Journal of Chromatography, 292 (1984) 295–304
Elsevier Science Publishers B.V., Amsterdam — Printed in The Netherlands

CHROM. 16,654

GAS CHROMATOGRAPHIC RESOLUTION AND ELUTION ORDERS OF SIMPLE DIASTEREOMERIC ALKENES

PHILIP E. SONNET
Insect Attractants, Behavior and Basic Biology Research Laboratory, Agricultural Research Service, U.S. Department of Agriculture, Gainesville, FL 32604 (U.S.A.)
(Received February 9th, 1984)

SUMMARY

An alkene in which the double bond is flanked by hydrocarbon asymmetric centers exists as a pair of diastereomers that often can be resolved by gas chromatography. The resolution of a series of such diastereomers on a bonded non-polar column is described. The elution order of the diastereomers, the variation of separation factors with the distance between the asymmetric centers, and the potential for using this information to analyze natural products for configuration and configurational purity are discussed.

INTRODUCTION

Many natural products that contain centers of asymmetry elude efforts to determine absolute configuration and configurational purity. In some instances, such as the branched hydrocarbons that occur commonly in plant waxes and on the cuticles of insects, the asymmetric center is imbedded in a hydrocarbon framework that offers no chemical handle. In other cases the amount of natural product available is too small for such standard techniques as polarimetry or chemical degradation. Insect semiochemicals epitomize this problem since many of the chiral compounds contain hydrocarbon asymmetric centers, such as $[-(CH_2)_nCHCH_3(CH_2)_m-$ where n and m are $\geqslant 2]$, and are available only in μg amounts. Thus most assignments of absolute configuration have been inferential based as they are upon biological testing[1].

Current research to solve such problems is directed along several independent lines. Chiral phases for enantiomer resolution by gas–liquid chromatography (GLC)[2–6] and high-performance liquid chromatography (HPLC)[7] are receiving intense attention. A second approach considers amplifying the asymmetry of the natural product by a process termed "liquid-crystal induced circular dichroism" (LCICD)[8,9]. Yet another approach, the subject of this work, is the historically oldest one of converting the compound in question to diastereomers for GLC analysis in a manner suitable for micro-level work. This of course, requires a chemical handle, and the usefulness of the process will hinge upon the distance that handle can be from the asymmetric center and still afford GLC resolution.

0021-9673/84/$03.00

Excellent reviews are available that deal with commonly employed diastereomer-forming derivatizations[10] and that discuss the bases for resolution of such diastereomers[11]. While rationales are available regarding GLC and HPLC resolutions, the recent efforts of Helmchen and co-workers[12,13], and Pirkle and co-workers[14,15] with respect to the HPLC resolutions of diastereomeric amides and carbamates are contributing greatly to a mechanistic foundation that will permit searching in a more directed manner for suitable derivatizing reactions and reagents in chromatography generally. In particular, in the absence of specific solvating (solute–solvent) effects, or solute intramolecular interaction, solute molecules will tend to align with the solvent molecules. This variable is superimposed on the tendency of the solute molecule to assume conformations that have the lowest (internal) potential energy as well. Thus, of a pair of diastereomers the one that can achieve alignment while in, or near, a preferred rotational conformation is retained longer by the solvent.

In early studies of positional isomerism (*para vs. meta vs. ortho* substituted benzenes), greater retention of *para* substituted solutes by a smectic liquid crystal GLC solvent was rationalized in terms of length-to-breadth ratio of the solute[16]. The elution orders of simple alkenes likewise tended to fit that perception since *trans*-alkenes, especially those removed from the chain termini, eluted later than the *cis*-alkenes when the solvent was nonpolar and encouraged solute alignment[17]. The idea of discriminating size and shape for flat, essentially two-dimensional molecules like the disubstituted aromatics, and linear molecules like long chain alkenes, was then extended to the three-dimensional case of diastereomers. We found that a series of closely related diastereomeric amides and carbamates were predictably separated by GLC, and the most effective solvent was the cholesteric liquid crystal, cholesterol *para*-chlorocinnamate (CpCC)[18]. Employing the likely solution conformation of such compounds[14], the more *trans*-like diastereomer was retained longer by the solvent.

