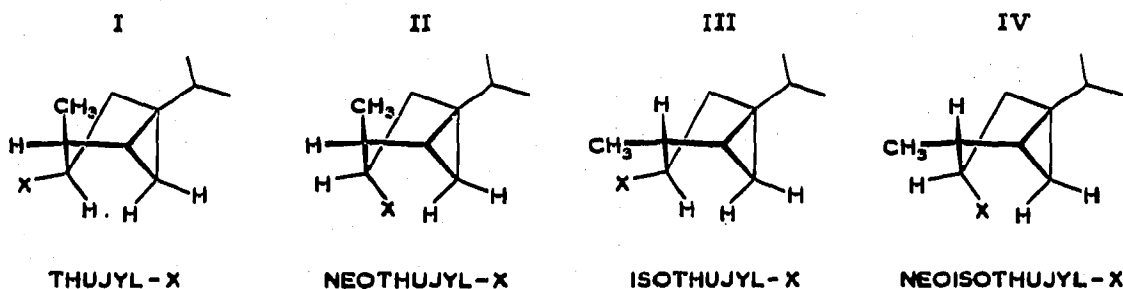


CHROM. 369I

Thin-layer chromatography of thujyl compounds

Column and thin-layer chromatography of certain epimeric compounds, *e.g.* menthylamines^{1,2}, bornylamines², menthols³, and cyclohexylamines⁴, have shown that the isomers with relatively shielded functional groups are eluted more readily by weakly polar solvents. The phenomenon is suggested to be general and to be useful for the rapid assignment of configurations or for indicating preferred conformations for compounds of known configuration⁴.

We here report the first systematic thin-layer chromatographic studies of thujyl compounds which enable the generality of these ideas to be extended to a bicyclic system. The thujones, thujols and thujylamines studied are of known configuration, I to IV^{5,6}, and have been shown by NMR spectroscopy to exist predominantly in *quasi-boat* conformations⁵⁻⁸.



Experimental

Pure specimens of the thujyl compounds were available⁶. Thin-layer plates (0.25 mm) were prepared with a Shandon apparatus using a slurry of silica gel (Merck G-grade, 30 g) and water (60 g), allowed to set for 5 min and then heated at 110° for 10 min while placed horizontally and for 60 min whilst vertical, before being stored in a desiccator.

Substrates (0.1 μ l, 10 % solution in hexane) were applied using a microsyringe and plates were developed with purified solvents (dried over molecular sieves) until the solvent front had risen 10 cm above the base-line. After removal of solvent, the plates were sprayed with a saturated solution of phosphomolybdic acid (analytical reagent grade) in ethanol and then heated at 110° for a few minutes to develop blue spots on a yellow background. Vanillin in concentrated sulphuric acid (2 %, v/v) also gave satisfactory traces, but diphenylpicrylhydrazyl⁹ as spray did not give good results.

The R_F values for the best solvent systems are given in Tables I and II.

Discussion

Good analytical separations were achieved. The only previous study in this field, that of thujols using only the conditions A of Table I, gave a similar elution order¹⁰.

Increase of the polarity or hydrogen-bonding ability of the solvent in the sequences A to D and E to F of Table I gave no complete reversal of the order of

TABLE I

THIN-LAYER CHROMATOGRAPHIC DATA FOR THUJOLS

Solvents: A = benzene; B = benzene-ethyl acetate (95:5); C = benzene-ethyl acetate (70:30); D = ethyl acetate; E = benzene-methanol (95:5); F = benzene-methanol (75:25); G = methanol; H = methanol; I = benzene. Conditions: (A-G) Plate activated in conventional manner (see Experimental section). (H,I) Plate activated 100°/0.5 mm for 3 h.

Compound	R_F values								
	A	B	C	D	E	F	G	H	I
(+)-Neoisothujol	0.27	0.38	0.70	0.80	0.50	0.67	0.74	0.76	0.14
(-)-Neothujol	0.20	0.31	0.62	0.80	0.44	0.66	0.77	0.80	0.09
(-)-Thujol	0.15	0.25	0.58	0.80	0.40	0.66	0.74	0.80	0.06
(+)-Isothujol	0.12	0.20	0.55	0.80	0.36	0.68	0.74	0.82	0.00

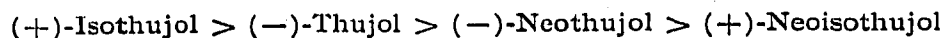
TABLE II

THIN-LAYER CHROMATOGRAPHIC DATA FOR THUJYLAMINES

Solvents: A = acetone-40-60° petroleum ether-880 aq. ammonia (50:25:1); B = acetone-40-60° petroleum ether-880 aq. ammonia (25:50:1); C = acetone-40-60° petroleum ether (25:50), saturated with ammonia gas; D = acetone-40-60° petroleum ether (50:25), saturated with ammonia gas.

