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Chiral recognition of carboxylic acids by Tröger's base derivatives

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ABSTRACT

The readily accessible optically active methoxy Tröger's base **3** and the corresponding α,α′-diphenyl carbinol derivative **5** are useful for the recognition and enantiomeric discrimination of representative chiral carboxylic acids.

1. Introduction

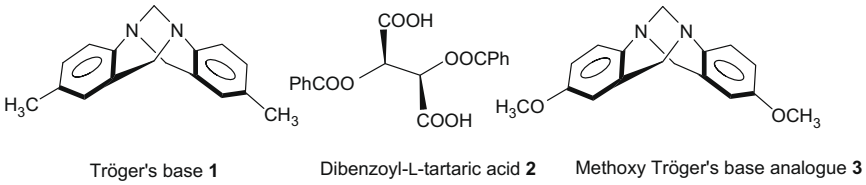
The study of chiral recognition phenomena is essential for many fields, such as resolution of racemic mixtures, the determination of enantiomeric purity of chiral compounds and the screening of chiral catalysts. Chiral carboxylic acids are the structural units of many natural products and drug molecules.[1] The growing use of enantiomerically pure carboxylic acids has led to the development of fast and reliable methodologies for the assessment of enantiomeric purity of chiral carboxylic acids.[2] Several approaches have been developed for the evaluation of chiral recognition, including spectroscopic, chromatographic and electrochemical techniques. Among these, NMR spectroscopy has the advantage of ease of use and requires no special equipment apart from the NMR spectrometer. Accordingly, NMR spectroscopy[3] is still widely used for the enantiomeric discrimination of amino acids, carboxylic acids, amines and amino alcohols by chiral synthetic receptors. However, few efficient chiral solvating agents are available for carboxylic acids.[4]

Recently, pincer-type receptors derived from cycloalkane 1,2-diamine[5] and the macrocyclic polyamides derived from L-/D-tartaric acids[6] were reported to exhibit chiral recognition towards certain chiral carboxylic acids. Rigid chiral macrocyclic dioxopolyamines derived from L-proline[7a] and chiral calix[4]azacrown ethers were also reported as chiral solvating agents.[7b]

In recent years, there has been renewed interest in the chiral separations and applications involving Tröger's base and its analogues.[8] During the course of our investigations on the synthesis, resolution and applications of Tröger's base and its analogues,[9] the use of certain Tröger's base analogues for the molecular recognition of adenine and biotin derivatives was reported.[10a,b] Selective recognition of dicarboxylic acids by the receptors derived from Tröger's base was also reported.[10c] Many of these applications as receptors deal with the geometry of Tröger's base skeleton. However, chiral recognition is a phenomenon where the chirality as well as the geometry of the Tröger's base skeleton can be exploited.[11] We have screened the chiral recognition property of the Tröger's base derivatives readily accessible by the methods developed in this laboratory.[9a] The results are described here (see Fig. 1).

2. Results and discussion

Preliminary studies indicated that the Tröger's base **1** itself is not very effective as a chiral enantiomer discriminating agent for carboxylic acids. For instance, when we recorded the ^{1}H NMR



Tröger's base **1** Dibenzoyl-L-tartaric acid **2** Methoxy Tröger's base analogue **3**

Figure 1.

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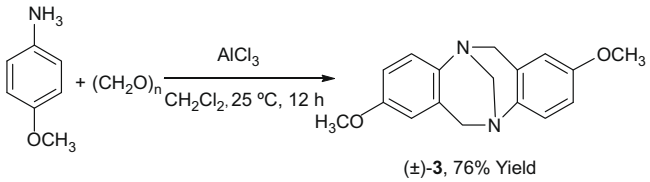


Scheme 1.

spectrum of (±)-2,3-diphenylsuccinic acid **7** in the presence of the chiral Tröger's base **1,** the methine proton signal of **7** was split into doublet by 9.6 Hz only. It was thought that increasing the electron density at the nitrogen centre by substituting a greater electron-donating substituent in the aromatic ring, would give better results**.** Accordingly, we have prepared the methoxy Tröger's base following a method developed in this laboratory.[9a] Thus, the reaction of *p*-anisidine with paraformaldehyde in the presence of $AlCl_3$ gave racemic methoxy Tröger's base in good yields (Scheme 1).

We have then examined the resolution of methoxy Tröger's base using different chiral acids and found that the methoxy Tröger's base could be readily resolved via the preparation of diastereomeric salts with *O,O′*-dibenzoyl-L-tartaric acid as resolving agent. The resolution was carried out in various solvents such as CH_2Cl_2, ethyl acetate and acetonitrile, and in all cases, the partially resolved methoxy Tröger's base was readily obtained. Optimum results were obtained in acetone when the racemic methoxy Tröger's base **3** and dibenzoyl-L-tartaric acid **2** were used in 1:1 ratio (Scheme 2). After isolation of the precipitate fraction, the (*R,R*)-enantiomer of the methoxy Tröger's base was obtained in >98% ee and from the filtrate fraction, the (*S,S*)-isomer was obtained in 30% ee.