We have previously made an unsuccessful effort to resolve simple dimethylalkanes (1,2; 1,3; 1,4; or 1,5)[19] and are not aware that such resolutions can be routinely accomplished. Evidently the manifold of solution conformations available to such diastereomeric pairs is such as to make the average length-to-breadth ratio equivalent. Insertion of a double bond between the branched, asymmetric carbons, however can cause a significant alteration in average size–shape through the introduction of some rigidity that the diastereomers are differentiated by the solvent. Reported here is the degree to which an alkene link can transmit chirality information between asymmetric centers, its effectiveness in the *cis* (*Z*), or *trans* (*E*) configuration, and its effectiveness as a function of separation of the centers in simple hydrocarbon systems. It will be evident then, that natural products that are, or can be converted to α-, β-, or γ-branched aldehydes, can be treated with a suitable chiral phosphorane to generate the subject alkenes and offer thereby a means to determine configuration of the natural product. As a corollary, the ideas expressed here have direct application in analysis to gauge the success of asymmetric organic synthesis as well.

EXPERIMENTAL

The DB-1 fused-silica column (0.25-μm film) was 15 m × 0.25 mm I.D. and was purchased from J & W Scientific Company (Orangevale, CA, U.S.A.). The CpCC

column was 44 m × 0.15 mm I.D. and was prepared in our laboratory from etched soft glass coated by the static method using a 0.2% (w/v) solution in dichloromethane. Its characteristics as a typical cholesteric liquid-crystal phase for GLC have been reported[17]. All work was done on a Varian 1400 instrument with a user-designed, all glass capillary system. The carrier gas was helium and the linear flow velocity 18 cm/sec. The inlet split ratio was *ca.* 100:1 and detector make-up gas (nitrogen) flow-rate was 30 ml/min.

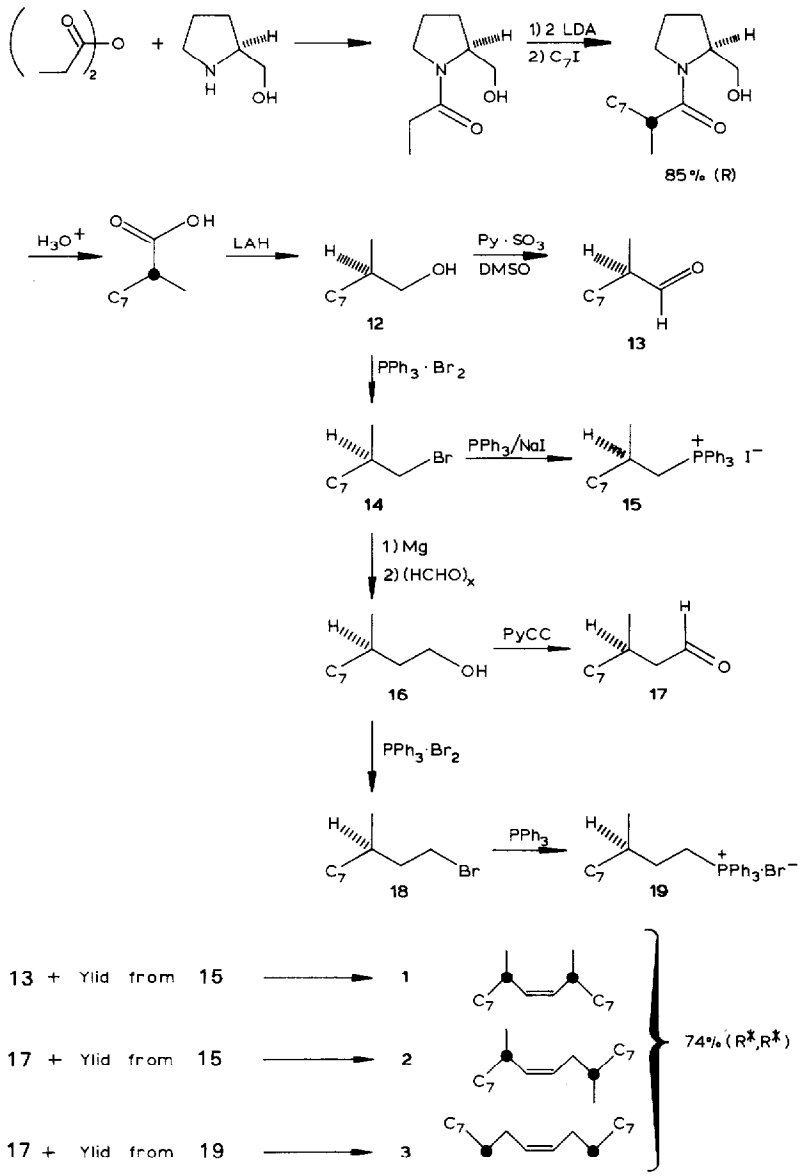


Fig. 1. Synthesis of (*Z*)-alkenes with a configurational bias. *n*-C_7H_{15} is drawn as C_7.

