion-exchanged in a saturated methanolic solution of NH_4PF_6 to give their PF_6^- salts. Similarly, receptors **6** and **7** were obtained from the steroidal bisbenzimidazole derivative **5** on refluxing with *o*-xylelene bromide and 1,8-bis(bromomethyl)naphthalene in acetonitrile for 18 h and 23 h, respectively, followed by their anion-exchange with NH_4PF_6.

2.2. Anion binding studies

The binding properties of these receptors **3**, **4**, **6** and **7** with various anions were investigated using ^{1}H NMR titration experiments. Significant changes in the chemical shifts (δ 1.00–2.50 ppm) of the C-2 protons of imidazolium moieties and (δ 0.40–0.70 ppm) of the methylene protons of acetyl units were observed upon addition of tetrabutylammonium salts of various anions to the solutions of the receptors in 10% CD_3CN in $CDCl_3$. The ^{1}H NMR titration curves for the receptors with different anions are given in Figure 2. The large downfield shifts indicate that anions bind with both



Scheme 2. Synthesis of benzimidazolium receptors.

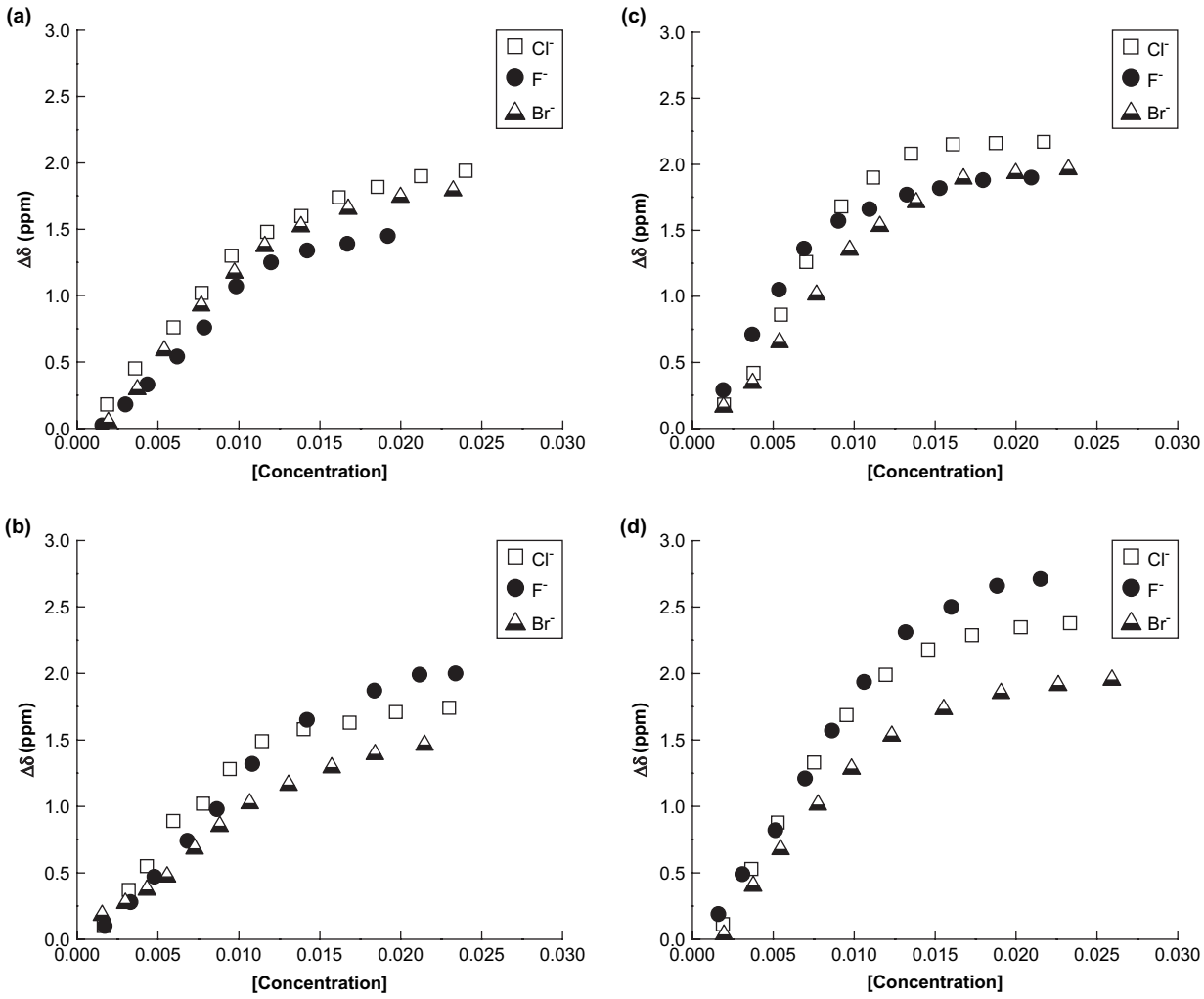


Figure 2. ^{1}H NMR titration curves for (a) receptor **3**, (b) receptor **4**, (c) receptor **6** and (d) receptor **7** with various anions.

methylenic and C-2 protons of imidazolium/benzimidazolium rings through C–H···X$^-$ and (C–H)$^+$···X$^-$ hydrogen bonds, respectively, in the cavity of the receptors. The association constants were calculated from the chemical shift changes of the C-2 protons of imidazolium/benzimidazolium rings by using WinEQNMR software,[8] which suggested 1:1 complex formation in each case. The values of the association constants are given in Table 1. The 1:1 stoichiometry of the complexation was confirmed by their Job's plots (Fig. 3).

The results clearly show that receptors **3** and **6** with *o*-xylelene group are selective for chloride ion whereas receptors **4** and **7** with naphthyl group are highly selective for fluoride ion. The selectivity of receptors **3** and **6** for chloride ion was rather unexpected. We expected these receptors to be more selective