The (*S,S*)-enantiomer was easily enriched by repeating the experiment using dibenzoyl-D-tartaric acid and the results are summarized in Table 1.

The precipitated diastereomeric salt **4**[(−)-**3**·(−)-**2**] (Table 1, entry 5) was crystallized from methanol and the X-ray crystal structure analysis was carried out (Fig. 2).[17] The asymmetric unit of the

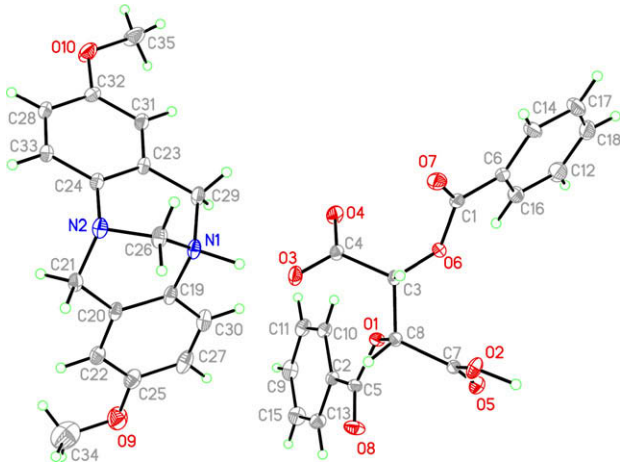
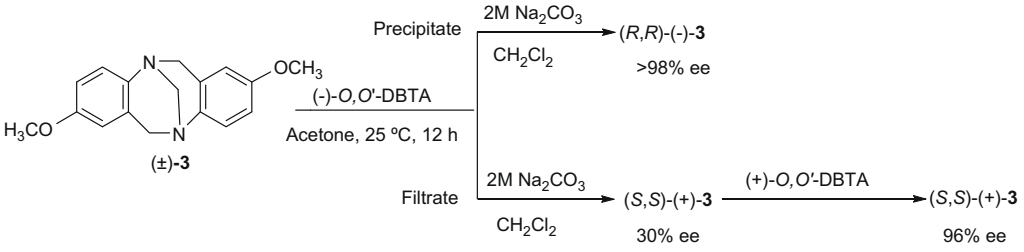


Figure 2. ORTEP representation of the crystal structure of the diastereomeric salt **4**[(−)-**3**·(−)-**2**] (thermal ellipsoids are drawn at 15% probability and all the hydrogen atoms are unlabelled for clarity).

crystal structure contains one molecule of methoxy Tröger's base and one molecule of dibenzoyl-L-tartaric acid (1:1). The ORTEP diagram (Fig. 2) clearly shows that only one proton from the two acid groups of (−)-DBTA transferred to nitrogen atom of methoxy Tröger's base **3** and the other nitrogen atom has not formed salt. This salt was packed in a helical fashion and the helix has formed because of the strong O–H···O and N–H···O hydrogen-bonding interactions (Fig. 3). The configuration of (−)-**3** was determined as 5*R*,11*R* relative to the chiral acid (*R,R*)-(−)-**2**. It is of interest to note here that whereas the methoxy Tröger's base **3** forms a salt with the dibenzoyl-L-tartaric acid, the Tröger's base **1** forms only a hydrogen-bonded complex.[9a] Clearly, the methoxy Tröger's base **3** is a stronger base as anticipated.

Generally, amines, diamines and amino alcohols exhibit chiral recognition towards carboxylic acids.[3b,7,12] Accordingly, we have also prepared the amino alcohol **5**, derived from the chiral meth-



Scheme 2.

Table 1
Resolution of racemic methoxy Tröger's base **3** using dibenzoyl-L-tartaric acid

Entry	(±)-**3** mmol (% ee)	DBTA (mmol)	Acetone (mL)	Methoxy Tröger's base **3** obtained from			
				Precipitate		Filtrate	
				% ee[a]/conf.	Yield[b] (%)	% ee[a]/conf.	Yield[b] (%)
1	2 (00)	1	20	79 (*R,R*)	24	19 (*S,S*)	73
2	2 (00)	2	20	83 (*R,R*)	34	43 (*S,S*)	60
3	2 (00)	2	25	86 (*R,R*)	35	28 (*S,S*)	60
4[c]	2 (28)	2	15	84 (*S,S*)	57	10 (*R,R*)	37
5	20 (00)	20	240	>98 (*R,R*)	30	30 (*S,S*)	66
6[c]	20 (30)	20	300	96 (*S,S*)	31	06 (*R,R*)	65

[a] The enantiomeric purities were based on the HPLC analysis by using CHIRALCEL OD-H column.
[b] The yields are of isolated products.
[c] In these experiments dibenzoyl-D-tartaric acid was used as resolving agent.

