amine 15. Elution with ether gave 195 mg (36%) of pure (NMR) 17 as a colorless viscous oil: ^{1}H NMR δ 1.14 (s, 9), 1.84 (s, 3), 6.07 (s, 1), 7.10 (s, 2), 7.21-7.34 (m, 3), 7.53-7.50 (m, 2); ^{13}C NMR δ 25.98, 32.78, 52.76, 65.41, 126.67, 127.84, 129.00, 146.63, 180.80; IR (CCl_4) 3480, 3425, 1685 cm^{-1}.

Carboxy(4-methoxyphenyl)methyl 1,1-Dimethylethyl Nitroxide Lithium Salt (22c). To a stirred solution of recrystallized 4-methoxyphenylacetic acid (**20c**, 166 mg, 1.00 mmol) in dry THF (2 mL) at -10 °C was added 0.85 mL (2.10 mmol) of 2.5 M *n*-BuLi in hexanes. The resulting yellow solution was stirred at 40 °C for 1 h [generation of the dianion (and also of the dianions derived from acids **20a,b**) was confirmed at this point by addition of a 50-μL aliquot of this solution to MeI (0.5 mL). After being stirred for 5 min at 25 °C, the solution was diluted with ether (5 mL) and then 10% HCl (0.5 mL) was added. The ether layer was separated, dried, and evaporated. An NMR ($CDCl_3$) spectrum of the residue indicated the clean formation of the corresponding α-methyl carboxylic acid in 90-95% yield], cooled to -78 °C, and then a solution of 2-methyl-2-nitrosopropane[20] (**21**, 130 mg, 1.5 mmol) in dry THF (2 mL) was added. The solution was allowed to warm to 25 °C over 3 h and then it was stirred for 30 min. The solution was cooled to 0 °C and allowed to stir open to air for 1 h. The resulting yellow-green solution was brought to pH 8 by addition of chilled 10% HCl. The organic solvent was evaporated, and the aqueous residue was diluted with H_2O (5 mL). The yellow aqueous solution was washed with ether (discarded), and then the aqueous phase was concentrated to dryness. The residue was dried under vacuum for 12 h. The resulting yellow solid was taken up in $CHCl_3$ (5 mL) and filtered. The filtrate was dried and evaporated to give 238 mg (95%) of crude **22c** as a yellow solid: ESR, an intense 6-line spectrum, a_N = 16.0 G, a_H = 4.9 G; IR ($CHCl_3$) 3373 (br), 1632 (sh), 1603 cm^{-1}.

α-Carboxy-α-phenylethyl 1,1-Dimethylethyl Nitroxide Lithium Salt (22a). The preparation was similar to that for **22c**. From 150 mg (1.00 mmol) of distilled 2-phenylpropionic acid (**20a**), 2.5 M *n*-BuLi in hexanes (0.84 mL, 2.10 mmol), and **21** (130 mg, 1.50 mmol) was obtained 201 mg (83%) of crude **22a** as a yellow solid: ESR, an intense 3-line spectrum, a_N = 17.0 G; IR ($CHCl_3$) 3380 (br), 1610 cm^{-1}.

Carboxyphenylmethyl 1,1-Dimethylethyl Nitroxide Lithium Salt (22b). The preparation was similar to that for **22c**. From recrystallized phenylacetic acid (**20b**, 136 mg, 1.00 mmol), 2.5 M *n*-BuLi in hexanes (0.84 mL, 2.10 mmol), and **21** (130 mg, 1.50 mmol) was obtained 194 mg (85%) of crude **22b** as a yellow solid: ESR, an intense 6-line spectrum, a_N = 16.0 G, a_H = 4.9 G; IR ($CHCl_3$) 3408 (br), 1626 cm^{-1}.

Carboxy[4-(dimethylamino)phenyl]methyl 1,1-Dimethylethyl Nitroxide Lithium Salt (22d). The preparation was similar to that for **22c**. From **20d**[21] (179 mg, 1.00 mmol), 2.5 M *n*-BuLi in hexanes (0.84 mL, 2.10 mmol), and **21** (130 mg, 1.50 mmol) was obtained 232 mg (95%) of **22d** as a crude yellow solid: ESR, an intense 6-line spectrum, a_N = 16.0 G, a_H = 5.0 G; IR ($CHCl_3$) 3367 (br), 1609 cm^{-1}.

Carboxy[4-(trimethylammonio)phenyl]methyl 1,1-Dimethylethyl Nitroxide, Iodide, Lithium Salt (22e). A solution of **22d** (100 mg, 0.41 mmol) in MeI (1 mL) was stirred for 24 h. The solvent was evaporated, and the residue was dried under vacuum for 12 h to yield 153 mg (97%) of crude **22e** as a hygroscopic yellow solid: ESR, an intense 6-line spectrum, a_N = 15.5 G, a_H = 4.0 G. It can be estimated from the ESR spectral intensity that about 60% of the mass of the yellow solid was **22e**.

***N*-[Carboxy(4-methoxyphenyl)methyl]-*N*-(1,1-dimethylethyl)hydroxylamine (23).** To a stirred solution of recrystallized *p*-methoxyphenylacetic acid (**20c**, 166 mg, 1.00 mmol) in dry THF (2 mL) at -10 °C was added 2.5 M *n*-BuLi in hexanes (0.85 mL, 2.10 mmol). The resulting yellow solution was stirred at 40 °C for 1 h and then it was cooled to -78 °C. A solution of **21** (130 mg, 1.5 mmol) in dry THF (2 mL) was added. The solution was allowed to warm to 25 °C over 3.5 h, and then the solution was quenched with chilled saturated NH_4Cl (10 mL). The mixture was filtered, the organic layer of the filtrate was separated, and the aqueous layer was extracted with ether. Chilled 10% HCl was added to the aqueous layer causing **23** to separate as a white precipitate (pH 5-6). This was collected and dried under vacuum for 24 h to yield 127 mg (50%) of analytically pure **23** as a white powder: mp 140-141 °C dec; ^{1}H NMR (CD_3OD) δ 1.40 (s, 9), 3.81 (s, 3), 4.89 (s, 1), 6.96-7.54 (AB q, 4, J = 8); IR (KBr) 3450, 3150, 1612 cm^{-1}. Anal. Calcd for $C_{13}H_{19}NO_4$: C, 61.64; H, 7.56; N, 5.53. Found: C, 61.50; H, 7.63; N, 5.45.

Oxidation of 23. A solution of **23** (1.2 mg, 4.7×10^{-3} mmol) in 10% aqueous LiOH (1 mL) was stirred under air and monitored by ESR. After 10-15 min an ESR spectrum identical with that obtained above for **22c** was obtained. The intensity of the ESR signal reached a maximum after 60-70 min and began to diminish after about 180 min.

Acknowledgment. This research was supported by PHS research grants GM-27137 to J.F.W.K and HL-33550 to G.M.R.