for fluoride ion due to their smaller cavity size as compared to receptor **1** with *m*-xylene spacer. It seems that in these receptors, the C-2 protons are projected outward due to the structural constraint and thus become more suitably orientated for binding of chloride ion rather than fluoride ion. In the case of naphthalene-bridged receptors **4** and **7**, which have very high affinity and selectivity for fluoride ion as compared to the *o*-xylene-bridged receptors, it has been found that the benzimidazolium receptor **7** shows two times more affinity for fluoride ion than the imidazolium receptor **4**. However, the imidazolium receptor **4** has much higher selectivity than the benzimidazolium receptor **7** for fluoride ion over chloride ion (six times vs four times). The distinct binding properties of these receptors may be of significance in terms of their suitability for applications in the design of sensors or ion-carriers for fluoride and chloride ions. Sometimes, high selectivity but slightly lower affinity of the receptor can be advantageous for using it as an ion-carrier due to easy release of the ion after transportation. For example, receptor **4** due to its lower affinity may be a better fluoride ion-carrier than the receptor **7**. The chloride selectivity of receptors **3** and **6** is also interesting as very few receptors are known, which bind chloride ion over fluoride ion.

Table 1
Association constants (K_a)[a] for 1:1 complexes of receptors with anions in 10% CD_3CN in $CDCl_3$ at 298 K

Receptor	Anion,[b] K_a (M^{-1})				
	F^-	Cl^-	Br^-	I^-	CH_3COO^-
3	300	1040	750	110	250
4	1800	310	230	120	350
6	700	2300	880	140	210
7	3200	800	450	150	850

[a] Estimated error <10%.
[b] Anions existed in their tetrabutylammonium salts.

3. Conclusion

In conclusion, we have synthesized various *o*-xylene and naphthalene-bridged deoxycholic acid-based imidazolium and benzimidazolium receptors, which show very different selectivity and affinity patterns for biologically important fluoride and chloride ions. In particular, the naphthalene-bridged receptors, which

