2:3 chloroform–hexane and twice with 7:3 chloroform–hexane. The resulting broad zone was divided into three equal parts. The top third was predominantly **4e**, the center was **4f**, and the bottom was **4g**. Rechromatography of each fraction gave pure samples (by IR and NMR comparison) of **4e** (13 mg), **4f** (12 mg), and **4g** (15 mg). In addition, benzoic acid (20 mg) was isolated.

B. With Sodium Hydride. Sodium hydride (55% dispersion in mineral oil, 4.4 mg) was added to a solution of **3e** (20 mg) in anhydrous ether and allowed to stand at room temperature for 15 min. Excess formic acid was added and the cloudy solution was filtered and concentrated to give a light-colored oil (16 mg). NMR analysis indicated the presence of a mixture of **4e**, **4f**, and **4g** in the ratio 1:0.1:1. The presence of the three esters was further confirmed by gas chromatographic analysis.

Benzoin *p*-Methoxybenzoate (6b). *p*-Methoxybenzoyl chloride (8.7 g) was added to a stirred solution of benzoin (11.1 g) in dry pyridine (50 mL). After being stirred for 2 h at room temperature, the solution was poured into cold, dilute sulfuric acid and worked up in the usual way to give crude ester (17.8 g, 95%). Crystallization from methanol gave **6b**, mp 99–100 °C, unchanged by further crystallization. IR 1720, 1690 cm^{-1}; UV (MeOH) 257 (ϵ 30000), 313 nm (350); NMR δ 7.9–8.3 (m, 4 H with superimposed doublet, J = 8 Hz), 7.2–7.7 (m, 8 H), 7.10 (1 H), 6.90 (d, J = 8 Hz, 2 H), 3.85 (3 H).

Anal. Calcd for $C_{22}H_{18}O_4$: C, 76.28; H, 5.24. Found: C, 76.18; H, 5.30.

Benzoin *p*-Chlorobenzoate (6a). Pure **6a** was obtained by reaction of *p*-chlorobenzoyl chloride with benzoin in pyridine using the procedure described above for **6b** followed by crystallization from ethanol, mp 112–113 °C: IR 1740, 1690 cm^{-1}; UV max (MeOH) 248 (ϵ 32000), sh 315 nm (400); NMR δ 7.9–8.3 (m, 4 H with superimposed doublet, J = 8 Hz, at 8.10), 7.3–7.7 (m, 10 H), 7.15 (1 H).

Anal. Calcd for $C_{21}H_{15}ClO_3$: C, 71.89; H, 4.37; Cl, 10.01. Found: C, 71.78; H, 4.33; Cl, 10.13.

***p*-Chlorobenzoin Benzoate (7a).** *p*-Chlorobenzoin[20] and benzoyl chloride in pyridine afforded **7a** by using the procedure described above. The pure sample was crystallized from methanol, mp 93–94 °C: IR 1720, 1690 cm^{-1}; NMR δ 7.9–8.3 (m, 4 H, with superimposed doublet at δ 8.00, J = 8 Hz), 7.3–7.7 (m, 10 H), 7.10 (1 H); MS, m/e (relative intensity) 350.0727 (M^+, 6), 211.0764 (100); $C_{21}H_{15}ClO_3$ requires 350.0744.

α,β-Stilbenediol Bis(*p*-chlorobenzoate) (9). The preparation was based on the procedure of Bauld[21] for the dibenzoate. A solution of benzil (2.1 g) in dry benzene (50 mL) was added dropwise to stirred magnesium turnings (0.24 g, activated with iodine) under nitrogen, and the resulting suspension was refluxed for 24 h. The dark solution was then treated with *p*-chlorobenzoyl chloride (5.0 g) and refluxed for an additional 30 min. Filtration and concentration afforded a crude product, which crystallized on standing. Two crystallizations from methanol gave **9** (1.3 g), mp 153–154 °C: IR 1740 cm^{-1}; NMR δ 7.3–8.1 (m); MS, m/e (relative intensity) 492.0562 (M^+ + 4, 3.2), 490.0580 (M^+ + 2, 16.5), 488.0594 (M^+, 27.1), 138.9929 (100); $C_{28}H_{18}Cl_2O_4$ requires 488.0605.