Chiral Trifluoro Diamines as Convenient Reagents for Determining the Enantiomeric Purity of Aldehydes by Use of ^{19}F NMR Spectroscopy

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N,N'-Dimethyl-1,2-bis[*o*-, *m*-, and *p*-(trifluoromethyl)phenyl]-1,2-ethanediamines have been prepared. The meta trifluoro diamine was used as a chiral reagent for determining the enantiomeric purity of chiral aldehydes.

NMR spectroscopy is widely used for the determination of optical purity of chiral organic compounds.[1] Among the variety of proposed chiral derivatives,[2] one of the most common is α-methoxy-α-(trifluoromethyl)phenylacetic

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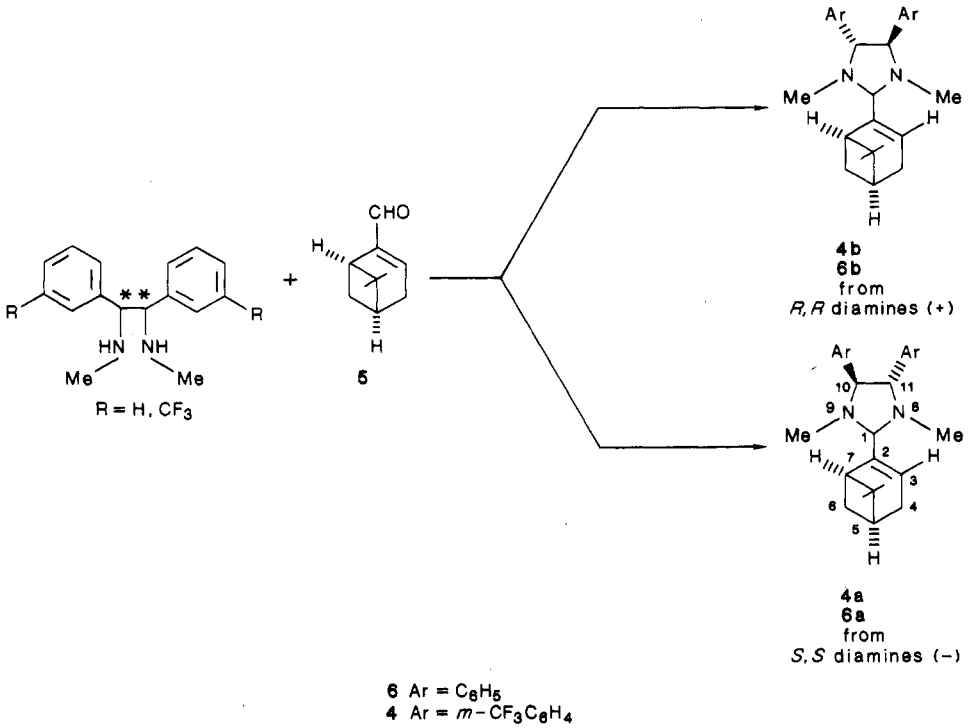
Scheme I



6 Ar = C_6H_5
4 Ar = *m*-$CF_3C_6H_4$

Table I. Diamines Obtained during the Coupling Reaction

diamine	*R*,R**/*R*,S**[a]	% yield[b] of 2
2a	70/30	40
2b	70/30	75
2c	80/20	80

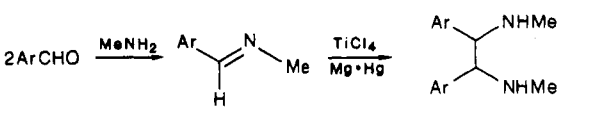
[a] Determined by ^{13}C and ^{1}H NMR analyses. [b] Yield of isolated mixture of *d,l* and meso.

acid, the Mosher reagent,[3] using the ^{19}F NMR signals from the trifluoromethyl group to determine the optical purity of alcohols, amines, etc. Few generally applicable methods exist for the determination of enantiomeric composition of chiral carbonyl compounds.[4] We have recently developed a diastereoselective, large-scale preparation of (*R*,R**)-(*d,l*)-*N,N'*-dimethyl-1,2-diphenyl-1,2-ethanediamine (**1**)[5,6] and its resolution with tartaric acid.[7] This reagent was used for optical purity determination and resolution of chiral aldehydes[8] via the formation of diastereomeric imidazolidines. During the course of our studies in the field of asymmetric synthesis of aldehydes, we have found that this methodology was not always adequate, especially when the ^{1}H and ^{13}C NMR signals of the aldehyde moiety of the imidazolidine interfere with those of the diamine unit. In this paper, we report that bis(trifluoromethyl) diamines **2** are suitable reagents for the determination of the enantiomeric purity of aldehydes and, most importantly, they are of general applicability even with small amounts of chiral aldehydes.

Figure 1. Part of the 250-MHz ^{1}H spectrum of a mixture of 70% **4b** and 30% **4a**.

Preparation and Resolution of Diamines

Racemic diamines (**2a–c**) were obtained by a two-step procedure from the commercially available ortho, meta, and para trifluoromethyl benzaldehydes, via the imines **3a–c**. Table I shows the results obtained during these coupling reactions; they fall into the same range as those previously reported[6] except for diamine **2a**. The low yield obtained for **2a** results probably from the steric hindrance of the ortho trifluoromethyl group. The racemic diamines were easily separated from the meso isomers by flash chromatography; however, only **2b** (meta) was easily re-



3a-c

1, Ar = C_6H_5
2a, Ar = *o*-$CF_3C_6H_4$
b, Ar = *m*-$CF_3C_6H_4$
c, Ar = *p*-$CF_3C_6H_4$