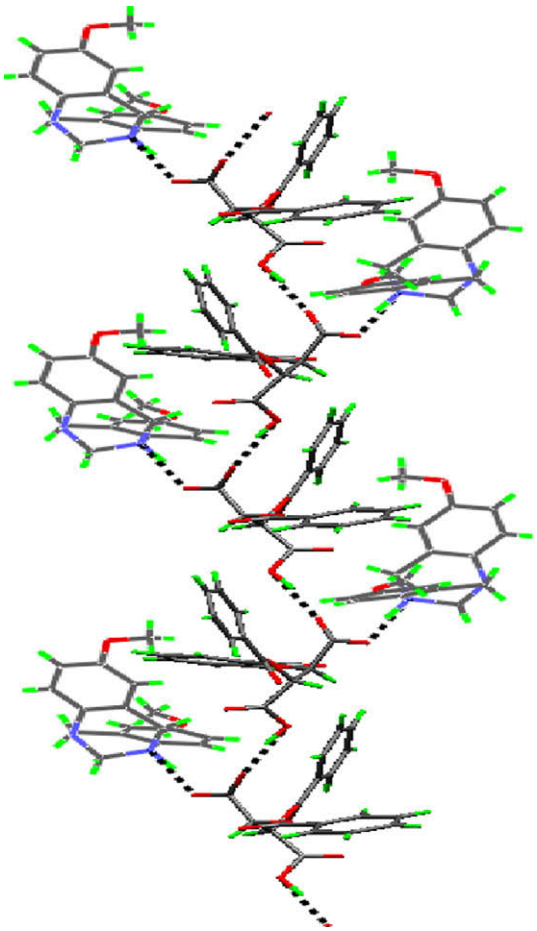


Figure 3. Packing diagram of the diastereomeric salt **4**[(−)-**3**·(−)-**2**] showing the helix formed due to strong O–H···O and N–H···O hydrogen-bonding interactions.

oxy Tröger's base **3** following a reported method for α-alkylation of tertiary amines (Scheme 3).[13]

We have employed ^{1}H and ^{31}P NMR spectroscopy to study the interaction of the chiral ligands (5*R*,11*R*)-**3** and (5*R*,6*S*,11*R*)-**5** with the racemic acid guests **6**–**10**. We observed that the methine proton signal of the carboxylic acids **6**–**9** appears as a sharp singlet and does not overlap with the signals of any of the protons in the host molecule. Hence, it is an ideal probe for the present studies. We recorded the ^{1}H NMR spectrum of (±)-2,3-diphenylsuccinic acid **7** in the presence of **3**. In this case, the methine proton signal was split into doublet by 12 Hz. Since the methoxy Tröger's base **3** gave better resolution, we continued our study with this amine. The samples for analysis were prepared by mixing equimolar amounts of the guests and chiral host **3** or **5**. The resulting chemical non-equivalences ($\Delta\Delta\delta$) are summarized in Table 2.

The methine proton signal of mandelic acid **6** was split into doublet by 4.8 Hz, 7.2 Hz in the presence of the chiral discriminating agents **3** and **5**, respectively, with upfield chemical shift. The $\Delta\delta$, chemical shift differences relative to the original signals in the absence of CSA, are in the range of 0.12–0.22. In the case of 2,3-diphenylsuccinic acid **7**, the methine proton signal was shifted upfield and split by 12 Hz in the presence of **3** (Fig. 4). The $\Delta\delta$ values are in the range of 0.08–0.11. The acid **7** did not show any splitting in the presence of **5**.

The 43% ee of (*S*,*S*)-**7** determined by ^{1}H NMR analysis in the presence of **3,** is in good agreement with the ee value determined by specific rotation (Fig. 5).

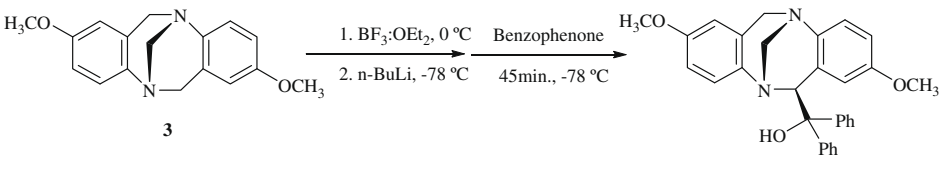
The methine proton signal of (*S*)-mandelic acid appeared at lower field than the (*R*)-mandelic acid in the presence of **3** and **5**. In the case of 2,3-diphenylsuccinic acid, the (*R*,*R*)-enantiomer appeared at lower field than the corresponding (*S*,*S*)-enantiomer in the presence of the chiral host **3.** It indicates that the (*S*,*S*)-enantiomer binds more strongly compared to its antipode with the host **3**. The results were confirmed by recording the ^{1}H NMR spectra of the samples containing non-racemic guests (acids) (Fig. 5).

