Journal of Chromatography, 503 (1990) 437–441
Elsevier Science Publishers B.V., Amsterdam — Printed in The Netherlands

CHROM. 22 180

Note

Chiral organosilicon compounds

II[a]. Comparison of gas–liquid chromatographic and NMR analyses of enantiomeric alcohols

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(First received August 9th, 1989; revised manuscript received November 28th, 1989)

The determination of enantiomeric excess is fundamental to the evalution of asymmetric induction methodologies and the literature reflects a continuing interest in techniques for enantiomer differentiation. These techniques include gas–liquid chromatographic (GLC) analysis using chiral stationary phases and chiral derivatization agents[2–5] and NMR analyses using chiral solvating agens[6,7], chiral platinum complexes[8] and chiral imidazolidine and boronic acid derivatization agents[9–11]. Whereas the derivatization capabilities of organosilicon compounds are well established, applications involving chiral organosilicon systems in synthesis and analysis have, until recently, received little attention[12,13]. NMR applications involving chiral silyl derivatives appear to be limited to studies by Richter[14], who used ^{1}H NMR analysis to examine stereoselectivity in the reactions of prochiral siloxanes, and, more recently, by Chan *et al.*[15], who used NMR (^{1}H, ^{13}C and ^{29}Si) methods to differentiate diastereomeric silyl acetal derivatives of enantiomeric alcohols. To our knowledge, no applications of chiral silyl probes in GLC have been reported. In this paper we compare GLC and NMR (^{1}H and ^{13}C) analyses of diastereomeric silyl acetals (**1–5**, Table I) [including the silyl acetals (**4**) examined by Chan *et al.*[15]], obtained by reacting selected racemic alcohols with excess of borneol- and/or menthol-derived chiral chlorosilanes [prepared from (−)-menthol and (−)-borneol as described in Part I[1]], under conditions which may be expected to minimize any kinetic resolution effects.

EXPERIMENTAL

The synthesis of the diastereomeric silyl acetals **1–5**, all of which gave satisfactory NMR, IR and high-resolution mass spectrometric analyses, was effected under anhydrous conditions in an inert atmosphere (nitrogen) as illustrated by the

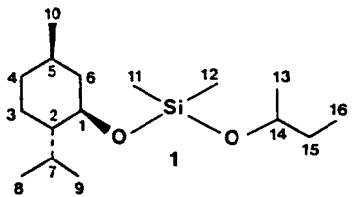
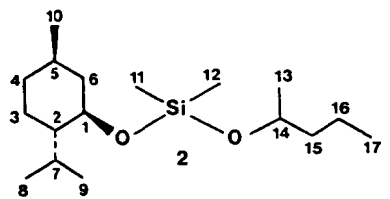
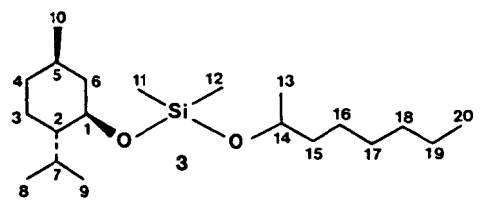
[a] For Part I, see ref. 1.

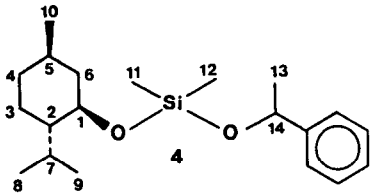
0021-9673/90/$03.50

TABLE I

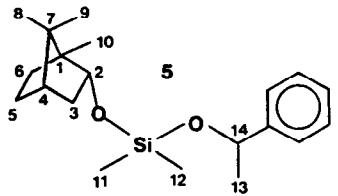
GLC AND NMR DATA FOR DIASTEREOMERIC SILYL ACETALS, $R^1(CH_3)_2SiOCH(R^2)R^3$

t_R = Retention times for 30- and 60-m columns followed, in each instance, by relative peak areas in parentheses. R_S = Peak resolution. α = Separation factor. δ_H = Chemical shifts followed, in parentheses, by relative signal intensity ratios, signal multiplicities and signal assignments. δ_C = ^{13}C P.n.d. signal shifts followed by signal assignments.

Compound	*t_R (min)*	*R_S*	*α*	*δ_H (ppm)*	*δ_C (ppm)*
 1	–	–	–	1.13, 1.14 (0.99:1.00; 2 × d[a]; 13-H)	45.39, 45.44; C-6
 2	–	–	–	1.13, 1.14 (0.91:1.00; 2 × d[b]; 13-H)	23.58, 23.66; C-13 45.39, 45.44; C-6
 3	35.60, 35.78 (0.88:1.00) 71.63, 71.84 (0.85:1.00)	0.69 0.75	1.005 1.003	1.13, 1.14 (0.81:1.00; 2 × d[c]; 13-H)	23.58, 23.66; C-13



41.14, 41.35 (1.00:1.00)	0.80	1.005	1.47, 1.48 (1.00:0.98; 2 × d[d]; 13-H)	15.92, 15.97; C-9 22.12, 22.23; C-8
84.37, 84.70 (0.95:1.00)	0.88	1.004	1.79, 1.96 (0.98:1.00; 2 × m; 6-$H_{eq.}$)	31.59 31.65; C-5 45.23, 45.37; C-6



43.00, 43.16 (1.00:0.98)	0.38	1.004	0.847, 0.851 (0.93:1.00; 2 × s; 8-, 9- or 10-H)	13.34, 13.47; C-10 28.25, 28.29; C-5
88.37, 88.68 (0.92:1.00)	0.63	1.004	1.56, 1.59 (0.90:1.00; 2 × t; 4-H)	39.13, 39.18; C-3 45.18, 45.22; C-4