(1) Yamaguschi, S. In *Asymmetric Synthesis*; Morrison, J. D., Ed.; Academic Press: New York, 1983; Vol. 1, p 124.
(2) For the most recent samples see: (a) Feringa, B. L.; Smaardijk, A.; Wynberg, H. *J. Am. Chem. Soc.* **1985**, *107*, 4798. (b) Hull, W. E.; Seeholzer, K.; Baumeister, M.; Ugi, I. *Tetrahedron* **1986**, *42*, 547. (c) Trost, B. M.; Belletire, J. L.; Godleski, S.; Mc Dougal, P. G.; Bulkovee, J. M. *J. Org. Chem.* **1986**, *51*, 2370. (d) Feringa, B. L.; Stritveen, B.; Kellog, R. M. *J. Org. Chem.* **1986**, *51*, 5484. (e) Terunuma, D.; Kato, M.; Kamei, M.; Uchida, H.; Ueno, S.; Nohira, H. *Bull. Chem. Soc. Jpn.* **1986**, *59*, 3581. (f) Sweeting, L. M.; Crans, D. C.; Whitesides, G. M. *J. Org. Chem.* **1987**, *52*, 2273. (g) Chan, T. H.; Peng, Q. J.; Wang, D.; Guo, J. A. *J. Chem. Soc., Chem. Commun.* **1987**, 325.
(3) Dale, J. A.; Bull, D. L.; Mosher, H. S. *J. Org. Chem.* **1969**, *34*, 2543.
(4) (a) Lemiere, G. L.; Dommisse, R. A.; Lepoivre, J. A.; Alderweireldt, F. C.; Hiemstra, H.; Wynberg, H.; Jones, J. B.; Toone, E. J. *J. Am. Chem. Soc.* **1987**, *109*, 1363. (b) Fujiwara, J.; Fukutani, Y.; Hasagawa, M.; Maruoka, K.; Yamamoto, H. *Tetrahedron Lett.* **1984**, *106*, 5004. (c) Maruoka, K.; Yamamoto, H. *Angew. Chem., Int. Ed. Engl.* **1985**, *24*, 668. (d) Mangeney, P.; Alexakis, A.; Normant, J. F. *Tetrahedron Lett.* **1987**, *28*, 2363. (e) Agami, C.; Meynier, F.; Berlan, J.; Besace, Y.; Brochard, L. *J. Org. Chem.* **1986**, *51*, 73.
(5) Betschart, C.; Seebach, D. *Helv. Chim. Acta* **1987**, *70*, 2215.
(6) Mangeney, P.; Tejero, T.; Alexakis, A.; Grojean, F.; Normant, J. F. *Synthesis* **1988**, 255.
(7) Mangeney, P.; Grojean, F.; Alexakis, A.; Normant, J. F. *Tetrahedron Lett.* **1988**, 2675.
(8) Mangeney, P.; Alexakis, A.; Normant, J. F. *Tetrahedron Lett.* **1988**, 2677.

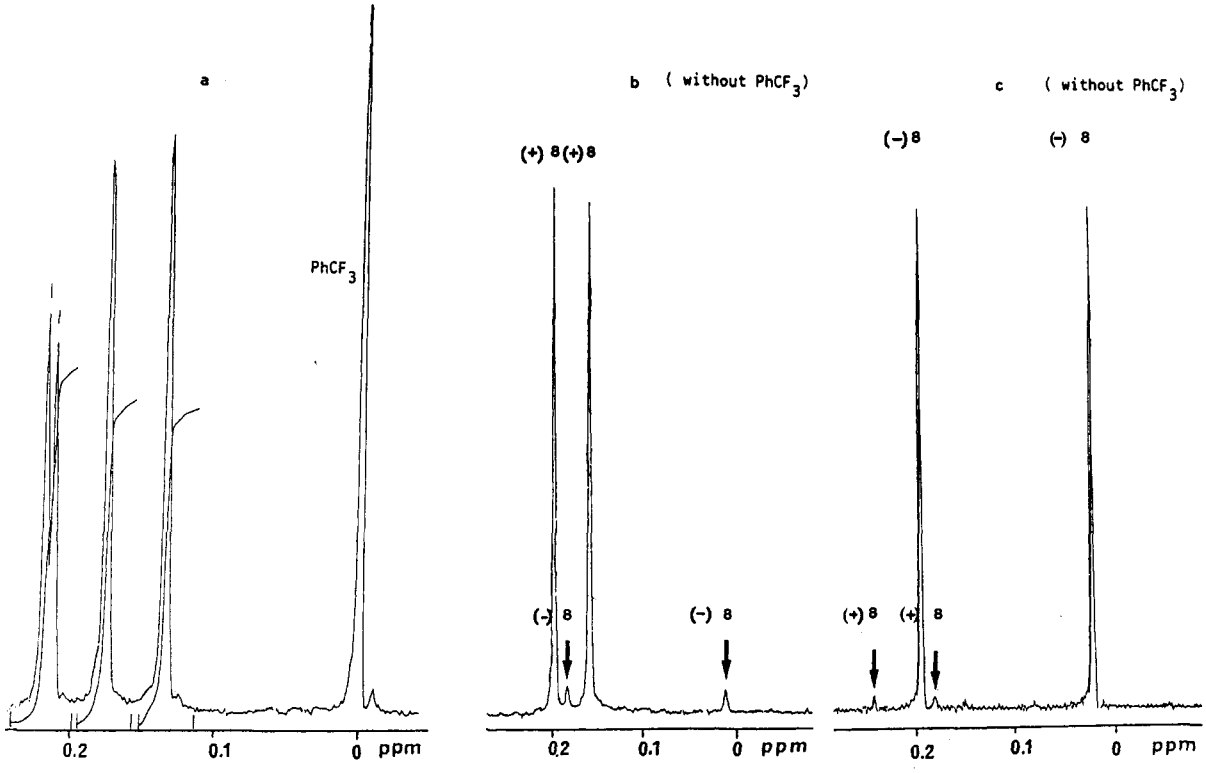


Figure 2. Part of 235-MHz ^{19}F NMR spectra of imidazolidines derived from (*R,R*)-**2b** and aldehyde **13** (a), (+)-**8** (b), and (−)-**8** (c).

solved by fractional recrystallization with optically active tartaric acid. The optical purity was measured by ^1H and ^{13}C NMR of the imidazolidine **4** derived from optically pure (−)-myrtenal **5** and was found to be ≥98%.

The absolute configuration of diamine **2b** was established by analogy with *N,N'*-dimethyl-1,2-diphenyl-1,2-ethanediamine (**1**)[9] (*S,S* configuration for (−) diamine **1**). Indeed, as for imidazolidine **6a** and **6b** (Scheme I), the ^1H NMR spectrum of imidazolidine **4a** shows a deshielded C_3-H signal and a shielded C_1-H signal relative to the corresponding signals observed for the imidazolidine **4b** (Scheme I, Figure 1). Therefore, as for DMPEDA (**1**), we have attributed the *R,R* configuration to (+) diamine **2b** and the *S,S* configuration to (−) diamine **2b**.

Determination of the Optical Purity of Chiral Aldehydes

The ability of the diamines (optically pure **2b**, (±)-**2a**, and (±)-**2c**) to induce nonequivalence, in the diastereomeric imidazolidines, suitable for optical purity measurements, was tested by recording the ^{19}F NMR spectra of the diastereomeric imidazolidines obtained from partially resolved citronellal[10] **7**.

Only imidazolidines prepared from **2a** and **2b** (ortho and meta) have chemical shifts sufficiently separated to allow accurate integration. However, with **2a** the formation of imidazolidine was not complete and thus could not be used for our purpose. Since **2b** is easier to prepare, we focused our study on this diamine. The diastereomeric imidazolidines of **2b** with a number of racemic and optically active aldehydes were prepared and the chemical shifts of their signals were recorded. The results are summarized in Table II.

The ^{19}F NMR spectra of imidazolidines prepared from a racemic aldehyde (**9**–**12**) shows four peaks of equal intensity corresponding to the CF_3 group (two peaks for each diastereomer). In each spectrum, at least two peaks are sufficiently separated to allow integration providing a measure of the diastereomeric excess (Figure 2).