In (±)-dibenzoyltartaric acid and (±)-ditoluoyltartaric acid, non-equivalence was observed for the *ortho*-C–H proton signal of the phenyl ring when **3** was used. The *ortho*-C–H proton appears as a doublet in the ^{1}H NMR spectrum of **8** or **9** in the absence of **3**. It was shifted downfield and split into two doublets by 21.2 Hz (Fig. 6c). The corresponding signal for (±)-ditoluoyltartaric acid was upfield shifted and split by 20.8 Hz in the presence of **3**. The $\Delta\delta$ values are in the range of 0.001–0.008. Whereas in the presence of the amino alcohol **5**, splitting was observed in the *ortho*-C–H proton as well as the methine proton signal. The signals were shifted upfield and the chemical shift differences ($\Delta\delta$) are in the range of 0.05–0.137. The methine proton signal of (±)-dibenzoyltartaric acid was split by 14.4 Hz (Fig. 6b) and the corresponding signal for (±)-ditoluoyltartaric acid was split by 20.4 Hz. The *ortho*-C–H proton doublet of dibenzoyl-D-tartaric acid and ditoluoyl-L-tartaric acid appeared at lower field in the presence of **3**. The methine proton signal of the dibenzoyl-L-tartaric acid and ditoluoyl-L-tartaric acid appeared at lower field when **5** was used.

It is of interest to note that in the past chiral cyclic phosphoric acid diesters derived from chiral BINOL were employed as chiral ligands and also catalysts in asymmetric organocatalysis.[14] Therefore, a relatively inexpensive method for determining their enantiomeric purity would be useful. We have employed the chiral methoxy Tröger's base **3** and the corresponding α,α′-diphenyl carbinol derivative **5** for ^{31}P NMR analysis of BINOL-phosphoric acid. Generally, BINOL-derived phosphoric acids are sparingly soluble or insoluble in $CDCl_3$. The 1,1′-binaphthyl-2,2′-diylphosphoric acid **10** is insoluble in $CDCl_3$ but it is soluble in the presence of **3** or **5**. In the ^{31}P NMR spectrum of BINOL-phosphoric acid, a singlet appearing at 4.5 ppm (in DMSO-d_6), is split into a doublet in the presence of **3** or **5** (Fig. 7). The resulting chemical anisochronies ($\Delta\Delta\delta$) measured using ^{31}P NMR are summarized in Table 3.

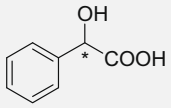
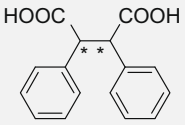
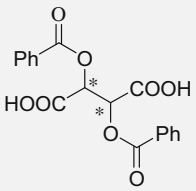
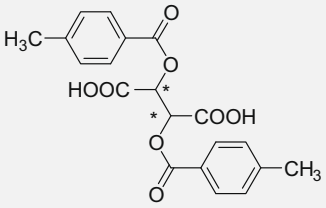
3. Conclusion

In conclusion, we have developed a convenient method to access the chiral methoxy Tröger's base. The chiral methoxy Tröger's base **3** and the corresponding α,α′-diphenyl carbinol derivative **5**



Scheme 3.

Table 2
Chemical shift changes ($\Delta\delta$) and chemical shift non-equivalence ($\Delta\Delta\delta$)[a] observed in ^{1}H NMR spectra of guest acids in the presence of hosts **3** and **5**

Guests	Observed signal	$\Delta\delta$ (ppm)		$\Delta\Delta\delta$ (Hz)	
		3	**5**	**3**	**5**
 mandelic acid, **6**	–CH	−0.13 −0.12 −0.205 −0.217	−0.122 −0.14 —	4 4.8[b]	7.2 —
 2,3-diphenylsuccinic acid, **7**	–CH	−0.08 −0.11	—	12	0
 *O,O′*-dibenzoyltartaric acid, **8**	*ortho*-CH of phenyl ring	+0.060 +0.008	−0.101 −0.137	21.2	14.4[c]
 *O,O′*-ditoluoyltartaric acid, **9**	*ortho*-CH of toluoyl ring	+0.001 −0.050	−0.05 0.102	20.8	20.4[c]

[a] All the ^{1}H NMR experiments were performed using 0.2 M, 1:1 (host to guest ratio) solution in $CDCl_3$ at 25 °C and 400 MHz spectrometer.
[b] In this case host to guest ratio was 2:1.
[c] The $\Delta\Delta\delta$ values correspond to the splitting observed for the methine proton.