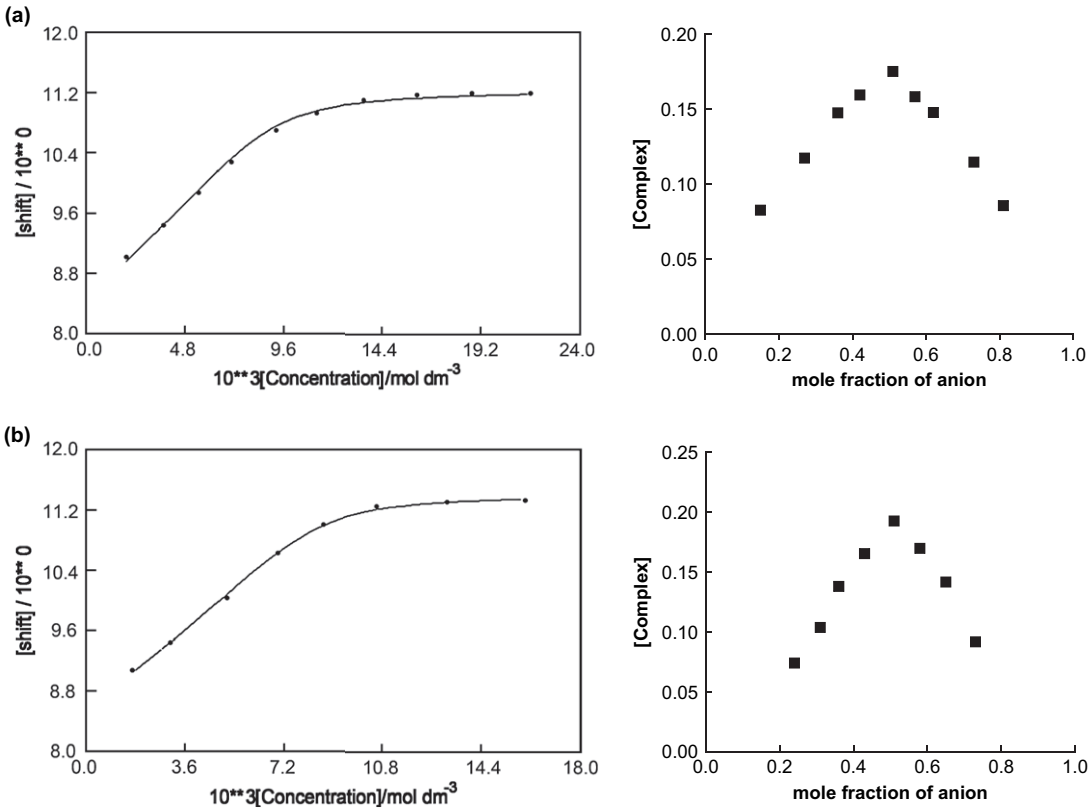


Figure 3. ^{1}H NMR titration fitted curves and Job plots for (a) receptor **6** and (b) receptor **7** with chloride and fluoride ions, respectively.

show very high selectivity for fluoride ion may be useful for designing fluoride ion-sensors and fluoride ion-carriers for analytical and medical applications.

4. Experimental

4.1. General

All the reagents used in the study were purchased from Sigma–Aldrich or Merck and were chemically pure. Reactions were carried out under nitrogen atmosphere and the solvents used were dried and distilled. Column chromatography was performed on silica gel (60–120 mesh) obtained from Merck. Melting points are uncorrected. ^{1}H and ^{13}C NMR spectra were recorded on a Bruker Spectrospin DPX 300 and chemical shifts in parts per million are reported with TMS as the internal standard. IR spectra were recorded on a Nicolet Protégé 460 Spectrometer, using KBr pellets high-resolution mass spectra were recorded on a VG-Fisons 'Autospec' Spectrometer.

4.2. Methyl 3α,12α-bis{*O*-(*N*$_1$-imidazole) acetyl}deoxycholate 2 and methyl 3α,12α-bis{*O*-(*N*$_1$-benzimidazole)acetyl}-deoxycholate 5

Compounds **2** and **5** were prepared using the experimental procedure given in Ref. 5f.

4.3. General procedure for the preparation of imidazolium/benzimidazolium cholaphane receptors

To a solution of steroidal bisimidazole/bisbenzimidazole derivative **2** or **5** (0.16 mmol) in acetonitrile (70 mL), *o*-xylelene bromide/1,8-bis(bromomethyl)naphthalene (0.16 mmol) was added and the solution was refluxed for 10/23 h. Then the solution was concentrated and recrystallized from hexane/chloroform to give the corresponding dibromide salt. Subsequently, dibromide salt of the receptor was added to a saturated methanolic solution of NH_4PF_6 and stirred for 1 h. The white precipitate of the product obtained was filtered, washed with methanol and then dried under vacuum. The product was recrystallized from chloroform/hexane.