Compound	R_F values			
	A	B	C	D
Amine from (+)-neoisothujol	0.79	0.88	0.91	0.73
Amine from (-)-neothujol	0.73	0.81	0.84	0.62
Amine from (+)-isothujol	0.63	0.71	0.66	0.45
Amine from (-)-thujol	0.55	0.65	0.56	0.33

elution of the thujols; but increased activation of the plates, conditions H and I, did allow such a change. Of the menthols, those isomers with low hydrogen-bonding ability due to relatively shielded hydroxyl groups migrated fastest in non-hydrogen-bonding solvents, whereas in eluting media of considerable hydrogen-bonding capacity the order was reversed, the isomers with less shielded hydroxyls now being favourably partitioned to the solvent³. Our results clearly indicate the hydrogen-bonding abilities to be



Except for a reversal of the former pair, this order would have been predicted from the conformations I and IV assuming that shielding by the methylene bridge is the major influence on hydrogen-bonding capacity.

Resolution of (-)-thujone and (+)-isothujone (derived from (-)-thujol and (+)-isothujol respectively by oxidation) could only be achieved with either toluene or dichloromethane as solvent when the R_F values were 0.28 and 0.33 (toluene) and 0.55 and 0.58 (dichloromethane). No polar component could be found to reverse the order, but our data are consistent with isothujone existing in a *quasi*-boat analogous

to III or IV and being less bonded to the stationary phase than its epimer in which the *quasi*-axial methyl group provides less shielding of the carbonyl function.

As with the thujones, a solvent pair could not be found that reversed the order of elution of the thujylamines from that of conditions A to D, Table II. However, under the last conditions, (—)-neothujol, (+)neoisothujol, (+)-isothujol, and (+)-sabinene (a terpene hydrocarbon) ran with R_F 0.78, 0.78, 0.74 and 0.80, which proves the conditions to be of the weakly hydrogen-bonding type in which the most sterically-hindered amine ran fastest. The observed order of hydrogen-bonding ability is thus

Thujylamine > Isothujylamine > Neothujylamine > Neoisothujylamine

which is expected from considerations of conformations I to IV, and does not show the reversal of the first pair that is found for the thujols. For the latter the order as determined by shielding by the methyl group is apparently easily reversed by small changes in conditions that are insufficient to alter the broader division caused by shielding by the methylene bridge.

In conclusion, the R_F values of these thujyl compounds can be rationalised on the correlation between configurations, conformations, and R_F values that had been previously proposed, and the results lend confidence to the extension of these ideas to other mono- and bicyclic compounds.

Department of Chemistry, University College,
London, W.C.1 (Great Britain)

D. V. BANTHORPE
K. W. TURNBULL

- 1 G. VAVON AND G. MEDYNSKI, *Compt. Rend.*, 229 (1949) 655.
- 2 B. GASTAMBIDE, *Ann. Chim. (Paris)*, 9 (1954) 257.
- 3 H. J. PETROWITZ, *Angew. Chem.*, 72 (1960) 921.
- 4 H. FELTKAMP AND F. KOCH, *J. Chromatog.*, 15 (1964) 314.
- 5 T. NORIN AND M. S. BERGQUIST, *Arkiv. Kemi*, 22 (1964) 137.
- 6 D. V. BANTHORPE AND H. F. S. DAVIES, *J. Chem. Soc.*, in press.
- 7 K. TORI, *Chem. Pharm. Bull. (Tokyo)*, 12 (1964) 1439.
- 8 H. E. SMITH, J. C. D. BRAND, E. H. MASSEY AND L. J. DURHAM, *J. Org. Chem.*, 31 (1966) 690.
- 9 G. BERGSTRÖM AND C. LAGERCRANTZ, *Acta Chem. Scand.*, 18 (1964) 560.
- 10 G. M. NANO AND A. MARTELLI, *Gazz. Chim. Ital.*, 94 (1964) 816.

Received July 10th, 1968

J. Chromatog., 37 (1968) 366-368