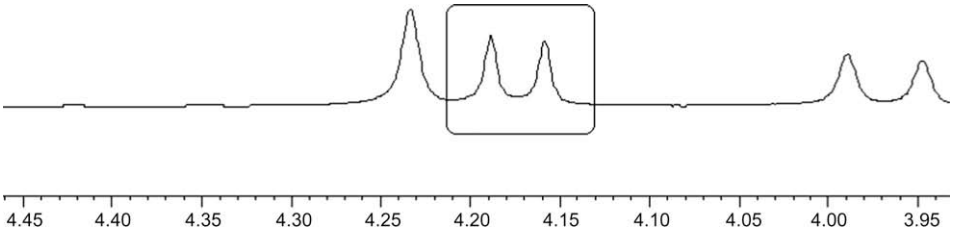


Figure 4. ^{1}H NMR spectrum of (±)-2,3-diphenylsuccinic acid **7** in the presence of the chiral methoxy Tröger's base **3** (1:1 ratio of 0.2 M solution in $CDCl_3$ at 25 °C).

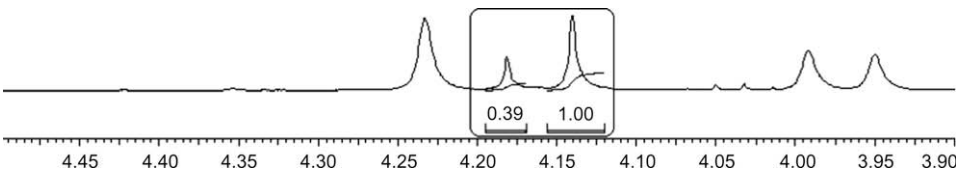


Figure 5. ^{1}H NMR spectra of 43% ee of (*S,S*)-**7** in the presence of **3** (1:1 ratio of 0.2 M solution in $CDCl_3$).

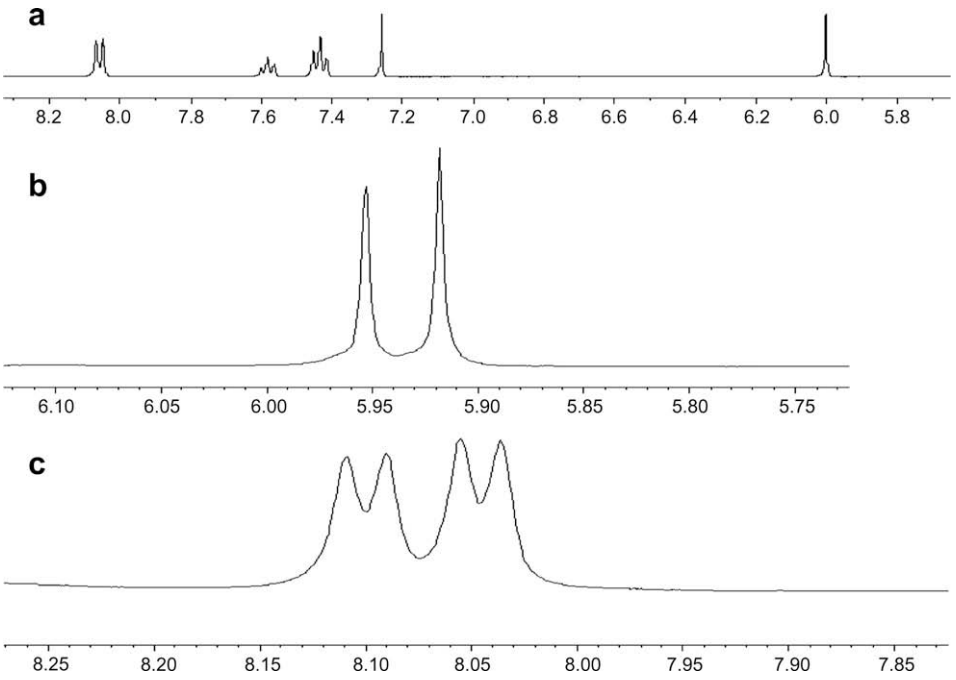


Figure 6. ^{1}H NMR spectrum of (a) (±)-dibenzoyltartaric acid in the absence of CSA, (b) (±)-dibenzoyltartaric acid in the presence of **5** (1:1 ratio of 0.2 M solution in $CDCl_3$ 25 °C) and (c) (±)-dibenzoyltartaric acid in the presence of **3** (1:1 ratio of 0.2 M solution in $CDCl_3$ at 25 °C).