Reaction of Benzoin *p*-Chlorobenzoate (6a) with Sodium Hydride in Benzene. A solution of **6a** (1 g) in benzene (70 mL) was boiled down to 50 mL and cooled under nitrogen, and sodium hydride (127 mg of 55% dispersion in mineral oil) was added. After a 12-h reflux under nitrogen, the brown solution was cooled and acidified with excess acetic acid. A small amount of insoluble material was filtered off and the filtrate concentrated to give a yellow oil (0.9 g). A portion (490 mg) was run twice on preparative plates with 4:1 hexane–chloroform, twice with 3:1 hexane–chloroform, and twice with 5:2 hexane–chloroform to give desoxybenzoin (45 mg), unidentified material (95 mg), a mixed fraction (150 mg) consisting, by NMR analysis, of a mixture of **6a**, **7a**, and **8a**, and pure samples of **7a** (48 mg; identity by comparison of IR and NMR spectra) and **8a** (105 mg).

The analytical sample of *p'*-chlorobenzoin benzoate (**8a**) was obtained by two crystallizations from methylene chloride–hexane, mp 119 °C: IR (chloroform) 1720, 1700 cm^{-1}: NMR δ 7.9–8.3 (m, 4 H), 7.3–7.7 (m, 10 H), 7.10 (1 H); MS, m/e (relative intensity) 352 (M^+ + 2, 2), 350 (M^+, 7), 105 (100).

Anal. Calcd for $C_{21}H_{15}ClO_3$: C, 71.89; H, 4.37. Found: C, 71.72; H, 4.29.

Reaction of Benzoin *p*-Methoxybenzoate (6b) with Sodium Hydride in Benzene. The reaction of **6b** (1 g) was run and worked up as described above for the *p*-chloro isomer to give a yellow oil (0.75 g). Preparative chromatography as described above in the reaction of **6a** gave benzil (14 mg), desoxybenzoin (17 mg), benzoin benzoate (20 mg), an unidentified fraction (15 mg), a fraction (120 mg) containing **6b**, **7b**, and **8b** (by NMR analysis), and a fraction (270 mg) containing **6b** and **8b** by NMR. A portion (108 mg) of the last fraction in methanol (5 mL) under nitrogen was treated with 2 mL of 2.8×10^{-2} N methanolic potassium hydroxide for 2 h at room temperature, then acidified, and concentrated. The residue was taken up in methylene chloride and filtered and the filtrate concentrated to give an oil (100 mg). This oil was chromatographed on two plates by running 4 times with 1:1 chloroform–hexane to give methyl benzoate (10 mg), benzil (4 mg), methyl *p*-methoxybenzoate (22 mg), benzoin (29 mg), *p*-methoxybenzoin (32 mg), and a trace (2 mg) of a yellow material, possibly *p*-methoxybenzil. The *p*-methoxybenzoin had mp 105–106 °C (lit.[22] mp 105.5 °C); other compounds were identified by TLC and spectral comparison with authentic samples.

Reaction of α,β-Stilbenediol Bis(*p*-chlorobenzoate) (9) with Sodium Phenoxide. A solution of **9** (225 mg) in dry benzene containing sodium phenoxide (160 mg) under nitrogen was treated with a few drops of dimethylformamide and stirred at room temperature. The solution darkened and then became yellow-orange. After 35 min, it was acidified with excess acetic acid, a small amount of insoluble material was filtered off, and the filtrate was concentrated under reduced pressure on a water bath. The crude material was run twice on three plates with chloroform to give phenyl *p*-chlorobenzoate (88 mg), phenol (90 mg), and a fraction (152 mg, 90%) consisting by NMR of a mixture of **6a**, **7a**, and **8a**. The ester fraction was run 5 times on four plates with 2:3 chloroform–hexane. A narrow bottom streak gave **8a** (32 mg). The broad upper streak was arbitrarily divided in half. The lower half was run 5 times with 20:1 hexane–ethyl acetate to give three separate streaks. The upper one gave **7a** (12 mg), the center streak gave **6a** (25 mg), and the lower streak gave additional **8a** (7 mg). Compounds were identified by spectral comparison with samples as described above.