Synthesis

(R)-2-methyl-1-nonanol (85%) [12]. Propionylation of (*S*)-prolinol that had been obtained from Aldrich was conducted as previously described[20] producing the N-propionyl derivative: b.p. 110–121°C (0.01 mmHg), yield quantitative. The alkylation of the propionyl group (Fig. 1) was conducted using 2 equiv. of lithium diisopropylamide and 2 equiv. of hexamethylphosphoric triamide (HMPT) per Li^+ in tetrahydrofuran (THF). The procedure for this alkylation using other alkyl halides than 1-iodoheptane has been described and the sense of configurational bias induced is known[20,21]. Deprotonation was conducted at room temperature (0.5 h), and the anionic species was C-alkylated with 1-iodoheptane at −78°C (2 h, then to 25°C overnight). After the usual work-up procedure[21], the product was hydrolyzed with 2 equiv. of perchloric acid in aq. THF under reflux (16 h). A sample of the crude 2-methylnonanoic acid was converted to an amide of (*S*)-α-methylbenzylamine for analysis of configuration (DB-1 column, 170°C, *k* values: 11.46, 12.54; α: 1.094, $R > 1$) (see Table I, third footnote). The order of elution of such amides is known[18] and confirms the stereobias assigned based on considerations of asymmetric induction noted above. The 2-methylnonanoic acid was 85% *R, i.e.* 70% enantiomeric excess (ee). Reduction of this acid with lithium aluminum hydride (LAH) in refluxing THF followed by work-up with aq. base, *etc.* gave after distillation 2-methyl-1-nonanol (12) in 53% yield from the propionamide of prolinol: b.p. 125°C (30 mmHg); $[\alpha]_D^{24}$ + 3.75° (*c*, 6.69, $CHCl_3$) for 70% ee; IR ($CHCl_3$) 3640 cm^{-1}; ^1H NMR (C^2HCl_3) 0.88 (3H, t, CH_3CH_2), 0.91 (3H, d, J = 6.8, CH_3CH), 3.45 (2H, m, CH_2OH) ppm; chemical ionization mass spectrometry (CI–MS): *m/e* 157 (M − 1), 141 (M + 1 − 18). This alcohol served to provide the other compounds of Fig. 1 with an established enantiomeric excess of 70%.

2-Methylnonanal (13). Alcohol 12 was oxidized to the corresponding aldehyde 13 in 72% (undistilled) yield using pyridine · SO_3 complex in dimethyl sulfoxide (DMSO) in the usual manner[22]. This procedure does not compromise the asymmetric center[23]: IR ($CHCl_3$) 1725 cm^{-1}; ^1H NMR (C^2HCl_3) 0.90 (6H, overlap of CH_3CH_2 and CH_3CH), 9.75 (1H, m, CHO) ppm.

2-Methyl-1-bromononane (14). The alcohol 12 was converted to the bromide 14 using triphenylphosphine dibromide in dichloromethane (25°C, 10 h)[24]. The crude product was chromatographed on silica gel (5% load) eluting with hexane. The solvent was removed, the bromide was analyzed by GLC (OV-1 glass capillary column, 3.3 m × 0.25 mm) and found to be free of 12, and was employed directly for the other transformations: ^1H NMR (C^2HCl_3) 0.88 (3H, t, CH_3CH_2), 1.01 (3H, d, J = 6.8 Hz, CH_3CH), 3.36 (2H, m, CH_2Br) ppm; CI–MS *m/e* 141 (M + 1 − HBr).

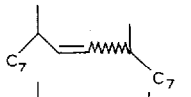
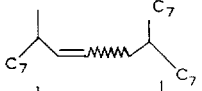
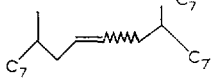
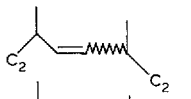
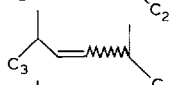
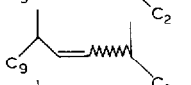
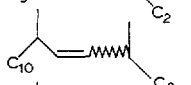
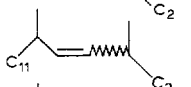
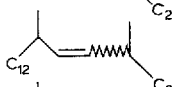
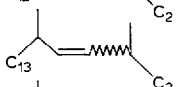
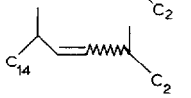
2-Methyl-1-nonyltriphenylphosphonium iodide (15). Because the bromide was only slowly displaced, the oily iodide was prepared and was then washed free of inorganics and organics as follows. The bromide (14) was heated in acetonitrile under reflux (48 − 64 h) with a slight excess of triphenylphosphine and 2 equiv. of sodium-iodidide. The solvent was removed by flash evaporation, and the residue was partitioned between water and dichloromethane. The organic layer was dried (magnesium sulfate) and concentrated; the residue was triturated with ether several times and then concentrated with hexane. The oily iodide salt was stored in dry THF over 4 Å molecular sieves and under dry nitrogen.