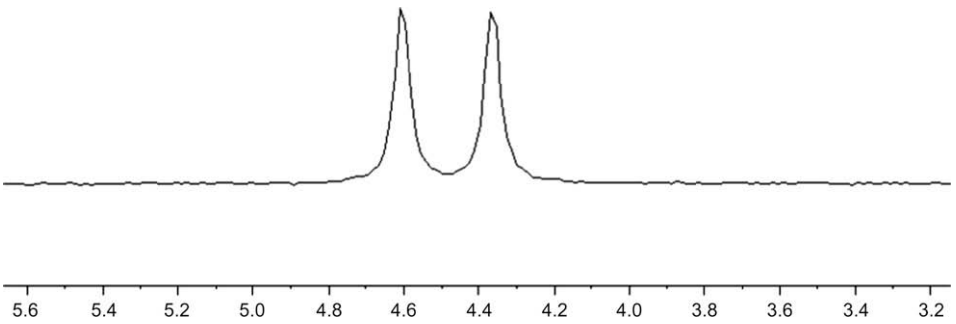


Figure 7. ^{31}P NMR spectrum of 1,1′-binaphthyl-2,2′-diylphosphoric acid in the presence of chiral methoxy Tröger's base **3** (0.1 M solution of the host to guest mixture in $CDCl_3$ at 25 °C).

Table 3
Chemical shift non-equivalence ($\Delta\Delta\delta$)[a] observed in ^{31}P NMR spectra of 1,1′-binaphthyl-2,2′-diylphosphoric acid **10** in the presence of hosts **3** and **5**

Ratio of amine/amino alcohol:acid	Observed signal	$\Delta\Delta\delta$ (Hz)	
		3	**5**
1:1	Phosphorus	39.2	42
1:2		11.2	36.5
1:4		—	31.7

[a] All the ^{31}P NMR experiments were performed using 0.1 M solution of the host to guest mixture in $CDCl_3$ at 25 °C and 161 MHz spectrometer.

exhibit good chiral recognition ability towards representative chiral carboxylic acids. Whereas, the chiral methoxy Tröger's base has shown a better enantio-discrimination towards the C_2-symmetric acids **7**–**9** and the C_1-symmetric **5** exhibited better discrimination towards unsymmetrical acids **6** and **10**. Accordingly, the chiral recognition studies of carboxylic acids using the readily accessible chiral methoxy Tröger's base **3** and its amino alcohol derivative **5** reported here have significant potential for further exploitation of the chemistry of this fascinating chiral moiety.

4. Experimental

Infrared spectra were recorded on Perkin–Elmer IR spectrophotometer Model 1310. ^{1}H NMR and ^{13}C NMR spectra were recorded on Bruker AV-400 Spectrometer with Chloroform-d as a solvent and TMS as reference (δ = 0 ppm). Chromatography was carried out using Acme's silica gel (100–200 mesh) or alumina. CH_2Cl_2 and THF were dried using the standard procedures.

4.1. Preparation of racemic methoxy Tröger's base 3

To a solution of *p*-anisidine (1.23 g, 10 mmol) and paraformaldehyde (0.60 g, 20 mmol) in CH_2Cl_2 (40 mL) was added the $AlCl_3$ (1.33 g, 10 mmol) under N_2 atmosphere. The reaction mixture was allowed to stir for 12 h at 25 °C and the reaction was quenched with cold water (10 mL). The reaction mixture was extracted in CH_2Cl_2 (2 × 15 mL) and the combined organic extracts were successively washed with water, brine solution and dried over anhydrous Na_2SO_4. After removal of the solvent, the residue was subjected to chromatography on alumina (basic) column using

30% ethyl acetate in hexane to elute the desired methoxy Tröger's base **3**, yield: 1.07 g (76%); mp 168–170 °C (lit.[15] mp 172–174 °C); IR (KBr): 3150, 1493, 1431, 1325, 1207, 1095, 960, 896, 829 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.06 (d, 2H, J = 8.8 Hz), 6.74 (d, 2H, J = 8.8 Hz), 6.42 (s, 2H), 4.64 (d, 2H, J = 16.4 Hz), 4.29 (s, 2H), 4.08 (d, 2H, J = 16.6 Hz), 3.70 (s, 6H); ^{13}C NMR ($CDCl_3$) δ 156.0, 140.9, 128.6, 125.9, 113.9, 110.9, 67.2, 58.9, 55.3.