Registry No. **3e**, 15138-21-3; **4e**, 21478-63-7; **4f**, 19347-08-1; **4g**, 19275-80-0; **6a**, 114678-98-7; **6b**, 114678-99-8; **7a**, 114679-00-4; **7b**, 38828-29-4; **8a**, 114679-01-5; **8b**, 38828-30-7; **9**, 114679-02-6; benzoic acid, 65-85-0; *p*-methoxybenzoyl chloride, 100-07-2; benzoin, 119-53-9; *p*-chlorobenzoyl chloride, 122-01-0; *p*-chlorobenzoin, 39774-18-0; benzoyl chloride, 98-88-4; benzil, 134-81-6; desoxybenzoin, 451-40-1; methyl benzoate, 93-58-3; methyl *p*-methoxybenzoate, 121-98-2; *p*-methoxybenzoin, 4254-17-5; *p*-methoxybenzil, 22711-21-3; phenyl *p*-chlorobenzoate, 1871-38-1; phenol, 108-95-2.

(20) Arnold, R. T.; Fuson, R. C. *J. Am. Chem. Soc.* **1936**, *58*, 1295.
(21) Bauld, N. L. *J. Am. Chem. Soc.* **1962**, *84*, 4345. We assume this compound to be the trans isomer.
(22) Kinney, C. R. *J. Am. Chem. Soc.* **1929**, *51*, 1592.

α-Methoxy-α-(trifluoromethyl)benzyl Isocyanate. A Convenient Reagent for the Determination of the Enantiomeric Composition of Primary and Secondary Amines

Aiko Nabeya* and Tadatoshi Endo

Tsurumi University, School of Dental Medicine, 2-1-3 Tsurumi, Tsurumi-ku, Yokohama, Japan 00230

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Several methods have been found for the determination of the enantiomeric composition of chiral amines by NMR analysis. These methods are based on the fact that diastereotopic nuclei have different chemical shifts. In order

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Table I. NMR Chemical Shifts of Diastereomeric Ureas and Urethanes Derived from (*S*)-(−)-α-Methoxy-α-(trifluoromethyl)benzyl Isocyanate[a]

			^{1}H			^{19}F	
entry	amine or alcohol	*R* or *S*	CH_3	$\|\Delta\delta\|$[b] for CH_3	other useful signal	CF_3	$\|\Delta\delta\|$ for CF_3
1	$CH_3CH_2CHCH_3$ (NH$_2$)	*RS*	0.628 1.004	0.38 (0.07)[c]	0.407[d] 0.805[d]	−1.523 −1.551	0.03 (0.10)
2	$CH_3CH_2CHCH_2NH_2$ (CH_3)	*R* *S*	0.515 0.577	0.06		−1.463 −1.463	0.00
3	CH_3, CH_3, $CHCHCH_3$ (NH$_2$)	*RS*	0.556 0.964	0.41	0.344; 0.422[e] 0.720; 0.770[e]	−1.486 −1.532	0.04
4	$PhCHCH_3$ (NH_2)	*R* *S*	0.979 1.332	0.35 (0.07)		−1.503 −1.503	0.00 (0.25)
5	CH_3CHNH_2 (1-Naph)	*R* *S*	1.144 1.485	0.34 (0.11)		−1.490 −1.623	0.13 (0.29)
6	CH_3, NH	*RS*	1.424 1.465	0.04		−4.465 −4.559	0.09
7	PhN=C(H)N, CH_2, O, CH_2, CH, CH_3	*R* *S*	1.395 1.395	0.00		−2.491 −2.565	0.07
8	PhN=C(H)N, CH_2, S, CH_2, CH, CH_3	*R* *S*	1.301 1.294	0.01		−2.777 −2.842	0.06
9	$CH_3CH_2CHCH_3$ (OH)	*R* *S*	1.058 1.179	0.12 (0.13)	0.864[f] 0.928[f]	−3.659 −3.704	0.05 (0.00)
10	CH_3, CH_3C, $CHCH_3$ (CH_3, OH)	*RS*	0.891[g] 1.114[g]	0.22 (0.07)	0.727[h] 0.782[h]	−3.077[i] −3.425 −3.710	 (0.22)
11	$PhCHCH_3$ (OH)	*R* *S*	*j* 1.512	(0.06)		 −3.685[k]	(0.20)
12	$PhCHCH_2CH_3$ (OH)	*R* *S*	0.711[g] 0.865	0.15 (0.08)		−3.498[g] −3.704	0.21 (0.38)