3-Methyl-1-decanol (16). The bromide 14 was allowed to react with magne-

TABLE I

GAS–LIQUID CHROMATOGRAPHIC DATA FOR DIASTEREOMERIC ALKENES

DB-1 capillary column (see Experimental) operated at the indicated temperatures. C_2 represents C_2H_5, C_7 is n-C_7H_{15}, and a methyl branch is simply a stick. The solvent efficiencies for the (*Z*)- and (*E*)-diastereomers are α_Z and α_E, respectively. The partition coefficient is k'^{36}.

Alkene structure	*T* (°C)	*k (relative configurations)*	α_Z	α_E
1 	170	5.85 (*Z,R*S**), 6.59 (*E,R*R**), 6.77 (*Z,R*R**), 7.15 (*E,R*S**)	1.157	1.085
2 	170	10.69 (*Z,R*R**), 11.15 (*Z,R*S**) 11.56 (*E,R*S**), 11.72 (*E,R*R**)	1.043	1.014*
3 	170	18.46 (*Z,R*S**), 18.69 (*Z,R*R**)	1.012*	—**
4 	30	11.85 (all isomers)	1.00	1.00
5 	35	9.62 (*Z*), 9.69 (*Z*), 10.23 (both *E*'s)	1.007*	1.00
6 	130	10.92 (*Z*), 11.23 (*Z*), 11.62 (*E*), 11.77 (*E*)	1.028*	1.013*
7 	150	7.00 (*Z*), 7.23 (*Z*), 7.54 (*E*), 7.62 (*E*)	1.033	1.011*
8 	150	10.77 (*Z*), 11.08 (*Z*), 11.38 (*E*), 11.46 (*E*)	1.029	1.007*
9 	170	7.77 (*Z,R*S**), 8.00 (*Z,R*R**), 8.31 (*E,R*R**), 8.38 (*E,R*S**)	1.030	1.008*
10 	170	11.46 (*Z*), 11.69 (*Z*), 12.08 (*E*), 12.15 (*E*)	1.020	1.006*
11 	170	16.38 (*Z*), 16.77 (*Z*), 17.15 (*E*), 17.23 (*E*)	1.024	1.005*

* Resolution was less than unity.
** Obscured by (*Z*)-isomer.

sium in anhydrous ether to form a Grignard reagent[25]. Reaction with paraformaldehyde (reflux, 16 h) and the usual work-up gave alcohol 16 in 85–90% yield: b.p. foamed badly; IR ($CHCl_3$) 3640 cm^{-1}; ^1H NMR (C^2HCl_3) 0.90 (6H, overlapped CH_3CH_2 and CH_3CH), 3.6 (2H, m, CH_2OH) ppm; CI–MS *m/e* 155 (M + 1 − 18).

3-Methyldecanal (17). Alcohol 16 was oxidized to 17 with pyridinium chlorochromate in dichloromethane in the usual manner[26] giving *ca.* 72% (undistilled) yield, IR ($CHCl_3$) 1705 cm^{-1}; ^1H NMR (C^2HCl_3) 0.90 (6H overlapped CH_3CH_2 and CH_3CH), 9.75 (1H, m, CHO) ppm; CI–MS *m/e* 171 (M + 1).

3-Methyl-1-bromodecane (18). The alcohol 16 was converted to its bromide

as described above for the preparation of 14 was employed directly for the next step.

3-Methyl-1-decyltriphenylphosphonium bromide (19). This transformation was performed with 1 equiv. of triphenylphosphine in acetonitrile (reflux. 2 h) and the salt was obtained by removing the solvent with heptane coevaporation. The oily bromide was stored in dry THF as above.