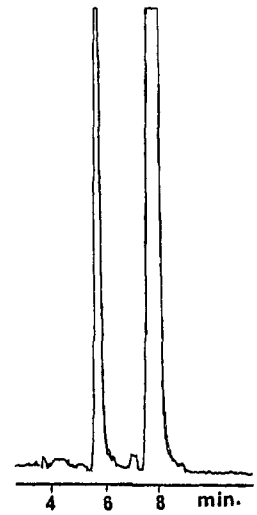


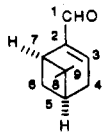
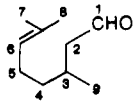
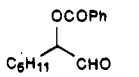
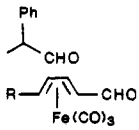
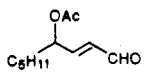
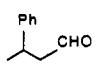
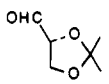
Figure 3. Chromatogram of imidazolidines derived from **13** and (*R,R*)-**2b** on a Zorbax SIL column. Solvent flow was 1 mL/min. The UV detection was performed with a Waters UV detector (λ = 263 nm).

As reported previously,[8] most diastereomeric imidazolidines are separable by usual chromatographic methods or by HPLC, providing an additional method for the determination of the enantiomeric excess (Table III) (figure 3) (except for aldehydes **5** and **10**).

We have compared the enantiomeric composition of aldehydes **7**, **8**, and **13** (see Table II) determined by optical rotation, by ^1H, ^{13}C, and ^{19}F NMR methods, and by HPLC. The agreement is good, as shown in Table IV. Moreover, we have compared the enantiomeric composition of enantiomerically enriched 3-phenylbutanal **13** (ee = 26%), $[\alpha]^{25}_D = -12°$ (*c* 0.7, Et_2O), with known methods. Thus,

(9) Meric, R.; Vigneron, J. P. *Tetrahedron Lett.* **1974**, 2059 and 2778.
(10) Citronellal was purchased from Fluka; Myrtenal and 2-phenylpropanal from Aldrich.

Table II. Chemical Shifts of ^{19}F NMR Signals for the CF_3 Groups of Imidazolidines Derived from (+)-2b and Various Chiral Aldehydes

aldehyde	compd no.	chemical shifts (^{19}F NMR),[a] ppm	de, %
	5	0.22, 0.19	100
		0.16, 0.24[b]	100
	7	0.12, 0.15, 0.17, 0.19	14
	(+)-8	0.16, 0.2	96
	(−)-8	0.01, 0.18	96
	9	0.03, 0.16, 0.2, 0.29	racemic
$R = C_4H_9$	10	0.07, 0.11, 0.15, 0.18	racemic
$R = CO_2H_3$	11	0.04, 0.09, 0.12, 0.13	racemic
	12	0.127, 0.131, 1.16, 0.17	racemic
	13	0.13, 0.17, 0.21, 0.22	28
	14	0.19, 0.35	100
		0.00, 0.14[b]	100

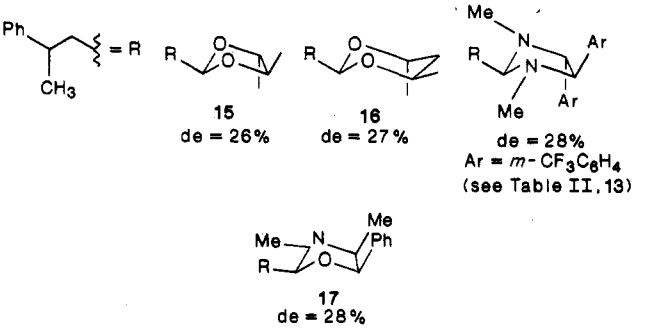
[a] ^{19}F NMR spectra were recorded on an AC250 spectrometer first without internal reference and then with $PhCF_3$ as internal reference ($\delta = 0$). [b] With (−)-**2b**.

Table III. HPLC Separation of Imidazolidines Derived from 2b and Various Aldehydes

compd no.	retention time,[a] min	solvent (Hex %–AcOEt, % TEA, 1%)	de	
5[b]	4.8	90–10	–	not resolved
5[c]	4.8	90–10	–	
7	4.8 (–), 5.28 (+)	95–5	12	
(+)-8	7.6	98–2	100[d]	
(−)-8	6.4	98–2	100[d]	
9	6.4, 5.4	95–5	0	
10	8.2	95–5	0	not resolved
11	5.72, 6.8	95–5	0	
12	8.7, 10.3	90–10	0	
13	5.8, 7.4	90–10	26	
14[b]	10.8	90–10	100[d]	
14[c]	4	90–10	100[d]	

[a] Prolabo SIL 55W or Zorbax SIL (DUPONT) 4.6 mm × 250 mm, solvent 1 mL/min; λ max 263 mm. [b] With (+)-**2b**. [c] With (−)-**2b**. [d] The diastereomeric imidazolidines are resolved, but in these cases, the minor diastereomer is not detectable.

the aldehyde was converted into the dioxolane **15** with (2*R*,3*R*)-2,3-butanediol,[4a] and dioxane **16** with (2*R*,4*R*)-2,4-pentanediol[4b] and also into the corresponding oxazolidine **17** with (1*R*,2*S*)-ephedrine.[4e] The agreement is again good and confirms that diamine **2b** is the reagent of choice for the determination of enantiomeric composition of chiral aldehydes.



^{19}F NMR spectroscopy seems to be one of the most sensitive methodologies. Indeed, it is the only way to detect the minor diastereomer for the aldehydes 8 (Table IV).

In conclusion, the measure of the enantiomeric composition of a chiral aldehyde via an imidazolidine is an excellent method for the following reasons: (1) high chemoselectivity, only aldehydes react with diamines, not ketones, very mild conditions are required to prepare the imidazolidine (Et_2O, molecular sieves, room temperature); (2) the C_2 axis of symmetry means a diasteromeric control in the formation of imidazolidine; (3) in order to avoid kinetic resolution, an excess of diamine can be employed, this excess is very easily removed by flash chromatography; (4) generally, an excellent separation of ^1H, ^{13}C, and ^{19}F NMR signals of the diastereomers is observed; (5) possibility of separation of diastereomeric imidazolidines by usual chromatographic methods and optical purity determination by HPLC.

Experimental Section

General. The ^1H, ^{13}C, and ^{19}F NMR spectra were recorded on a Bruker AC250 spectrometer. ^1H and ^{19}F NMR and spectra were recorded in C_6D_6 solutions and ^{13}C NMR spectra in $CDCl_3$ solutions; all chemical shifts for ^1H and ^{13}C are reported with respect to Me_4Si ($\delta = 0$). Chemical shifts for ^{19}F are given from Ph-CF_3 as internal standard. In order to improve resolution, ^{19}F NMR spectra were recorded with F-H irradiation. This was not necessary, except for imidazolidine derived from **12**. HPLC separations were performed on a Prolabo SIL S5W or Zorbax SIL column. Solvent flow was 1 mL/min. The UV detection was performed with a Waters UV detector (λ = 263 nm). The optical rotations were measured with a Perkin-Elmer 141 polarimeter.