[a] Measured in $CDCl_3$ using TMS as an internal standard in ^{1}H and CF_3COOH as an external standard in ^{19}F NMR. All spectra were taken on a JEOL GSX-270 spectrometer (270 MHz). [b] $|\Delta\delta| = |\delta(S,R) - \delta(S,S)|$. [c] Values in parentheses are of MTPA amides or esters (ref 8a for CH_3 and ref 8b for CF_3). [d] Protons at C-4. [e] Methyl protons of isopropyl moiety. Nonequivalence of the two methyls is observed. [f] Protons at C-4. [g] Broad. [h] Methyl protons of *t*-Bu. [i] Three signals, and the two of them are broad. [j] The urethane was not obtained. [k] Broad and split.

to induce such magnetic nonequivalence, several types of chiral reagents have been used so far: chiral derivatizing reagents to make diastereomeric compounds,[1] chiral solvents in which diastereomeric solvates are formed,[2] and chiral lanthanide[3] or other shift reagents[4] to form diastereomeric complexes or salts. In the course of our study on the ring-opening reaction of azetidines, it has become desirable to have a convenient way to determine the enantiomeric composition of amines by ^{1}H or ^{19}F NMR analysis. Utilization of diastereomers in which the chiral centers are linked covalently seemed preferable in the sense that the diastereomers have definite NMR spectra and the chemical shift differences are generally large in these diastereomers. Among the chiral derivatizing reagents known thus far, α-methoxy-α-(trifluoromethyl)-phenylacetic acid chloride[1e] is the most prominent and has been widely used for amines and alcohols. However, one disadvantage in using the acid chloride is having to add a dehydrochlorinating agent to make the derivatives and to remove the hydrochloride before taking the NMR. To avoid this problem, we have undertaken the synthesis of an isocyanate with the α-methoxy-α-(trifluoromethyl)-benzyl moiety, which should give the diastereomeric ureas by the addition rather than the condensation reaction, and the diastereomers are expected to be useful for both ^{1}H and ^{19}F NMR analyses.

(*S*)-(−)-α-Methoxy-α-(trifluoromethyl)benzyl isocyanate ((*S*)-1) was prepared from (*R*)-(+)-α-methoxy-α-(trifluoromethyl)phenylacetic acid ((*R*)-(+)-MTPA) via the acid azide through the Curtius rearrangement. It is generally accepted that the Curtius rearrangement occurs with complete retention of configuration at the migrating alkyl center.[5] Actually, it was found that the *R* acid gave the

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(2) Pirkle, W. H.; Hoover, D. J. *Topics in Stereochemistry*; Eliel, E. L., Allinger, N. L., Wilen, S. H., Eds.; Wiley-Interscience: New York, 1982; Vol. 13, p 263.

(3) Sullivan, G. R. *Topics in Stereochemistry*; Eliel, E. L., Allinger, N. L., Eds.; Wiley-Interscience: New York, 1978; Vol. 10, p 287.

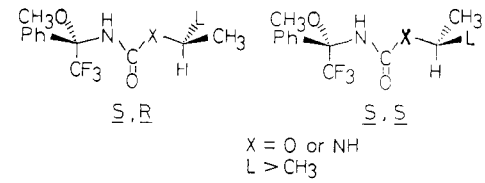
(4) (a) Mikołajczyk, M.; Omelańczuk, J.; Leitloff, M.; Drabowicz, J.; Ejchart, A.; Jurczak, J. *J. Am. Chem. Soc.* **1978**, *100*, 7003. (b) Villani, F. J., Jr.; Costanzo, M. J.; Inners, C. R.; Mutter, M. S.; McClure, D. E. *J. Org. Chem.* **1986**, *51*, 3715.