*4.3.1. Cholaphane **3**(Br)$_2$*

Yield: 74%; Mp: 175 °C; IR (KBr) 2946, 2866, 1740, 1630, 1563, 1449 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 0.73 (s, 3H, 18-Me), 0.86 (d, J=6.6 Hz, 3H, 21-Me), 0.90 (s, 3H, 19-Me), 1.06–2.35 (26H, steroidal H), 3.67 (s, 3H, OCH_3), 4.40 (br s, 1H, 3β-H), 4.64–6.30 (m, 9H, benzylic CH_2, $OCOCH_2$, 12β-H), 6.99–8.03 (m, 8H, ArH, ImH), 9.78 (s, 1H, ImH-2), 10.23 (s, 1H, ImH-2); ^{13}C NMR ($CDCl_3$) δ 174.6, 165.4, 164.8, 136.9, 136.7, 132.5, 131.8, 131.4, 131.1, 130.5, 123.9, 122.7, 80.2, 79.0, 51.5, 50.8, 48.9, 47.4, 45.0, 41.8, 35.3, 34.9, 34.7, 33.9, 31.1, 30.5, 27.2, 26.4, 26.1, 25.1, 24.6, 23.4, 22.7, 22.4, 17.5, 12.1; TOF MS(ES$^+$) 806.8224: $(M-Br)^+$; Anal. Calcd for $C_{43}H_{58}N_4O_6Br_2\cdot 3H_2O\cdot 1CH_3CN$: C, 55.05; H, 6.88; N, 7.13. Found: C, 54.94; H, 6.75; N, 7.0.

*4.3.2. Cholaphane-receptor **3**(PF$_6$)$_2$*

Yield: 83%; Mp: 180–183 °C; IR (KBr) 2948, 1744, 1625, 1567, 1450 cm^{-1}; ^{1}H NMR (10% CD_3CN in $CDCl_3$) δ 0.72 (s, 3H, 18-Me), 0.82 (br s, 3H, 21-Me), 0.89 (s, 3H, 19-Me), 1.08–2.32 (26H, steroidal H), 3.64 (s, 3H, OCH_3), 4.41 (br s, 1H, 3β-H), 4.60–5.70 (m, 9H, benzylic CH_2, $OCOCH_2$, 12β-H), 7.09–7.56 (m, 8H, ArH, ImH), 8.05 (s, 1H, ImH-2), 8.63 (s, 1H, ImH-2); ^{13}C NMR ($CD_3CN/CDCl_3$) δ 173.69, 164.08, 163.59, 135.49, 135.34, 131.86, 131.18, 130.76, 130.60, 130.29, 129.90, 129.60, 123.73, 121.73, 121.37, 79.21, 78.31, 50.48, 49.85, 49.61, 49.14, 48.25, 46.51, 44.29, 41.04, 34.52, 34.05, 33.93, 33.34, 33.20, 30.05, 29.87, 29.75, 26.39, 25.77, 25.29, 24.55, 23.97, 22.56, 21.57, 16.43, 11.16; HRMS(ES$^+$): calcd for $C_{43}H_{58}N_4O_6\cdot F_6P$ 871.3998 $(M-PF_6)^+$, found: 871.4025.

*4.3.3. Cholaphane **4**(Br)$_2$*

Yield: 77%; Mp: 214 °C; IR (KBr) 2944, 2866, 1739, 1630, 1565, 1447 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 0.72 (s, 3H, 18-Me), 0.80 (d, J=5.7 Hz, 3H, 21-Me), 0.88 (s, 3H, 19-Me), 1.09–2.33 (26H, steroidal H), 3.65 (s, 3H, OCH_3), 4.49 (br s, 1H, 3β-H), 4.90–5.81 (m, 5H, $OCOCH_2$, 12β-H), 6.10–6.81 (m, 4H, naphthalenic CH_2), 7.10–8.20 (m, 10H, ArH, ImH), 10.22 (s, 1H, ImH-2), 10.33 (s, 1H, ImH-2); ^{13}C NMR ($CDCl_3$) δ 174.6, 174.5, 165.0, 164.9, 137.9, 137.3, 129.7, 126.3, 125.7, 124.3, 123.9, 122.6, 122.08, 79.94, 78.99, 54.3, 51.5, 50.8, 49.1, 47.5, 45.03, 41.8, 41.2, 35.9, 35.3, 34.7, 34.5, 34.4, 34.1, 33.9, 33.8, 31.5, 31.05, 30.6, 28.9, 27.6, 27.2, 26.8, 26.5, 26.02, 25.2, 25.0, 22.6, 22.5, 20.6, 20.3, 19.3, 18.6, 17.6, 14.2, 14.0, 12.1, 11.3; HRMS(ES$^+$): calcd for $C_{47}H_{60}N_4O_6Br$ 855.3696 (M−Br)$^+$, found: 855.3682.