Condensations to generate alkenes 1, 2 and 3. The phosphonium iodides were dissolved in dry THF under nitrogen and converted to ylids with commercial butyllithium (0–25°C, 0.25 h). The orange–red solutions were cooled to −78°C and HMPT (2 equiv.) was added. Then the aldehyde was added neat, and the mixture was stirred for another 0.25 h in the cold. It was allowed to come to ambient temperature and worked up in the usual manner. The crude (*Z*)-alkenes (< 3% *E*) were purified by passage through a column of silica gel (2% load) eluting with hexane to provide 75–80% yields of 1, 2, and 3: IR ($CHCl_3$) absence of 965 cm^{-1} band of 1,2-disubstituted (*E*)-alkene; ^1H NMR (C^2HCl_3) 0.88 (12H, m, CH_3's), 1.25 (CH_2 envelope), 5.01 (2H, m, = CH_2). The allylic H's were exhibited at 2.0 as a multiplet for = $CHCH_2$ and/or at 2.4 as a multiplet for $CHCH(CH_3)$ in these alkenes as appropriate for their structures. CI–MS: (1), *m/e* 281 (M + 1), 280 (M), 197 ($C_{14}H_{29}$) for both diastereomers; (2), *m/e* 295 (M + 1), 294 (M), 211 ($C_{15}H_{31}$); (3), *m/e* 309 (M + 1), 225 ($C_{16}H_{33}$); diastereomers of 2 and 3 not separated by GC–MS system.

Other compounds described in Table I were synthesized by the same methods just described either in racemic form or with a known configurational bias. All new compounds were characterized by infrared (Perkin-Elmer Model 467 spectrophotometer). ^1H NMR (Nicolet 300 MHz Fourier transform (FT) NMR), and CI–MS (Finnigan Model 3200 chemical-ionization mass spectrometer using isobutane, and equipped with a GLC inlet served by a Varian 1400 instrument and an OV-101 column (31 m × 0.25 mm I.D.).

Because the availability and configurational purity of (*S*)-2-methyl-1-butanol prompts consideration of a derived phosphonium salt as a chiral auxiliary for assessing the configurational bias of certain natural products, the following preparation is described.

(S)-2-Methyl-1-butyltriphenylphosphonium iodide. The alcohol was obtained from Tridom-Fluka (Hauppauge, NY, U.S.A.) ($[\alpha]^{20}_{546}$ − 7.3 ± 1°; *c*, 10, ethanol) and was converted to a lithium salt with an equiv. of butyllithium in dry THF under nitrogen. The HMPT (2 equiv. per Li^+) was added and methanesulfonylchloride (1 equiv.) was added dropwise with ice-cooling of the mixture. After 2 h at 25°C, sodium iodide (1.5 equiv.) was added and the mixture was warmed to reflux overnight. After the usual work-up, the iodide was distilled: b.p. 49°C (67 mmHg, 54% yield. The iodide was converted to a phosphonium salt with 1 equiv. of triphenylphosphine in acetonitrile under reflux (48 h). The mixture was concentrated employing addition of heptane to facilitate evaporation of the acetonitrile, and the residue was crystallized under ether to give the (*S*)-iodide in 70% yield: m.p. 172–3°C (ethyl acetate–ethanol), ^1H NMR (C^2HCl_3) 0.82 (3H, t, J = 7.4 Hz, CH_3CH_2), 0.98 (3H, d, J = 6.7 Hz, CH_3CH), 1.5 (2H, m, CH_3CH_2CH), 1.9 (1H, m, *CH*), 3.6 (2H, m, CH_2p^+) ppm, $[\alpha]^{21}_d$ + 3.1° (*c*, 6.5, $CHCl_3$).

RESULTS AND DISCUSSION

In order to minimize specific solute–solvent interactions and thereby maximize the effects of size–shape discrimination of diastereomeric pairs of alkenes, a commercial capillary column of DB-1 was chosen as representative of a commercially available phase. Then a number of diastereomeric alkenes, 1–11 (Table I and Fig. 1) were synthesized. The general approach to configuration analysis of the (*Z*)- and (*E*)-alkenes was to prepare a suitable synthetic intermediate with a known configurational bias. For example, 2-methyl-1-nonanol (12), was synthesized by a route known to produce an excess of the (*R*)-configuration in the product[20,21]. In fact, the ratio *R*:*S* was 0.85:0.15 as determined by GLC analysis of an appropriate intermediate (see Experimental). The alcohol 12 was then converted to other suitable compounds, namely 13–19 (Fig. 1), by standard chemical methods. Each of those materials carry the same configurational bias as the alcohol 12 since none of the transformations jeopardizes the asymmetric center. The desired diastereomeric alkenes were then constructed by means of Wittig condensation[27] of the biased synthetic intermediates employing conditions that would maximize the (*Z*)-alkene content[28]. The product alkene would be 72% *R* at both centers (0.85 × 0.85), and 2% *S* at both centers (0.15 × 0.15), or stated in terms of relative stereochemistry (thereby indicating the diastereomer, the (*R**,*R**)-alkene would predominate by *ca.* 74:26 over the (*R**, *S**). This ratio of roughly 3:1 was manifest in the GLC peak areas. Isomerizations of *Z* to *E* were conducted with nitrous acid[29] and, in each instance, growth of the minor areas due to (*E*)-alkenes occurred at the expense of the original GLC pair. When the diastereomeric (*E*)-alkenes were resolved by GLC, the 3:1 diastereomer ratio was observed as expected. Similar tactics were employed to obtain the other alkenes described and the data for elution of diastereomers.