S isocyanate without any racemization. The *S* isocyanate ((*S*)-**1**) gave an optically pure urea derivative on addition either to (*S*)- or (*R*)-1-(1-naphthyl)ethylamine. The urea derivative with the *S* amine ((*S*,*S*)-**2**) (Table I, entry 5) has a doublet at 1.485 ppm attributable to the methyl protons in the amine residue and not at 1.144 ppm where the corresponding doublet is found in the urea derivative of (*S*)-**1** and *R* amine ((*S*,*R*)-**2**), and vice versa, the urea derived from (*S*)-**1** and *R* amine has a doublet only at 1.144 ppm in the NMR spectrum. In the ^{19}F NMR, (*S*,*S*)-**2** has a peak at −1.623 ppm (with trifluoroacetic acid as an external standard), while in (*S*,*R*)-**2**, a peak is found at −1.490 ppm.

With other primary and secondary amines also, the isocyanate has been proven to be a useful chiral derivatizing agent. Addition of (*S*)-**1** to a $CDCl_3$ solution of an amine in a slight excess gives a sample for the NMR. The signal of OCH_3 of **1** is found further downfield (around 3.3 ppm) than the methyl proton signals in usual amine residues so that the presence of excess **1** does not interfere with the ^{1}H NMR analysis. Additional information was obtained in many cases from the ^{19}F NMR to ascertain or supplement the ^{1}H NMR data. Thus our original purpose to determine the enantiomeric composition of 2-(phenylimino)-6-methyltetrahydro-1,3-oxazine[6] (Table I, entry 7) was attained by the ^{19}F NMR analysis, despite the fact that the ^{1}H NMR did not show any discernible nonequivalence of the methyl protons between the diastereomers. Results obtained with amines are summarized in Table I.

Alcohols react with **1** much more slowly than do amines. Addition of **1** to a solution of 5 mg of 2-butanol in 0.6 mL of $CDCl_3$ (for NMR sample) did not give the urethane at all after several hours. However, in the presence of DABCO in a more concentrated solution (5 mg of the alcohol in 0.1 mL of $CDCl_3$), the urethane formation was complete in 2 h, and an NMR sample was obtained after dilution with $CDCl_3$. In both the ^{1}H and ^{19}F NMR, the shift differences of both diastereomers ((*S*)-**1** with (*S*)-2-butanol, and (*S*)-**1** with (*R*)-2-butanol) are large enough to afford quantitative analysis (Table I, entry 9). With 3,3-dimethyl-2-butanol (Table I, entry 10) and 1-phenyl-1-propanol (entry 12), the urethane formation proceeded smoothly as in the case with 2-butanol. However, some of these urethanes showed line broadening or unusual splitting of the peaks in the NMR, probably owing to the hindered rotation of the bonds around the urethane linkages.[7] With (*R*)-1-phenylethanol, (*S*)-**1** failed to react under similar reaction conditions, while the *S* alcohol gave the urethane (*S*,*S*)-**3** with (*S*)-**1** (Table I, entry 11) quite smoothly. *R* isocyanate ((*R*)-**1**) gave the urethane ((*R*,*R*)-**3**) with the *R* alcohol and its NMR spectrum was identical with that of (*S*,*S*)-**3**. Results with alcohols are included in Table I.

In summary, it is concluded that **1** is a convenient chiral derivatizing agent for primary and secondary amines due to the fact that one only has to add **1** in a slight excess to an NMR sample solution of an amine to obtain a definite NMR spectrum of the diastereomers. No separation or purification process is required after addition of **1** unless the OCH_3 region is of primary concern. Further, the shift differences of the signals ($\Delta\delta$) are usually large enough between the diastereomers to enable quantitative analysis by ^{1}H or ^{19}F NMR, and these magnitudes of nonequivalences are roughly on the same order as those observed for the comparable MTPA amides or esters.[8] However, **1** is not widely applicable for use with alcohols because it sometimes fails to react with hindered alcohols under the conditions described, and some of the urethanes derived from it show line broadening or unusual splitting of the peaks in the ^{1}H or ^{19}F NMR spectra. Inspection of Table I has revealed that the CH_3 signal in the *S*,*R* urea or urethane always appears at a higher field than that in the *S*,*S* isomer. Such configuration chemical shift correlations have extensively been elucidated for chiral derivatizing reagents.[9] On the basis that *Z* conformation is the preferred one in urethanes[10] (and also in ureas by analogy), we propose the configuration correlation models for the diastereomers as depicted below,