*4.3.4. Cholaphane-receptor **4**(PF$_6$)$_2$*

Yield: 85%; Mp: 218–220 °C; IR (KBr) 2945, 1742, 1640, 1565, 1461 cm^{-1}; ^{1}H NMR (10% CD_3CN in $CDCl_3$) δ 0.68 (s, 3H, 18-Me), 0.77 (br s, 3H, 21-Me), 0.83 (s, 3H, 19-Me), 1.06–2.25 (26H, steroidal H), 3.61 (s, 3H, OCH_3), 4.30–5.80 (m, 10H, 3β-H, naphthalenic CH_2, 12β-H, $OCOCH_2$), 7.13–8.10 (m, 10H, ArH, ImH), 8.28 (s, 1H, ImH-2), 8.64 (s, 1H, ImH-2); ^{13}C NMR (CD_3CN/$CDCl_3$) δ 173.4, 164.1, 163.4, 136.2, 135.4, 132.9, 131.3, 128.7, 128.6, 126.8, 125.5, 125.1, 124.0, 123.8, 121.9, 120.9, 79.3, 78.2, 53.8, 52.2, 50.3, 49.8, 49.2, 48.6, 46.6, 44.3, 41.0, 34.5, 33.9, 33.8, 33.6, 31.1, 29.9, 29.8, 29.7, 26.2, 25.8, 25.1, 24.8, 24.2, 22.6, 21.6, 16.2, 11.1; HRMS(ES$^+$): calcd for $C_{47}H_{60}N_4O_6\cdot F_6P$ 921.4155 (M−PF$_6$)$^+$, found: 921.4444.

*4.3.5. Cholaphane **6**(Br)$_2$*

Yield: 71%; Mp: 220 °C; IR (KBr) 2944, 2867, 1739, 1617, 1564, 1444 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 0.68 (s, 3H, 18-Me), 0.86 (s, 3H, 21-Me), 0.95 (s, 3H, 19-Me), 1.02–2.50 (26H, steroidal H), 3.69 (s, 3H, OCH_3), 4.64 (br s, 1H, 3β-H), 5.19 (s, 1H, 12β-H), 5.30–6.50 (m, 6H, $OCOCH_2$, benzylic CH_2), 6.90–7.15 (m, 3H, benzylic CH_2, ArH), 7.30–8.40 (m, 11H, ArH, BIH), 10.94 (s, 1H, BIH-2), 11.13 (s, 1H, BIH-2); ^{13}C NMR ($CDCl_3$) δ 174.5, 164.6, 163.8, 143.1, 142.9, 132.1, 131.5, 131.2, 130.6, 131.2, 129.9, 129.4, 128.9, 127.8, 127.6, 115.0, 114.7, 112.8, 112.4, 79.1, 78.4, 51.4, 49.3, 48.7, 48.4, 47.1, 41.8, 35.3, 34.7, 34.4, 34.2, 34.06, 31.1, 31.0, 30.5, 28.8, 27.0, 26.7, 26.4, 25.6, 25.3, 23.1, 22.8, 22.4, 17.5, 12.0, 11.2; HRMS(ES$^+$): calcd for $C_{51}H_{62}N_4O_6Br$ 905.3853 (M−Br)$^+$, found: 905.3837.