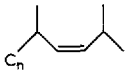
The results of these analyses are given in Table I. Clearly, the separation of diastereomers is greatest when the allylic carbons themselves are asymmetric and the alkene has the (*Z*)-structure. As expected, when one of the branching methyl groups is shifted away from the double bond, separation diminishes. Most intriguing is that the elution order of diastereomers appears to invert each time the asymmetric center is shifted. Thus, when the branches of a (*Z*)-alkene are in a 1,4-relationship the (*R**,*S**)-diastereomer elutes first (alkenes 1, 3 and 9). The (*R**,*R**)-isomer, however, elutes first for the (*Z*)-1,5-dimethylalkene 2, and when each methyl branch has been shifted by one carbon to produce a 1,6-dimethylalkene, the (*R**,*S**)-isomer elutes first again (alkene 3). The separations mediated by (*E*)-alkenes were poorer, but the elution order appears to be reversed from that of the corresponding (*Z*)-alkene (compare 1 and 2).

Table II summarizes the separation factors observed for a set of (*Z*)-1,4-dimethylalkenes. The members of the set differ in the length of one of the alkyl groups. Separation tended to improve with increasing chain length to a point and then remained constant. Presumably the greater difference in size between "branch-- and the "chain" is a factor in producing a preferred alignment. Thus separations will be maximal if the alkene link and the asymmetric centers are more internalized in the hydrocarbon chain as, for example, in compound 1.

In order for these diastereomer-forming reactions to have utility for configuration analysis, one side of the alkene must be available with a strong configurational

TABLE II

EFFECT OF HYDROCARBON CHAIN LENGTH ON SEPARATION FACTOR OF *Z*-DIASTEREOMERS



n	α^*
2	1.00
3	1.007
9–14	1.020–1.033

* The elution order in this series is *R*,S**, then *R*,R**.

bias. In fact, commercially available (*S*)-2-methyl-1-butanol is >99.5% pure, and is easily converted to a chiral phosphonium salt that can be stored for later use in natural product analysis. Reactions with this salt produces alkenes of structure $RCH=CHCH(CH_3)C_2H_5$ where the italized segment arises from the chiral auxiliary, and the RCH= portion is derived from either a chiral aldehyde whose configuration is under investigation, or an aldehyde derived by oxidation of an alcohol or ozonolysis of an alkene to produce a chiral aldehyde that may now be derivatized for analysis. In other words, compounds such as those of Table II are generated. If this particular phosphonium salt that relies on solvent discrimination between methyl and ethyl substituents proves too weak to effect satisfactory resolution, one can easily prepare a quantity of a pure 2-methyl-1-alkanol of either, or both, configurations[30] and bearing a suitably longer alkyl group to effect the desired resolution. At this point it appears that the limit to resolution imposed by distance between asymmetric centers requires that the natural product's asymmetry reside preferably on the α-, β- or γ-carbon of the aldehyde (or proaldehyde).

In addition, we noted that 4,8-dimethyldecanal (20, Fig. 2), an aggregation pheromone of two pest beetle species, *Tribolium castaneum* (Herbst) and *T. confusum* Jacquelin duVal[31] challenges direct analysis for configuration with two methyl branches that are fairly well removed from functionality. Careful work with synthetics indicated that both species of insect respond to the (4*R*,8*R*)-stereoisomer[32]. The following indicates the potential for evaluating the natural configuration of the 4-carbon and its actual configurational purity. Condensation of racemic (synthetic) 4,8-dimethyldecanal (Zoecon, Palo Alto, CA, U.S.A.) with phosphonium salt 15 produced an alkene, 21, that was resolved into a pair of diastereomers presumably based