in which the CF_3 group in the isocyanate residue and the C–H in the alcohol or amine residue are both placed cis to the carbonyl group.[9] In the *S*,*R* diastereomer, the methyl group in the alcohol or amine moiety is eclipsed with the phenyl group in the isocyanate residue. As a result, the methyl hydrogens are more shielded in the *S*,*R* than in the *S*,*S* isomer where the methyl group is not eclipsed with the phenyl group.

Experimental Section

Melting points (taken on a Laboratory Device MEL-TEMP) and boiling points are uncorrected. Infrared spectra were obtained on a Shimazu IR-400 spectrometer. Proton, carbon-13, and fluorine NMR spectra were recorded on a JEOL GSX-270 (270 MHz) spectrometer using $CDCl_3$ as a solvent. Optical rotations were measured on a JASCO DIP-SL polarimeter. α-Methoxy-α-(trifluoromethyl)phenylacetic acid (*R* and *S*) and all primary amines and secondary alcohols used here were obtained commercially (Aldrich). 2-Methylazetidine, (*S*)-2-(phenylimino)-6-methyltetrahydro-1,3-oxazine, and the corresponding thiazine were prepared according to the method given in a previous paper.[11]

α-Methoxy-α-(trifluoromethyl)benzyl Isocyanate (1). (*R*)-(+)-MTPA (5 g, 0.02 mol) was converted to the acid hydrazide through the ester. The hydrazide (syrup) was dissolved in 20 mL of 2 N HCl and the acid solution was washed with benzene to remove the unreacted ester. Then the acid solution was placed in a three-necked flask along with 20 mL of benzene. While the content of the flask was cooled with ice and stirred vigorously, a solution of 1.7 g of $NaNO_2$ in 2 mL of water was added dropwise. After addition, the contents of the flask were transferred to a separatory funnel, and the benzene solution was washed with a saturated NaCl solution and dried (Na_2SO_4). The azide solution was submitted to the Curtius rearrangement. Evolution of gas was observed at a temperature range of 30–65 °C. After removal of benzene, the residue was distilled to give 2.4 g (52%) of an off-white liquid: bp 46–47 °C/1 mm; IR (liquid film) 2260 cm^{-1} (N=C=O); ^{1}H NMR 3.344 (s, OCH_3); ^{13}C NMR 51.877 (OCH_3); ^{19}F NMR −6.665 (CF_3); $[\alpha]^{25}_D$ −44.4° (*c* 3.85 g in 100 mL, benzene).

(5) Hine, J. *Physical Organic Chemistry*; McGraw-Hill: New York, 1962; p 336.
(6) A tautomeric form, 2-anilino-6-methyl-4,5-dihydro-1,3-oxazine should be considered also. However, the carbamoylation was found to take place exclusively at the ring nitrogen in this case. As to the site of the carbamoylation in such systems, research is now in progress.
(7) Pirkle, W. H.; Simmons, K. A.; Boeder, C. W. *J. Org. Chem.* **1979**, *44*, 4891.
(8) (a) For ^{1}H NMR: Dale, J. A.; Mosher, H. S. *J. Am. Chem. Soc.* **1973**, *95*, 512. (b) For ^{19}F NMR: Sullivan, G. R.; Dale, J. A.; Mosher, H. S. *J. Org. Chem.* **1973**, *38*, 2143.
(9) Yamaguchi, S. *Asymmetric Synthesis*; Morrison, J. D., Eds.; Academic Press: New York, **1983**; Vol. *1*, p 125, and papers cited therein.
(10) Pirkle, W. H.; Hauske, J. R. *J. Org. Chem.* **1977**, *42*, 1839.
(11) Iwakura, Y.; Nabeya, A.; Nishiguchi, T.; Ohkawa, K. *J. Org. Chem.* **1966**, *31*, 3352.