*4.3.6. Cholaphane-receptor **6**(PF$_6$)$_2$*

Yield: 80%; Mp: 228–230 °C; IR (KBr) 2958, 1746, 1572, 1438 cm^{-1}; ^{1}H NMR (10% CD_3CN in $CDCl_3$) δ 0.66 (s, 3H, 18-Me), 0.84 (s, 3H, 21-Me), 0.95 (s, 3H, 19-Me), 1.15–2.40 (26H, steroidal H), 3.67 (s, 3H, OCH_3), 4.46 (br s, 1H, 3β-H), 4.70–5.60 (m, 9H, 12β-H, benzylic CH_2, $OCOCH_2$), 7.00–7.70 (m, 12H, ArH, BIH), 8.02 (s, 1H, BIH-2), 8.54 (s, 1H, BIH-2); ^{13}C NMR (CD_3CN/$CDCl_3$) δ 173.6, 163.5, 163.4, 140.9, 140.4, 131.2, 131.1, 130.9, 130.6, 130.4, 129.6, 128.0, 127.5, 127.4, 127.0, 113.2, 113.0, 112.7, 50.5, 47.9, 47.8, 47.2, 46.9, 46.5, 44.2, 41.0, 34.0, 33.8, 33.6, 33.4, 33.3, 30.7, 30.3, 30.1, 29.8, 26.3, 26.1, 25.6, 24.8, 24.7, 22.4, 22.1, 16.5, 11.2; HRMS(ES$^+$): calcd for $C_{51}H_{62}N_4O_6\cdot F_6P$ 971.4311 (M−PF$_6$)$^+$, found: 971.4298.

*4.3.7. Cholaphane **7**(Br)$_2$*

Yield: 73%; Mp: 208–210 °C; IR (KBr) 2940, 2866, 1738, 1620, 1565, 1444 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 0.65 (s, 3H, 18-Me), 0.82 (s, 3H, 21-Me), 0.95 (s, 3H, 19-Me), 1.06–2.40 (26H, steroidal H), 3.67 (s, 3H, OCH_3), 4.64 (br s, 1H, 3β-H), 5.20–7.10 (m, 9H, $OCOCH_2$, 12β-H, naphthalenic CH_2), 7.36–8.10 (m, 14H, ArH, BIH), 11.16 (s, 1H, BIH-2), 11.40 (s, 1H, BIH-2); ^{13}C NMR ($CDCl_3$) δ 174.4, 164.6, 164.2, 143.4, 143.0, 135.8, 137.3, 131.9, 131.6, 131.4, 131.0, 130.3, 130.0, 128.7, 128.6, 127.6, 127.4, 126.8, 126.0, 125.5, 115.4, 115.2, 113.02, 112.7, 79.20, 53.8, 52.9, 51.5, 49.1, 48.9, 48.5, 47.2, 45.0, 44.9, 41.2, 35.9, 35.4, 34.3, 33.8, 31.4, 31.3, 31.1, 30.6, 28.9, 25.5, 25.1, 23.3, 22.8, 22.5, 20.3, 19.3, 18.6, 17.6, 14.2, 12.2, 11.3; HRMS(ES$^+$): calcd for $C_{55}H_{64}N_4O_6Br$ 955.4009 (M−Br)$^+$, found 955.4034.

*4.3.8. Cholaphane-receptor **7**(PF$_6$)$_2$*

Yield: 84%; Mp: 210–212 °C; IR (KBr) 3080, 2938, 1745, 1614, 1572, 1445 cm^{-1}; ^{1}H NMR (10% CD_3CN in $CDCl_3$) δ 0.70 (s, 3H, 18-Me), 0.84 (s, 3H, 21-Me), 0.89 (s, 3H, 19-Me), 1.13–2.43 (26H, steroidal H), 3.67 (s, 3H, OCH_3), 4.41 (br s, 1H, 3β-H), 5.00–6.90 (m, 9H, $OCOCH_2$, 12β-H, naphthalenic CH_2), 7.40–8.15 (m, 14H, ArH, BIH), 8.69 (s, 1H, BIH-2), 9.11 (s, 1H, BIH-2); ^{13}C NMR ($CDCl_3$/CD_3CN) δ 173.7, 164.8, 163.5, 142.0, 140.8, 135.8, 134.5, 132.2, 131.5, 131.2, 131.1, 130.9, 130.1, 129.1, 127.9, 127.7, 127.3, 127.2, 126.2, 125.5, 125.1, 124.3, 113.0, 112.7, 81.2, 78.7, 53.0, 50.9, 50.0, 49.1, 48.4, 47.5, 47.3, 47.0, 44.5, 41.6, 35.3, 34.9, 34.4, 33.4, 31.1, 30.4, 30.0, 29.7, 27.1, 26.6, 25.2, 25.0, 23.0, 22.3, 16.8, 11.7; HRMS(ES$^+$): calcd for $C_{55}H_{64}N_4O_6\cdot F_6P$ 1021.4468 (M−PF$_6$)$^+$, found 1021.4490.