Preparation of Imines. General Procedure. The (trifluoromethyl)benzaldehyde (158 g, 1 mol) is added with stirring to a 40% aqueous solution of methylamine (100 mL, 1.3 mol) at 0 °C. After 1 h at room temperature, the imine is extracted with Et_2O (3 × 100 mL), dried (Na_2CO_3), and distilled.

***N*-((2-(Trifluoromethyl)phenyl)methylidene)methanamine (3a)** (159 g, 85%): bp 140 °C (40 mm); ^1H NMR ($CDCl_3$) δ 8.52 (s, 1 H, C-H imine), 8.2–7 (m, 4 H, H aromat), 3.41 (s, 3 H, N-CH_3); IR (neat) 3080, 2940, 2910, 2880, 2760, 1700, 1645, 1560, 1310, 765 cm^{-1}.

Table IV. Comparison of the Various Ways Investigated To Determine the Enantiomeric Purity of Some Aldehydes via Their Imidazolidines Derived from 2b

compd no.	$[\alpha]^{25}_D$ (c, solvent)	ee from α_D, %	^1H[a]	^{13}C[a]	^{19}F	HPLC
7	+2 (2.5, $CHCl_3$)	11	13	12	14	12
(+)-8	+50 (0.7, Et_2O)	–	100[b]	100[b]	96	100[b]
(−)-8	−50 (0.7, Et_2O)	–	100[b]	100[b]	96	100[b]
13	−12 (0.2, Et_2O)	26	25	24	28	26

[a] See ref 8. [b] The diastereomeric imidazolidines are resolved, but in these cases, the accuracy of the method is not enough to detect the minor diastereomer.

***N*-((3-(Trifluoromethyl)phenyl)methylidene)methanamine (3b)** (163 g, 87%): bp 88 °C (24 mm); ^{1}H NMR ($CDCl_3$) δ 8.31 (s, 1 H, C-H imine), 8.1–7.4 (m, 4 H, H aromat), 3.55 (s, 3 H, N-CH_3); IR (neat) 3080, 2960, 2840, 1710, 1650, 1330, 800, 690 cm^{-1}.

***N*-((4-(Trifluoromethyl)phenyl)methylidene)methanamine (3c)** (160 g, 85%): bp 68 °C (0.1 mm); ^{1}H NMR ($CDCl_3$) δ 8.39 (s, 1 H, C-H imine), 7.6 (d, 2 H, J = 4 Hz, CH aromat), 7.3 (d, 2 H, J = 4 Hz, C-H aromat), 3.52 (s, 3 H, N-CH_3); IR (neat) 3040, 2940, 2840, 1705, 1645, 1320, 850, 750 cm^{-1}.

Preparation of Diamines 2a–c. General Procedure. To a solution of mercuric chloride (5.3 g, 0.02 mol) in distilled THF (150 mL) is added 70–80 mesh magnesium powder (18.2 g, 0.75 mol). The resulting mixture is stirred at room temperature under nitrogen for 20 min. The turbid supernatant liquid is removed, and the remaining amalgam is washed with three portions of THF (3 × 100 mL). The resulting amalgam is taken up in THF (850 mL), cooled to 0 °C, and treated dropwise with titanium tetrachloride (82 mL, 0.75 mol). The yellow-green mixture is allowed to warm to room temperature for 30 min and is then cooled at 0 °C. A solution of the imine (93.5 g, 0.5 mol) in THF (50 mL) is added, and the black reaction mixture is stirred at 0 °C for 12 h and then allowed to warm to room temperature. The reaction is quenched with a saturated aqueous solution of K_2CO_3 (250 mL) at 0 °C and stirred for 30 min at 0 °C. Ethylenediamine (100 mL) is carefully added at 0 °C, and the mixture is stirred at room temperature for 1 h.

The resulting mixture is diluted with THF (200 mL) and filtered through Celite. The filtrate is concentrated in vacuo, diluted with ether (200 mL), and washed with 1 N HCl (3 × 150 mL). The acidic aqueous solution is neutralized with 4 N NaOH and extracted with ether (3 × 100 mL). The combined ether extracts are washed with brine, dried over K_2CO_3, and concentrated in vacuo. Pure *d,l* diamines were obtained by column chromatography (SiO_2, ether saturated with NH_4OH).

***N,N'*-Dimethyl-1,2-bis(2-(trifluoromethyl)phenyl)-1,2-ethanediamine (2a)** (41 g, 22%): ^{1}H NMR ($CDCl_3$) δ 8–7.1 (m, 8 H, H aromat), 4.2 (s, 2 H, C-H benz), 2.1 (s, 6 H, N-CH_3), 2 (s, 2 H, NH); ^{13}C NMR ($CDCl_3$) δ 132, 130, 128.5, 127, 125.5 (C aromat + CF_3), 64.3 (C benz), 34.25 (N-CH_3); IR (KBr) 3300, 3240, 1320, 1160, 1125, 1070 cm^{-1}. Anal. Calcd for $C_{18}F_6H_{18}N_2$ (376.340): C, 57.45; H, 4.82. Found: C, 57.50; H, 4.67.

***N,N'*-Dimethyl-1,2-bis(3-(trifluoromethyl)phenyl)-1,2-ethanediamine (2b)** (90 g, 48%): ^{1}H NMR ($CDCl_3$) δ 7.6–7 (m, 8 H, H aromat), 3.55 (s, 2 H, C-H benz), 2.37 (s, 6 H, N-CH_3), 1.7 (s, 2 H, NH); ^{13}C NMR ($CDCl_3$) δ 141.4, 131.8, 128.7, 125.2, 124.6, 124.1 (C aromat + CF_3), 71.3 (C benz), 34.6 (N-CH_3).

***N,N'*-Dimethyl-1,2-bis(4-(trifluoromethyl)phenyl)-1,2-ethanediamine (2c)** (96 g, 51%): ^{1}H NMR ($CDCl_3$) δ 7.4 (d, 4 H, J = 4 Hz, C-H aromat), 7.15 (d, J = 4 Hz, C-H aromat), 3.6 (s, 2 H, C-H benz), 2.2 (s, 6 H, N-CH_3), 2.1 (s, 2 H, NH); IR (KBr) 3300, 3240, 1320, 1160, 1120, 1080 cm^{-1}. Anal. Calcd for $C_{18}F_6H_{18}N_2$ (376.340): C, 57.45; H, 4.82. Found: C, 57.51; H, 4.66.

Resolution of Diamine 2b. To a solution of (+)-tartaric acid (0.4 g, 2.6 mmol) in absolute ethanol (40 mL) was added solid diamine **2b** (1 g, 2.6 mmol). The solution was maintained at room temperature until crystallization was complete. The white precipitate was then removed by filtration to give 0.56 g of (+)-**2b** tartaric salt.