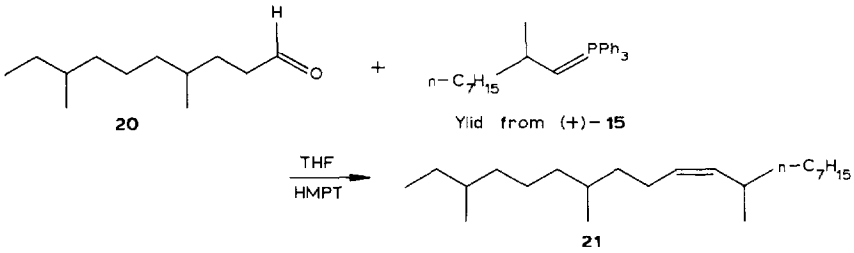


Fig. 2. Derivatization of synthetic trogodermal.

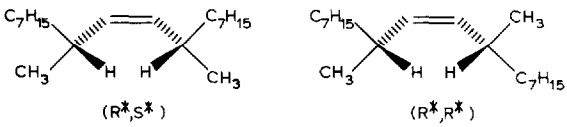


Fig. 3. Possible solution conformation preference of (*Z*)-1,4-dimethylalkenes.

on the 1,6-dimethylalkene relationship. The expected elution order based on this work is: *R**,*S** first, and at 170°C the *k* values were 12.85 and 13.08 (α = 1.018). Similarly, the use of a CpCC (see above) liquid phase gave *k* values of 10.81 and 11.03 (α = 1.020) at 155°C*. Although the separations were not complete, it does appear that this approach would have value in assigning configuration for the 4-carbon of this aldehyde**.

Other natural product structures that might be investigated fruitfully in this manner, and using known substrates as models to ensure knowledge of elution order, are those of faranal (pharaoh's ant trail marker)[33], terrestrol (bumble bee pheromone)[34] by oxidation of the natural alcohol to an aldehyde first, japonilure (Japanese beetle pheromone) by ozonolysis of the pheromone to an aldehyde; and the melon fly sex pheromone[35] also by a prior ozonolysis.

A rationalization of the elution order of the (*Z*)-1,4-dimethylalkenes is depicted in Fig. 3. With the asymmetric carbons rotated to minimize internal potential energy the hydrogens on those carbons would probably be perturbed slightly in either direction from the position depicted. Nevertheless the (*R**,*S**)-diastereomer is cisoid in nature, whereas the (*R**,*R**)-isomer is more elongated. Viewed in this manner the latter would align better with the chains of the polymeric solvent employed as the GLC liquid phase and be retained longer.

Current effort is directed toward developing a chiral auxiliary that will provide improved separation of diastereomers and thereby permit precise evaluation of configuration for aldehydes that have methyl branching at the γ-carbon atom and, if possible, yet further removed from the carbonyl group. In addition we are seeking to improve detectability of the derivatives with suitable substituents in the chiral auxiliary.

ACKNOWLEDGEMENTS

The author expresses his indebtedness to the following people of this laboratory: A. T. Proveaux for GC–MS data, E. Adamek for the NMR spectral data, B. Dueben for valuable assistance with some of the chromatography, and R. R. Heath for helpful discussion in the preparation of this manuscript. Mention of a commercial or proprietary product does not constitute an endorsement by the USDA.

---

* In our experience liquid crystal phases ought to perform better than currently available GLC phases for nonpolar solutes whose separations are based primarily on molecular shape, especially since the separation factor can be improved by operating the system at temperatures below the lowest transition temperature (super-cooling).

** An amide formed between α-naphthylethylamine and 4,8-dimethyldecanoic acid (obtained by oxidizing the aldehyde) also gave a partial resolution with the DB-1 column (220°C): α 1.012, *k* values >25, $R \ll 1.0$. For GLC resolution, the generation of diastereomeric alkenes appears to be an improvement over the more traditional method of preparing diastereomeric amides.