4.2. Resolution of methoxy Tröger's base analogue 3 using dibenzoyl-L-tartaric acid

The dibenzoyl-L-tartaric acid (7.2 g, 20 mmol) and the racemic methoxy Tröger's base **3** (5.64 g, 20 mmol) were taken in acetone (240 mL) and the contents were stirred at 25 °C for 12 h. The precipitate was collected and crystallized by dissolving in hot acetone. The crystals were suspended in a mixture of CH_2Cl_2 (50 mL) and 2 N Na_2CO_3 and stirred until the dissolution occurred. The organic layer was separated and the aqueous layer was extracted with CH_2Cl_2 (2 × 25 mL). The combined organic extracts were washed with brine (10 mL), dried over anhydrous Na_2SO_4 and evaporated to obtain the product (*R,R*)-**3** enantiomer (1.7 g, 30% yield, >98% ee). $[\alpha]_D^{25} = -242 \pm 5$ (*c* 0.22, $CHCl_3$). The filtrate was concentrated and the residue was treated as outlined above to obtain the (*S,S*)-**3** enantiomer (3.7 g, 66% yield, 30% ee). The (*S,S*)-**3** isomer with 30% ee was further enriched by repeating the resolution experiment using dibenzoyl-D-tartaric acid to obtain the sample of 96% ee. $[\alpha]_D^{25} = +236 \pm 5$ (*c* 0.22, $CHCl_3$). The samples were also analyzed by HPLC using the chiral column to assess the enantiomeric purities.[16]

4.3. Preparation of the α,α′-diphenyl carbinol derivative 5 of methoxy Tröger's base

To an oven-dried round-bottomed flask equipped with a stir bar, septum, cooled under nitrogen, were added chiral methoxy Tröger's base **3** (1.12 g, 4 mmol) and 30 mL of dry THF. The solution was cooled to 0 °C, BF_3:OEt_2 (0.58 mL, 4.1 mmol) was added and allowed to stir for 15 min. The solution was cooled to −78 °C and allowed to stir for 10 min. *n*-BuLi (2.7 mL of 1.6 M solution in hexanes, 4.1 mmol) was added and the resulting orange–red solution was stirred for 10 min. Then to this benzophenone (0.75 g, 4.1 mmol, in dry THF) was added slowly through syringe, the orange–red colour disappeared at the end of addition and the solution was allowed to stir for 45 min at −78 °C. The reaction was quenched by the careful addition of cold water (5 mL). The reaction mixture was extracted in diethyl ether (2 × 15 mL) and the combined organic extracts were successively washed with water, brine solution and dried over anhydrous Na_2SO_4. After removal of the solvent, the residue was subjected to chromatography on silicagel using 20% ethyl acetate in hexane to elute the desired amino alcohol **5**.[16] Yield: 1.07 g (58%); mp 148–150 °C; $[\alpha]_D^{25} = +27 \pm 1$ (*c* 0.5, $CHCl_3$); IR (KBr): 3416, 3057, 3003, 2924, 2852, 1493, 1344, 1238, 1035, 702 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.54 (d, 2H, J = 8 Hz), 7.33–7.13 (m, 9H), 6.91 (d, 1H, J = 8.8 Hz), 6.72 (dd, 1H, J_1 = 2.8 Hz, J_2 = 6 Hz), 6.65 (dd, 1H, J_1 = 2.8 Hz, J_2 = 6 Hz), 6.28 (d, 1H, J = 2.8 Hz), 5.75 (s, 1H), 5.58 (d, 1H, J = 2.8 Hz), 4.67 (s, 1H), 4.38 (d, 1H, J = 16.8 Hz), 3.84 (d, 1H, J = 16.8 Hz), 3.61 (s, 3H), 3.54 (d, 1H, J = 13.2 Hz), 3.30 (d, 1H, J = 13.2 Hz), 3.14 (s, 3H); ^{13}C NMR ($CDCl_3$) δ 156.4, 155.3, 144.5, 142.1, 141.8, 140.9, 129.7, 128.7, 128.3, 128.2, 127.9, 127.4, 127.2, 126.3, 125.5, 116.5, 114.0, 111.1, 110.5, 78.9, 77.6, 61.9, 58.4, 55.4, 54.7.

4.4. NMR Shift experiments

NMR shift experiments were performed on a 400 MHz spectrometer at 25 °C and the samples for analysis were prepared by mixing the equimolar amounts of host **3** or **5** with the guests **6**–**11**. The final volume was adjusted with $CDCl_3$ to 0.5 mL.