The diamine was regenerated by alkaline treatment (NaOH, 1 N) and extracted with ether (3 × 200 mL). The combined ether solutions were dried (Na_2CO_3) and evaporated to give 0.4 g of diamine; $[\alpha]^{25}_D$ +15° (*c* 0.5, $CHCl_3$).

This diamine was treated again as above to yield 0.2 g of optically pure (+)-**2b** ($[\alpha]^{25}_D$ = +17° (*c* 0.5, $CHCl_3$). The remaining diamines were treated in a similar manner with (+)-tartaric acid for the (+)-diamine and (−)-tartaric acid for the (−)-diamine until complete resolution (425 mg, of (+)-diamine, 425 mg of (−)-diamine, 85%): white crystals; mp 115 °C (Et_2O); IR (KBr) 3300, 3240 (N–H), 1325 (CF_3), 1160, 1130, 1070 cm^{-1}; Anal. Calcd for $C_{18}F_6H_{18}N_2$ (376.340): C, 57.45; H, 4.82. Found: C, 57.52; H, 4.65.

Preparation of Imidazolidines. General Procedure. To a stirred solution of (+)-diamine **2b** (0.13 mmol) in ether (10 mL) at room temperature in the presence of molecular sieves (4-Å) (1 g) was added an ethereal solution of aldehyde (0.13 mmol, 10 mL). The mixture was stirred for approximately 1 h or until reaction was complete as indicated by TLC. After completion the molecular sieves were filtered off, and the obtained solution was evaporated under vacuum to give the corresponding pure imidazolidine.

^{1}H and ^{13}C NMR Data for Imidazolidines Obtained from Aldehydes 5–14 (see Table II) (the minor diastereomer is noted as c′). **(−)-Myrtenal[10] (5 with (+)-2b)**: ^{1}H NMR (C_6D_6) δ 7.6–7.1 (m, 8 H, H aromat), 5.75 (m, 1 H, C_3-H), 4.18 (s, 1 H, C_1-H), 3.8 (d, J_{A-B} = 8.1 Hz, 1 H, C-H benz), 3.48 (d, J_{A-B} = 8.1 Hz, 1 H, C-H benz), 2.6–2.3 (m, 6 H, C_4-H_2, C_5-H, C_6-H_2, C_7-H), 2.19 and 2.14 (2 s, 6 H, N-CH_3), 1.37 and 0.98 (2 s, 6 H, C_9-H_3 and C_{10}-H_3); ^{13}C NMR ($CDCl_3$) δ 148.4, 140.9, 131.5, 131.1, 128.7, 128.6, 124.7, 124.5, 123.9 (C aromat + C_2 + C_3 + CF_3), 89.6 (C_1), 77.2 (C benz), 44.2 (C_7), 40.9 (C_5), 38.2 (N-CH_3), 37.1 (C_8), 35 (N-CH_3), 32.7 and 31.6 (C_4 and C_6), 26.7 and 21.8 (C_9 and C_{10}).

(−)-Myrtenal (5 with (−)-2b): ^{1}H NMR δ 7.9–6.7 (m, 8 H, H aromat), 5.4 (m, 1 H, C_3-H), 4.16 (s, 1 H, C_1-H), 3.68 (d, J_{A-B} = 8 Hz, 1 H, C-H benz), 3.38 (d, J_{A-B} = 8 Hz, 1 H, C-H benz), 2.6–2.15 (m, 6 H, C_4-H_2, C_5-H, C_6-H_2, C_7-H), 2.08 and 2 (2 s, 6 H, N-CH_3), 1.5 and 0.97 (2 s, H, C_9-H_3 and C_{10}-H_3); ^{13}C NMR ($CDCl_3$) δ 149.8, 149.9, 140.8, 131.4, 131.3, 131.1, 128.6 128.5, 124.7, 124.6, 124.4, 124.1, 124, 123.4 (C aromat + C_2 + C_3 + CF_3), 89.1 (C_1), 77.3 and 77.2 (C benz), 44 (C_7), 41 (C_5), 37.9 (C_8), 37.7 and 34.1 (N-CH_3), 31.7 and 31.3 (C_4 and C_6), 26.3 and 21.6 (C_9 and C_{10}).

Citronellal[10] (7): ^{1}H NMR (C_6D_6) δ 6.8–7 (m, 8 H, H aromat), 5.36 and 5.3 (2 m, 1 H, C′$_6$H + C_6-H), 3.9 and 3.8 (dd, J_{1-2} = 7.2 Hz, J'_{1-2} = 4.2 Hz (t, J_{1-2} = 6 Hz), 1 H, C′$_1$-H + C_1-H), 3.4 (2 d, J_{A-B} = 3 Hz, 1 H, C-H benz + C′-H benz), 3.2 (d, J_{A-B} = 8.3 Hz, 0.62 H, C-H benz), 3.22 (d, J_{A-B} = 8.3 Hz, 0.38 H, C-H benz), 2.15 and 1.97 (2 s, 1.86 H, N-CH_3), 2.1 and 2.02 (2 s, 1.14 H, N′-CH_3), 2–1.8 (m, 2 H, C_2-H + C_2′-H_2), 1.75–1.2 (m, 11 H, C_7-H_3 + C_7′-H_3, C_8-H_3 + C_8′-H_3, C_3-H + C_3′-H, C_4-H_2, C′$_4$-H_2, C_5-H_2 + C_5′-H_2), 1.08 d, J'_{9-3} = 6.6 Hz, 1.14 H, C_9′-H_3), 1 (d, J_{9-3} = 6.6 Hz, 1.86 H, C_9-H_3); ^{13}C NMR ($CDCl_3$), δ 142.5, 142.2, 132, 131.7, 129.4, 129.3, 128.3, 128, 127.6, 125.6, 125 (C aromat + CF_3), 83.7 and 83.5 (C_1 + C_1′), 80 and 79.8 (C benz + C′ benz), 76.5 and 76.2 (C benz + C′ benz), 41.4 and 40.4–39.1 and 38.2–38.7 and 38 (N-CH_3 + N′-CH_3 and C_2 + C_2′), 35 and 34.5 (C_5 + C_5′), 29.5 and 29.4 (C_3 + C_3′), 26.4, 26.2, 26.1 (C_7 + C_7′ and C_4 + C_4′), 21 and 20.2 (C_8 + C_8′), 16 (C_9 + C_9′).