Likewise was prepared the (*R*)-(+) isocyanate, (*R*)-**1** from (*S*)-MTPA, and the specific rotation was as follows: $[\alpha]^{25}_{D}$ +41.4° (*c* 3.81 g in 100 mL, benzene).

1-[(1-Naphthyl)ethyl]-3-[α-methoxy-α-(trifluoromethyl)-benzyl]urea (2). Into a solution of 85 mg of (*S*)-1-(1-naphthyl)ethylamine in 1 mL of benzene was added a solution of 120 mg of (*S*)-**1** in 1 mL of benzene, and the reaction mixture was allowed to stand until white crystals separated out. The crystals were collected and recrystallized from benzene to give an analytical sample: mp ca. 150 °C; ^{1}H NMR 1.485 (d, CH_3), 3.554, 3.560 (each s, OCH_3);[12] ^{13}C NMR 22.12 (CCH_3), 45.29 (*C*H), 51.37, 51.40 (OCH_3),[12] 154.37 (*C*=O).

Anal. Calcd for $C_{22}H_{21}N_2O_2F_3$ (402.2): C, 65.69; H, 5.27; N, 6.96. Found: C, 66.04; H, 5.31; N, 6.77.

A sample for NMR analysis was prepared by mixing 5 mg of (*S*)-1-(naphthyl)ethylamine and 8 mg of **1** in 0.6 mL of $CDCl_3$ in an NMR sample tube. Both the ^{1}H and ^{19}F NMR spectra were identical with those obtained above for the pure sample of (*S,S*)-**2** except for the presence of a signal at 3.3 ppm (OCH_3 of **1**) in the former and at −6.67 (CF_3 of **1**) in the latter.

Other NMR samples of urea derivatives were prepared in the same way.

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Registry No. (*S*)-**1**, 114693-11-7; (*R*)-**1**, 114693-12-8; **2**, 114693-15-1; (*R*)-(+)-MTPA (hydrazide), 114693-13-9; (*S*)-MTPA (hydrazide), 114693-14-0; (*RS*)-$CH_3CH_2CH(NH_2)CH_3$, 33966-50-6; (*R*)-$CH_3CH_2CH(CH_3)CH_2NH_2$, 36272-22-7; (*S*)-$CH_3CH_2CH(CH_3)CH_2NH_2$, 34985-37-0; (*RS*)-$(CH_3)_2CHCH(NH_2)CH_3$, 110509-11-0; (*R*)-$PhCH(NH_2)CH_3$, 3886-69-9; (*S*)-$PhCH(NH_2)CH_3$, 2627-86-3; (*R*)-CH_3CH(1-Naph)NH_2, 3886-70-2; (*S*)-CH_3CH(1-Naph)NH_2, 10420-89-0; (*R*)-$CH_3CH_2CH(OH)CH_3$, 14898-79-4; (*S*)-$CH_3CH_2CH(OH)CH_3$, 4221-99-2; (*RS*)-$(CH_3)_3CCH(OH)CH_3$, 20281-91-8; (*S*)-$PhCH(OH)CH_3$, 1445-91-6; (*R*)-$PhCH(OH)CH_2CH_3$, 1565-74-8; (*S*)-$PhCH(OH)CH_2CH_3$, 613-87-6; (*RS*)-2-methylazetidine, 52730-18-4; (*R*)-2-(phenylimino)-6-methyltetrahydro-1,3-oxazine, 114693-16-2; (*S*)-2-(phenylimino)-6-methyltetrahydro-1,3-oxazine, 114693-17-3; (*R*)-2-(phenylimino)-6-methyltetrahydro-1,3-thiazine, 114693-18-4; (*S*)-2-(phenylimino)-6-methyltetrahydro-1,3-thiazine, 114693-19-5.