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References

1. (a) Armani, G.; Bottari, F.; Saettone, M. F. *Farmaco Sci.* **1972**, *27*, 870; (b) Hannessian, S. *Total Synthesis of Natural Products: The Chiron Approach*; Pergamon: Oxford, 1983; (c) Valentine, D., Jr.; Johnsun, K. K.; Priester, W.; Sun, R. C.; Toth, K.; Saucy, G. *J. Org. Chem.* **1980**, *45*, 3698; (d) Maier, N. M.; Franco, P.; Lindner, W. *J. Chromatogr., A* **2001**, *906*, 3.
2. Eliel, E. L.; Wilen, S. H. *Stereochemistry of Organic Compounds*; John Wiley & Sons: New York, 1994.
3. (a) Pirkle, W. H.; Hoover, D. *J. Top. Stereochem.* **1982**, *13*, 263; (b) Parker, D. *Chem. Rev.* **1991**, *91*, 1441; (c) Wenzel, T. J.; Wilcox, J. D. *Chirality* **2003**, *15*, 256; (d) Gloria, U.-B.; Piero, S. *Chirality* **2005**, *17*, S243.
4. (a) Yuan, Q.; Fu, E. Q.; Wu, X. J.; Fang, M. H.; Xue, P.; Wu, C. T.; Chen, J. H. *Tetrahedron Lett.* **2002**, *43*, 3935; (b) Yang, D.; Li, X.; Fan, Y.-F.; Zhang, D.-W. *J. Am. Chem. Soc.* **2005**, *127*, 7996; (c) Li, Z. B.; Lin, J.; Zhang, H.-C.; Sabat, M.; Hyacinth, M.; Pu, L. *J. Org. Chem.* **2004**, *69*, 6284; (d) Enzo, T.; Mauro, B.; Franco, F.; Bruna, M.; Luciano, M.; Silvio, A. *Inorg. Chem.* **2003**, *42*, 4891.
5. Peña, C.; González-Sabín, J.; Alfonso, I.; Rebolledo, F.; Gotor, V. *Tetrahedron* **2008**, *64*, 7709.
6. Li, B.; Yang, X.; Wu, X.; Luo, Z.; Zhong, C.; Fu, E. *Supramol. Chem.* **2006**, *18*, 507.
7. (a) Yang, X.; Wu, X.; Fang, M.; Yuan, Q.; Fu, E. *Tetrahedron: Asymmetry* **2004**, *15*, 2491; (b) Demitras, H. N.; Bozkurt, S.; Durmaz, M.; Yilmaz, M.; Sirit, A. *Tetrahedron: Asymmetry* **2008**, *19*, 2020.
8. (a) Sergeyev, S. *Helv. Chim. Acta* **2009**, *92*, 415; (b) Valík, M.; Strongin, R. M.; Král, V. *Supramol. Chem.* **2005**, *17*, 347.
9. (a) Satishkumar, S.; Periasamy, M. *Tetrahedron: Asymmetry* **2006**, *17*, 1116; (b) Satishkumar, S.; Periasamy, M. *Indian J. Chem.* **2008**, *47B*, 1080.
10. (a) Wilcox, C. S.; Adrian, J. C.; Webb, T. H.; Zawacki, F. J. *J. Am. Chem. Soc.* **1992**, *114*, 10189; (b) Adrian, J. C., Jr.; Wilcox, C. S. *J. Am. Chem. Soc.* **1989**, *111*, 8055; (c) Goswami, S.; Ghosh, K. *Tetrahedron Lett.* **1997**, *38*, 4503.
11. Wilen, S. H.; Qi, J. Z.; Williard, P. G. *J. Org. Chem.* **1991**, *56*, 485.
12. Wang, W.; Shen, X.; Ma, F.; Li, Z.; Zhang, C. *Tetrahedron: Asymmetry* **2008**, *19*, 1193; (b) Wang, W.; Ma, F.; Shen, X.; Zhang, C. *Tetrahedron: Asymmetry* **2007**, *18*, 832; (c) Yang, X.; Wang, G.; Zhong, C.; Wu, X.; Fu, E. *Tetrahedron: Asymmetry* **2006**, *17*, 916.
13. (a) Kessar, S. V. et al *J. Chem. Soc., Chem. Commun.* **1991**, 568; (b) Harmata, M.; Carter, K. W.; Jones, D. E.; Kahraman, M. *Tetrahedron Lett.* **1996**, *37*, 6267.
14. (a) Akiyama, T. *Chem. Rev.* **2007**, *107*, 5744; (b) Poulsen, T. B.; Jørgensen, K. A. *Chem. Rev.* **2008**, *108*, 2903.
15. Mason, S. F.; Vane, G. W.; Schofield, K.; Wells, R. J.; Whitehurst, J. S. *J. Chem. Soc. B* **1967**, 553.
16. HPLC analysis of **3** and **5** was carried out on CHIRALCEL OD-H column using hexane/2-propanol = 95:5 as mobile phase, flow rate: 1.0 mL/min.
17. *Crystal data*: for complex (−)**2**·(−)**3** molecular formula: $C_{35}H_{32}N_2O_{10}$, MW = 640.63, monoclinic, space group: $P2_1$, a = 10.640(2) Å, b = 14.726(3) Å, c = 11.347(2) Å, β = 114.366(2)°, V = 1619.64 Å^3, Z = 2, ρ_c = 1.314 mg m^{-3}, μ = 0.097 mm^{-1}, T = 298(2) K. Of the 14,906 reflections collected, 6356 were unique (R_{int} = 0.0288).Refinement on all data converged at R_1 = 0.0489, wR_2 = 0.1328 (Deposition number CCDC 740895).