Citronellal (7 + Racemic Diamine 2c): ^{1}H NMR (C_6D_6) δ 7.5–6.9 (m, 8 H, H aromat), 5.3 (m, 1 H, C_6-H), 3.9 and 3.83 (dd, J_{1-2} = 7.8 Hz, J_{1-2} = 4.4 Hz (t, J_{1-2} = $J_{1-2'}$ = 6 Hz), 1 H, C_1-H), 3.41 and 3.28 and 3.21 (3 d, J_{A-B} = 9.1 Hz, 2 H, C-H benz), 2.29 and 2.11 and 2.04 and 1.99 (4 s, N-CH_3), 1.08 and 1 (2 d, J_{9-3} = 6.5 Hz, 3 H, C_9-H_3); ^{13}C NMR ($CDCl_3$) δ 144.7, 144.5, 144.2, 131.4, 128.5, 128.3, 128.2, 128, 127, 125.3, 125.2, 124.9, 124.8, 121.6 (C aromat + CF_3), 83.3 and 83.2 (C_1), 79.3 and 79.2 (C benz), 76.1 and 75.7 (C benz), 41, 39.9, 38.2, 37.4 (4 N-CH_3), 38.4, 35.2, 34.6, 29, 28.8, 25.7, 25.5, 20.6, 19.9, 17.7.

(+)-2-(Benzoyloxy)heptanal[8] (8): ^{1}H NMR (C_6D_6) δ 8.4–6.7 (m, 13 H, H aromat), 5.62 (m, 1 H, C_2-H), 3.98 (2 d, J_{A-B} = 8.4 Hz, C-H benz, J_{1-2} = 1.4 Hz, 2 H, C_1-H), 3.5 (d, J_{A-B} = 8.4 Hz, 1 H, C-H benz), 2.29 (s, 3 H, N-CH_3), 2.13 (s, 3 H, N-CH_3); ^{13}C NMR ($CDCl_3$) δ 166.3 (CO), 140.9, 140, 133, 131.9, 131.4, 131.2, 130.7, 124.8, 124.6, 124.5, 124.1, 124 (C aromat + CF_3), 84.9 (C_1), 78.7 (C benz), 77 (C benz), 75.1 (C_2), 42.1 and 33.3 (2 N-CH_3), 31.9, 31.1, 25.8, 22.6, 14 (C_5H_{11}).

(−)-2-(Benzoyloxy)heptanal (8); ^{1}H NMR (C_6D_6) δ 8.4–6.8 (m, 13 H, H aromat), 5.85 (dt, J_{2-3} = 10 Hz, J_{2-1} = 2.8 Hz, 1 H, C_2-H), 4.15 (d, J_{2-1} = 2.8 Hz, 1 H, C_1-H), 3.76 (d, J_{A-B} = 8.5 Hz, 1 H, C-H benz), 3.4 (d, J = 8.5 Hz, 1 H, C-H benz), 2.27 and 2.21 (2 s, 6 H, 2 N-CH_3); ^{13}C NMR ($CDCl_3$) δ 166.3 (CO), 140.5, 139.6, 135.5, 134.5, 133, 131.8, 131.1, 130.8, 130.5, 130.2, 120.7, 129, 128.8, 128.7, 128.5, 128.4, 126.9, 124.8 (C aromat + CF_3), 85.1 (C_1), 77 and 76.1 (C benz), 75.2 (C_2), 40.4 and 33.8 (N-CH_3), 31.9, 31, 25.7, 22.8, 14 (C_5H_{11}).

2-Phenylpropanal[10] (9): ^{1}H NMR (C_6D_6) δ 7.75–6.7 (m, 13 H, H aromat), 4.03 (d, J_{2-1} = 2.9 Hz, 0.5 H, C_1-H), 3.82 (d, J_{1-2} = 3.4 Hz, 0.5 H, C_1′-H), 3.7 (2 d, J_{A-B} = 8.7 Hz and 8.8 Hz, 1 H, C-H benz), 3.45 (d, J_{A-B} = 8.8 Hz, 0.5 H, C-H benz), 3.37 (d, J_{A-B} = 8.7 Hz, 0.5 H, C-H benz), 3.1 (m, 1 H, C_2-H), 2.06 and 2.02 and 1.96 and 1.75 (4 s, 6 H, N-CH_3 + N′-CH_3), 1.45 and 1.42 (2 d, J_{1-3} = 1.9 Hz, 3 H, C_3-H_3 + C_3′ − H_3); ^{13}C NMR ($CDCl_3$) δ 144.5, 144, 142, 141.8, 140, 132, 132.8, 131.8, 131.2, 129.2, 128.8, 128.7, 128.6,

128.5, 128.4, 128.2, 128, 126.2, 124.4, 124.3 (C aromat + CF_3), 91 and 89.3 (C_1 + C_1'), 78.3 and 76.8 (C benz + C′ benz), 74.5 and 74 (C benz + C′ benz), 43.5, 43.2, 41.9, 40.7 (2 N-CH_3 and 2 N′-CH_3), 35.6–33.7 (C_2), 17.2, 15.3 (C_3).

(*E*,*E*)-2,4-Nonadienal iron tricarbonyl complex[11] (10): ^{1}H NMR (C_6D_6) δ 7.8–6.8 (m, 8 H, H aromat), 4.7 and 4.55 (2 m, 2 H, C_4-H and C_3-H), 3.6–3.05 (m, 3 H, C_1-H + C-H benz), 2.5, 2.4, 2, 1.9 (4 s, 6 H, N-CH_3 + N′-CH_3), 1.6–0.7 (m, 11 H, C_4H_9 + C_5-H and C_2-H); ^{13}C NMR ($CDCl_3$) δ 210 ($FeCO_3$), 140.5, 131.6, 131.2, 131, 128.8, 128.5, 124.9, 124.5 (C aromat + CF_3), 88.1, 87, 86.2, 84.1, 82.2, 82 (C_1 + C_3 + C_4), 78.6 (C benz), 76.5 (C benz), 65.8 and 65.7–62.6 (C_2 + C_5), 40, 39.3, 37.4, 34.4, 34.3, 34.2, 33.9, 22.4, 13.9 (N-CH_3 + C_4H_9).

Methyl 6-Oxo-(*E*,*E*)-2,4-hexadienoate iron tricarbonyl complex[11] (11): ^{1}H NMR (C_6D_6) δ 7.9–6.8 (m, 8 H, H aromat), 5.7 (dd, J_{4-5} = 8.7 Hz, J_{4-3} = 5.2 Hz, 0.5 H, C_4-H), 5.6 (dd, J_{4-5} = 8.7 Hz, J_{4-3} = 5.2 Hz, 0.5 H, C_4-H), 4.7 (dd, J_{3-2} = 8.7 Hz, J_{3-4} = 5.2 Hz, 0.5 H, C_3-H), 4.5 (dd, J_{3-2} = 8.7 Hz, J_{3-4} = 5.2 Hz, 0.5 H, C_3-H), 3.65–3.05 (m, 6 H, C_1-H, CO_2CH_3, C-H benz), 2.32 (s, 1.5 H, N-CH_3), 2.22 (s, 1.5 H, N-CH_3), 1.98 (1, 1.5 H, N-CH_3), 1.8 (s, 1.5 H, N-CH_3), 1.3–0.9 (m, 2 H, C_2-H and C_5-H); ^{13}C NMR ($CDCl_3$) δ 210 ($FeCO_3$), 172 (CO), 140.7, 140.2, 140.1, 131.9, 131.5, 131.2, 131, 129.1, 129, 124.8 (C aromat + CF_3), 87.2, 87, 85.5, 84.5, 83.3 (C_1 + C_3 and C_4), 79–78.8 (C benz + C′ benz), 75.9–74.8 (C benz + C′ benz), 65 and 61.7 (C_5), 51.9 (OCH_3), 47.4 and 46.6 (C_2 + C_2'), 40.5, 40.2, 37.2, 34.4 (N-CH_3).