4.4. ^{1}H NMR titration method

All NMR experiments were performed on Bruker DPX300 (300 MHz) Spectrometer at 298 K. A solution (10 mM) of receptor in $CDCl_3$/CD_3CN was titrated with small aliquots from a stock solution of the tetrabutylammonium salt (40–60 mM) in the same solvent. The changes in the chemical shift of the C-2 protons of imidazolium/benzimidazolium moieties in the receptors were monitored. The association constants were determined by using WinEQNMR program. Every titration was repeated at least once.

Acknowledgements

We thank the CSIR, New Delhi for the research fellowship to M.C.

Supplementary data

NMR, mass spectra and binding isotherms are available in Supplementary data. Supplementary data associated with this article can be found in the online version, at doi:10.1016/j.tet.2008.04.065.

References and notes

1. (a) Sessler, J. L.; Gale, P. A.; Cho, W.-S. *Anion Receptor Chemistry*; Royal Society of Chemistry: Cambridge, UK, 2006; (b) Schmidtchen, F. P.; Berger, M. *Chem. Rev.* **1997**, *97*, 1609–1646; (c) Gale, P. A. *Coord. Chem. Rev.* **2000**, *199*, 181–233; (d) Gale, P. A. *Coord. Chem. Rev.* **2003**, *240*, 191–221; (e) Gale, P. A. *Acc. Chem. Res.* **2006**, *39*, 465–475; (f) Gale, P. A.; Garcia-Garrido, S. E.; Garric, J. *Chem. Soc. Rev.* **2008**, *37*, 151–190.
2. (a) Kirk, K. L. *Biochemistry of the Halogens and Inorganic Halides*; Plenum: New York, NY, 1991; (b) Kleerekoper, M. *Endocrinol. Metab. Clin. North Am.* **1998**, *27*, 441–452; (c) Matuso, S.; Kiyomiya, K. i.; Kurebe, M. *Arch. Toxicol.* **1998**, *72*, 798–806; (d) Laisalmi, M.; Kokki, H.; Soikkeli, A.; Markkanen, H.; Yli-Hankala, A.; Rosenberg, P.; Lindgren, L. *Acta Anaesthesiol. Scand.* **2006**, *50*, 982–987.
3. (a) Black, C. B.; Andrioletti, B.; Try, A. C.; Ruiperez, C.; Sessler, J. L. *J. Am. Chem. Soc.* **1999**, *121*, 10438–10439; (b) Mason, S.; Llinares, J. M.; Morton, M.; Clifford, T.; Bowman-James, K. *J. Am. Chem. Soc.* **2000**, *122*, 1814–1815; (c) Furtura, H.; Maeda, H.; Osuka, A. *J. Am. Chem. Soc.* **2001**, *123*, 6435–6436; (d) Takeuchi, M.; Shioya, T.; Swager, T. M. *Angew. Chem., Int. Ed.* **2001**, *40*, 3372–3376; (e) Camolo, S.; Gale, P. A.; Hursthouse, M. B.; Light, M. E.; Warriner, C. N. *Tetrahedron Lett.* **2003**, *44*, 1367–1369; (f) Kang, S. O.; Llinares, J. M.; Powell, D.; VanderVelde, D.; Bowman-James, K. *J. Am. Chem. Soc.* **2003**, *125*, 10152–10153; (g) Jose, D. A.; Kumar, D. K.; Ganguly, B.; Das, A. *Org. Lett.* **2004**, *6*, 3445–3448; (h) Lee, J. Y.; Cho, E. J.; Mukamel, S.; Nam, K. C. *J. Org. Chem.* **2004**, *69*, 943–950; (i) Yin, Z.; Li, Z.; Yu, A.; He, J.; Cheng, J.-P. *Tetrahedron* **2004**, *45*, 6803–6806; (j) Chellappan, K.; Singh, N. J.; Hwang, I.-C.; Lee, J. W.; Kim, K. S. *Angew. Chem., Int. Ed.* **2005**, *44*, 2899–2903; (k) Kim, K. S.; Kim, H.-S. *Tetrahedron* **2005**, *61*, 12366–12370; (l) Albrecht, M.; Marita de Groot, T.; Bahr, M.; Weinhold, E. *Synlett* **2005**, 2095–2097; (m) Mascal, M. *Angew. Chem., Int. Ed.* **2006**, *45*, 2890–2893; (n) Jun, E. J.; Swamy, K. M. K.; Bang, H.; Kim, S.-J.; Yoon, J. *Tetrahedron Lett.* **2006**, *47*, 3103–3106; (o) Ghosh, K.; Adhikari, S. *Tetrahedron Lett.* **2006**, *47*, 8165–8169; (p) Oton, F.; Tarraga, A.; Espinosa, A.; Velasco, M. D.; Molina, P. *J. Org. Chem.* **2006**, *71*, 4590–4598; (q) Yu, M.; Zhao, G.; Lin, H. *J. Mol. Recognit.* **2007**, *20*, 69–73; (r) Han, F.; Bao, Y.; Yang, Z.; Fyles, T. M.; Zhao, J.; Peng, X.; Fan, J.; Wu, Y.; Sun, S. *Chem.—Eur. J.* **2007**, *13*, 2880–2892; (s) Lin, C.-I.; Selvi, S.; Fang, J.-M.; Chou, P.-T.; Lai, C.-H.;