(12) Such an NMR nonequivalence of OCH_3 was also observed in the ureas derived from 1-phenylethylamine (Table I, entry 4), 2-(phenylimino)-6-methyltetrahydro-1,3-oxazine (entry 7) and thiazine (entry 8).

Linear Electric Field Effects on ^{13}C NMR Shifts in Saturated Aliphatic Frameworks: Scope and Limitations[1]

Hans-Jörg Schneider,* Eckehard F. Weigand, and Norman Becker

Fachrichtung Organische Chemie der Universität des Saarlandes, D-6600 Saarbrücken 11, West Germany

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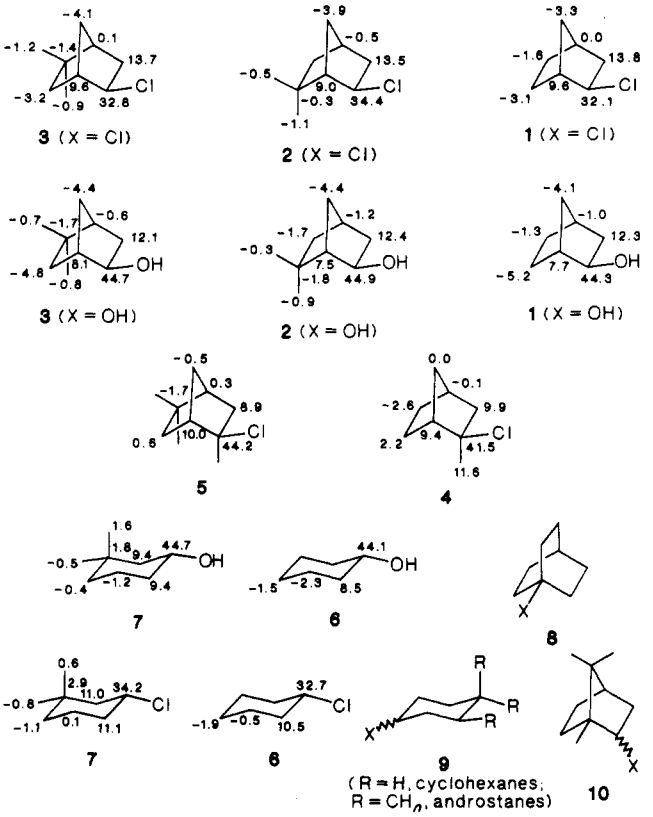
Introduction

The transmission of polar substituent effects through aliphatic bonds is one of the rare cases of a common basis for organic reaction as well as of NMR shielding mechanisms. Local electron density variations by through-space field or by inductive through bond substituent effects and their influence on chemical rates and equilibria have been in the focus of many physical-organic studies[2] but have been to a lesser degree scrutinized with respect to their visibility in NMR screening constants. ^{13}C NMR shifts[3] are known to be particularly sensitive to such electron density variations and do often show intuitively expected patterns in similar compounds. Related electric field as well as inductive effects have been studied widely with unsaturated but not so much with saturated systems.[4] In the present paper ^{13}C NMR shielding variations are observed in newly prepared norbornane derivatives and are compared to related aliphatic frameworks; at the same time we try to explore the possibilities of classical linear electric field calculations in such systems.

Chart I. Substituent-Induced Shielding Values (in ppm) Relative to the Parent Hydrocarbon



Substituent Effects on ϑ-Positions. The significance of linear electric through-space field effects (LEF) has been first pointed out for protons[5] as well as later for heavier nuclei,[6] including ^{13}C.[7] We have shown that the C-ϑ-shift variations in 12 substituted cyclohexanes[8a] can be de-

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(2) See, e.g.: Ferguson, N. L. *Organic Molecular Structure*; Willard Grant: Boston, 1975; p 72 ff.

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(5) (a) Raynes, W. T.; Buckingham, A. D.; Bernstein, H. J. *J. Chem. Phys.* **1962**, *36*, 3481. (b) ApSimon, J. W.; Beierbeck, H. *Can. J. Chem.* **1971**, *49*, 1328 and earlier papers. (c) Zücher, F. *Progr. NMR Spectrosc.* **1967**, *2*, 205.

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