4-Acetoxy-2(*E*)-nonenal[8] (12): ^{1}H NMR (C_6D_6) δ 7.6–6.8 (m, 8 H, H aromat), 5.6 (m, 2 H, C_2-H and C_3-H), 5.5 (m, 1 H, C_4-H), 4.1 (d, J_{1-2} = 8.7 Hz, 1 H, C_1-H), 3.5 (2 d, J_{A-B} = 7 Hz, 1 H, C-H benz), 3.24 (2 d, J_{A-B} = 7 Hz, 1 H, CH benz), 2.13, 2.1, 2, 1.99 (4 s, 6 H, N-CH_3 + N′-CH_3), 1.77–1.76 (2 s, $OCOCH_3$ + $OCOCH_3$), 1.7–0.8 (m, 11 H, C_5H_{11}); ^{13}C NMR ($CDCl_3$) δ 140.5, 131.6, 131.2, 131, 128.8, 128.5, 124.9, 124.5 (C aromat + C_2 + C_3 + CF_3), 86.7 and 86.6 (C_1 + C_1'), 77.5 and 77.7 (C benz), 77 and 76.7 (C′ benz), 74 and 73.9 (C_4 + C_4'), 37.45 and 37.4 (N-CH_3), 35.15 and 35.2 (N′-CH_3), 34.5, 31.5, 24.9, 22.5, 13.9 (C_5H_{11}).

3-Phenylbutanal[13] (13): ^{1}H NMR (C_6D_6) δ 7.7–6.7 (m, 13 H, H aromat), 3.63, 3.28, 3.1 (3 m, 4 H, C_1-H + C_1'-H + C_3-H + C_3'-H, C-H benz + C′-H benz), 2.2–1.5 (m, + 4s (2.11 + 1.97 + 1.9 + 1.5), 8 H, C_2-H_2 + C_2'-H_2 + N-CH_3 + N′-CH_3), 1.36 (d, J = 6.4 Hz, 1.8 H, C_4-H_3), 1.26 (d, J= 6.4, 1, 2 H, C_4'-H_3); ^{13}C NMR ($CDCl_3$) δ 147.9, 147.3, 141.9, 141.6, 141.2, 140, 131.5, 131.4, 131.2, 131, 129, 128.7, 128.6, 127.3, 127.2, 127, 126.5, 126.1, 124.8, 124.7, 124.6, 124.5, 124.4, 124.3, 124 (C aromat + CF_3), 83.3 and 83 (C_1 + C_1'), 79.7 and 79.35 (C benz + C′ benz), 75.9 and 75.8 (C benz + C′ benz), 41.6 and 40.4, 39.8 and 38.3 (N-CH_3 + N′-CH_3), 36.3 and 36.24 (C_2 + C_2'), 35 and 34.5 (C_3 + C_3'), 24.5 and 22 (C_4 + C_4').

(*R*)-2,3-Isopropylideneglyceraldehyde[12] (14 with (+)-2b): ^{1}H NMR (C_6D_6) δ 7.9–6.7 (m, 8 H, H aromat), 4.1 (td, J_{2-3} = 7.3 Hz, J_{1-2} = 3 Hz, 1 H, C_2-H), 3.89 (d, J_{A-B} = 8.7 Hz, 1 H, C-H benz), 3.8 (d, J_{2-3} = 7.3 Hz, 2 H, C_3-H_2), 3.66 (d, J_{1-2} = 3 Hz, 1 H, C_1-H), 3.4 (d, J_{A-B} = 8.7 Hz, 1 H, C-H benz), 2.12 (2 s, 6 H, N-CH_3), 1.63 (s, 3 H, C_5-H), 1.4 (s, 3 H, C_6-H); ^{13}C NMR ($CDCl_3$) δ 140.8, 140.2, 138.5, 138, 132, 128.2, 128.6, 124.1, 124, 123.5 (C aromat + CF_3), 109 (C_4), 83.5 (C_1), 78.7–77.6 (C benz), 75.4 (C_2), 66.2 (C_3), 40.2–33.9 (N-CH_3), 26.6–25.6 (C_5 and C_6).

(*R*)-2,3-Isopropylideneglyceraldehyde (14 with (−)-2b): ^{1}H NMR (C_6D_6) δ 7.5–6.7 (m, 8 H, H aromat), 4.18 (m, 2 H, C_2-H and C-H benz), 4 (m, 2 H, C_3-H_2), 3.25 (m, 2 H, C_1-H, C-H benz), 2.17 (s, 6 H, N-CH_3), 1.48–1.4 (2 s, 6 H, C_5-H and C_6-H); ^{13}C NMR ($CDCl_3$) δ 140.8, 140, 131.8, 131.4, 131.3, 128.8, 128.4, 125, 124.9, 124.8, 124.7, 124.6, 124.5 (C aromat + CF_3), 110 (C_4), 85.3 (C_1), 78.7–76.9 (C benz), 75.1 (C_2), 66.6 (C_3), 42.5–34 (N-CH_3), 26.6–25 (C_5 and C_6).

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The Urea Connection. Intramolecular Diels–Alder Reactions of Ureas

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Intramolecular Diels–Alder reactions with a urea tether afford adducts in good yields, yet the analogous carbamates fail to cyclize.

The intramolecular Diels–Alder reaction has become a powerful tool for constructing complex natural products.[1] As its potential continues to be probed, researchers have become increasingly aware that the atomic makeup of the tether can significantly affect the success of the reaction. In a classic set of experiments Boeckman and co-workers reported that while the ether **1** (X = H, H) cyclized to form **2**, the corresponding ester **1** (X = O) could not be induced to cyclize.[2] Babayan discovered that the ammonium salt **3** cyclized at 100 °C, whereas the tertiary amine **4** did not cyclize[3] (Scheme I). Many functional groups have been empolyed as part of the tether. Herein we report the first use of the urea moiety as part of a tether.

In connection with our studies on the intramolecular Diels–Alder reactions of indoles,[4] we required a tether that was sturdy enough to withstand thermolysis, oxidation, and mild reduction conditions and also amenable to selective cleavage at a later stage in the synthesis. The carbamate **5** was initially examined. Carbamate **5** was prepared in 50% yield by treating the sodium salt of indole-3-carboxaldehyde (**6**) with carbon dioxide gas followed by

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