[a] J = 6.18 and 6.03 Hz, respectively.
[b] J = 5.94 and 6.15 Hz, respectively.
[c] J = 5.85 and 6.03 Hz, respectively.
[d] J = 6.34 and 6.30 Hz, respectively.

following example. A solution of chloro(menthyloxy)dimethylsilane (2.98 g, 12 mmol)[1] in diethyl ether (10 ml) was added dropwise to a stirred solution of racemic 1-phenylethanol (0.98 g, 8 mmol) (the *racemic* alcohol substrates exhibited zero optical rotation) and triethylamine (1.2 g, 12 mmol) in diethyl ether (20 ml). After stirring overnight, the resulting slurry was poured into aqueous sodium hydrogencarbonate. Extraction with diethyl ether, concentration *in vacuo* and flash chromatography on silica [elution with hexane–ethyl acetate (95:5)] gave, as a diastereomeric mixture, menthyloxydimethyl(1-phenylethoxy)silane (**4**) (1.9 g, 71%). Isolated yields for the other silyl acetals were: (**1**) 72%, (**2**) 76% (**3**) 50% and (**5**) 57%.

The silyl acetals **1**–**5** were chromatographed, as 0.1–0.2% solutions in diethyl ether, on a Hewlett-Packard 5890A gas chromatograph fitted with a J&W DB225 fused-silica capillary column (0.25 μm film thickness) [30 m × 0.25 mm I.D. (for a 60-m column, two 30-m columns were joined)] and using helium as the carrier gas at a flow-rate of 41 ml/min, optimized temperature programmes [*e.g.*, for the silyl acetals **4**, 60–140°C at 4°C/min, 140–170°C at 1°C/min], an inlet purge time of 0.5 min and flame ionization detection using synthetic air and hydrogen as detector feed gases. The inlet and detector temperatures were set at 210°C.

^{1}H (500 MHz) and ^{13}C (125 MHz) NMR spectra were obtained for C^2HCl_3 solutions on a Bruker WM 500 spectrometer.

RESULTS AND DISCUSSION

Silyl acetal mixtures (**1**–**5**) were chromatographed on a standard 30-m capillary column. Under optimum temperature-programmed conditions, resolution of the components (see Fig. 1) was obtained for each of the diastereomeric systems **3**, **4** and

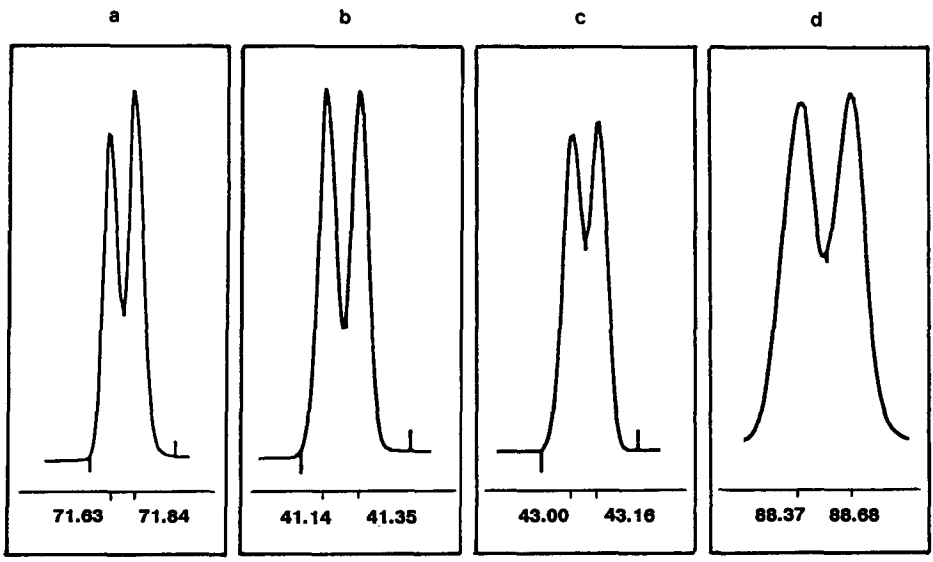


Fig. 1. Partial gas chromatograms illustrating resolution of the diastereomeric components of silyl acetals: (a) **3**, 60-m column; (b) **4**, 30-m column; (c) **5**, 30-m column; (d) **5**, 60-m column. Retention times of components are indicated in minutes.

5; doubling the column length increased the peak resolution in each instance (Table I). Peak splitting was not observed for the silyl acetals **1** and **2** [$R^2 = CH_3$, $R^3 = C_2H_5$, *n*-C_3H_7 (Table I)]. It seems that significant differences between the substituents (R^2 and R^3) are necessary if GLC resolution of the respective diastereomers is to be achieved and, although ^1H and ^{13}C NMR chemical shift non-equivalence was observed for all five of the systems examined, the signal doublings are more numerous and significant in the spectra of the silyl acetals **4** and **5** where the substituents are markedly different (*i.e.* $R^2 = CH_3$, $R^3 = C_6H_5$).

The results reflect a close correlation between GLC and ^1H NMR integral ratios and illustrate the potential of chiral silyl derivatization agents in the GLC analysis of enantiomers. Further research is expected to involve the development of more effective enantio-differentiating chiral silyl probes and extension to other functional groups.

ACKNOWLEDGEMENTS

The authors thank Mr. Ivan Antonowitz (CSIR) for obtaining the high-field NMR spectra, and Rhodes University and the Foundation for Research Development (CSIR) for generous financial support.

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