Cheng, Y.-M. *J. Org. Chem.* **2007**, *72*, 3537–3542; (t) Zhang, Y.; Yin, Z.; He, J.; Cheng, J.-P. *Tetrahedron Lett.* **2007**, *48*, 6039–6043; (u) Zhang, Y.; Yin, Z.; Li, Z.; He, J.; Cheng, J.-P. *Tetrahedron* **2007**, *63*, 7560–7564; (v) Bates, G. W.; Gale, P. A.; Light, M. E. *Chem. Commun.* **2007**, 2121–2123.

4. (a) Yun, S.; Ihm, H.; Kim, H. G.; Lee, C.-W.; Indrajit, B.; Oh, K. S.; Gong, Y. J.; Lee, J. W.; Yoon, J.; Lee, H. C.; Kim, K. S. *J. Org. Chem.* **2003**, *68*, 2467–2470; (b) Yoon, J.; Kim, S. K.; Singh, N. J.; Kim, K. S. *Chem. Soc. Rev.* **2006**, *35*, 355–360.
5. (a) Davis, A. P.; Joos, J.-B. *Coord. Chem. Rev.* **2003**, *240*, 143–156; (b) Sisson, A. L.; Clare, J. P.; Taylor, L. H.; Charmant, J. P. H.; Davis, A. P. *Chem. Commun.* **2003**, 2246–2247; (c) Clare, J. P.; Ayling, J. A.; Joos, J.-B.; Sisson, A. L.; Margo, G.; Pérez-Payán, M. N.; Lambert, T. N.; Shukla, R.; Smith, B. D.; Davis, A. P. *J. Am. Chem. Soc.* **2005**, *127*, 10739–10746; (d) Bhattarai, K. M.; del Amo, V.; Magro, G.; Sisson, A. L.; Joos, J.-B.; Charmant, J. P. H.; Kantacha, A.; Davis, A. P. *Chem. Commun.* **2006**, 2335–2337; (e) Davis, A. P. *Coord. Chem. Rev.* **2006**, *250*, 2939–2951; (f) Chahar, M.; Upreti, S.; Pandey, P. S. *Tetrahedron* **2007**, *63*, 171–176.
6. Ghosh, S.; Choudhary, A. R.; Guru Row, T. N.; Maitra, U. *Org. Lett.* **2005**, *8*, 1441–1444.
7. Khatri, V.; Upreti, S.; Pandey, P. S. *Org. Lett.* **2006**, *8*, 1755–1758.
8. Hynes, M. J. *J. Chem. Soc., Dalton Trans.* **1993**, 311–312.