REFERENCES

1 J. M. Brand, J. Chr. Young and R. M. Silverstein, in W. Herz, H. Grisebach and G. W. Kirby (Editors), *Progress in the Chemistry of Organic Natural Products*, Vol. 37, Springer, New York, 1979, pp. 95–98.
2 T. Saeed, P. Sandra and M. Verzele, *J. Chromatogr.*, 186 (1979) 611.
3 H. F. Graeme, N. Nicholson and E. Bayer, *Angew. Chem. Int. Ed. Engl.*, 17 (1978) 363.
4 B. Koppenhoefer, K. Hintzer, R. Weber and V. Schurig, *Angew. Chem. Int. Ed. Engl.*, 19 (1980) 471.
5 N. Oi, H. Kitahara and T. Doi, *J. Chromatogr.*, 207 (1981) 252.
6 W. A. König, I. Benecke and S. Sievers, *J. Chromatogr.*, 238 (1982) 427.
7 W. H. Pirkle and J. M. Finn, *J. Org. Chem.*, 47 (1982) 4037.
8 G. Gottarelli, B. Samori, C. Fuganti and P. Grasselli, *J. Am. Chem. Soc.*, 103 (1981) 472.
9 P. L. Rinaldi and M. Wilk, *J. Org. Chem.*, 48 (1983) 2141.
10 B. Halpern, in K. Blau and G. S. King (Editors), *Handbook of Derivatives for Chromatography*, Heyden, Philadelphia, PA, 1978, pp. 464–492.
11 E. Gilv-Av and D. Nurok, *Advances in Chromatography*, Vol. 10, Marcel-Dekker, New York, 1980, pp. 99–171.
12 G. Helmchen, G. Nill, D. Flockerzi, W. Schühle and M. S. K. Youssef, *Angew. Chem. Int. Ed. Engl.*, 18 (1979) 62.
13 G. Helmchen, G. Nill, D. Flockerzi and M. S. K. Youssef, *Angew. Chem. Int. Ed. Engl.*, 18 (1979) 63.
14 W. H. Pirkle, K. A. Simmons and C. W. Boeder, *J. Org. Chem.*, 44 (1979) 4891.
15 W. H. Pirkle and J. R. Hauske, *J. Org. Chem.*, 42 (1977) 1839.
16 M. J. S. Dewar and J. P. Schroeder, *J. Org. Chem.*, 30 (1965) 2296, 3485.
17 R. R. Heath, J. R. Jordan, P. E. Sonnet and J. H. Tumlinson, *J. High Resolut. Chromatogr. Chromatogr. Commun.*, 2 (1979) 712.
18 P. E. Sonnet and R. R. Heath, *J. Chromatogr.*, 238 (1982) 41.
19 P. E. Sonnet and R. R. Heath, unpublished results.
20 D. A. Evans and J. M. Takacs, *Tetrahedron Lett.*, 21 (1980) 4273.
21 P. E. Sonnet and R. R. Heath, *J. Org. Chem.*, 45 (1980) 3137.
22 J. R. Parikh and W. von E-Doering, *J. Amer. Chem. Soc.*, 89 (1967) 5505.
23 D. A. Evans and J. Bartroli, *Tetrahedron Lett.*, 23 (1982) 807.
24 L. F. Fieser and M. Fieser, *Reagents for Organic Synthesis*, Vol. 1, Wiley, New York, 1967, p. 1247.
25 L. F. Fieser and M. Fieser, *Reagents for Organic Synthesis*, Vol. 1, Wiley, New York, 1967, p. 415.
26 E. J. Corey and J. W. Suggs, *Tetrahedron Lett.*, 16 (1975) 2647.
27 E. Vedejs, G. P. Meier and K. A. J. Snoble, *J. Amer. Chem. Soc.*, 103 (1981) 2823.
28 P. E. Sonnet, *Org. Prep. Proceed. Int.*, 6 (1974) 269.
29 C. Litchfield, R. D. Harlow, A. F. Isbell and R. Reiser, *J. Amer. Oil Chem. Soc.*, 42 (1965) 73.
30 P.E. Sonnet, *J. Org. Chem.*, 47 (1982) 3793.
31 T. Suzuki, *Agric. Biol. Chem.*, 44 (1980) 2519.
32 T. Suzuki and K. Mori, *Appl. Entomol. Zool.*, 18 (1983) 134.
33 F. J. Ritter, I. E. M. Brüggemann-Rotgans, P. E. J. Verwiel, C. J. Persoons and E. Talman, *Tetrahedron Lett.*, 18 (1977) 2617; and later refs.
34 L. Ahlquist, S. Stallberg-Stenhagen, *Acta Chem. Scand.*, 25 (1971) 1685, and refs. cited therein.
35 K. Ohinata, M. Jacobson, R. M. Kobayashi, D. L. Chambers, M. S. Fujimoto and H. H. Higa, *J. Environ. Sci. Health*, A17 (1982) 197.
36 L. S. Ettre, *J. Gas Chromatogr.*, 1 (1963) 36.