Journal of Chromatography, 100 (1974) 240–242

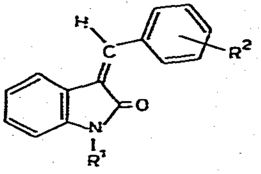
CHROM. 7761

Note

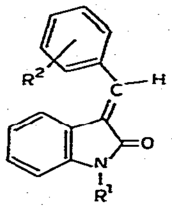
Thin-layer chromatographic separation of some substituted 3-benzylidene-indol-2(3H)-ones

ROY W. DAISLEY
Department of Pharmacy, Brighton Polytechnic, Brighton, Sussex BN2 4GJ (Great Britain)
and
JOHN WALKER
Pharmacy Department, Chelsea College, University of London, London S.W.3 (Great Britain)
(Received May 22nd, 1974)

During our investigations into the synthesis and stereochemistry of some substituted 3-benzylidene-1-methylindol-2(3H)-ones[1] it became necessary to develop a suitable method for the rapid separation and quantitation of the *cis* (Ia–f) and *trans* (IIa–f) isomers formed. Thin-layer chromatography (TLC) was chosen because of its rapidity and simplicity, quantitation being achieved by using the method described earlier[2]. The resulting R_F values were found to be useful in assessing the relative configurations of these isomers.



Ia–f



IIa–f

	R^1	R^2
(a)	CH_3	H
(b)	CH_3	4-Cl
(c)	CH_3	3,4-diMeO
(d)	CH_3	4-F
(e)	CH_3	4-MeO
(f)	H	H

EXPERIMENTAL

Glass plates (8 × 15 cm) were coated with a layer (250 μm) of Silica Gel PF_{254} (Merck, Darmstadt, G.F.R.) according to Stahl[3]. The plates were activated (110° for 30 min) and the samples applied in methanol solution 2 cm from the bottom of the plate and at 2-cm intervals. The chromatoplates were developed at room temperature in equilibrated tanks lined with filter paper until the solvent front was 1 cm from the top of the plate. The solvents used were: (A) diethyl ether–cyclohexane (4:1); (B) petroleum ether (b.p. 60–80°)–diethyl ether (1:1); (C) diethyl ether; (D) diethyl ether–methylene dichloride (1:19); (E) diethyl ether–methylene dichloride (19:1). The developed plates were examined visually.

RESULTS AND DISCUSSION

Table I shows the R_F values of compounds I and II. In all cases the *cis* isomers (Ia–f) have higher R_F values than their *trans* counterparts (IIa–f). This phenomenon is probably due to the fact that the *trans* isomer is more coplanar and also allows adsorption to occur via the carbonyl and exocyclic double bonds. This latter effect cannot occur in the *cis* isomers due to the steric hindrance caused by the phenyl ring in preventing approach of these double bonds to the adsorbent surface.

TABLE I

$R_F \times 100$ VALUES OF A SERIES OF *cis* AND *trans* ISOMERS

TLC of *cis* isomers (Ia–f) and corresponding *trans* isomers (IIa–f) using solvent systems A–E.

Compound	*Solvent system*				
	A	*B*	*C*	*D*	*E*
Ia	72	52	90	82	94
IIa	56	36	76	60	82
Ib	80	56	93	85	98
IIb	62	29	78	64	92
Ic	38	25	65	40	68
IIc	33	20	54	33	56
Id	67	56	97	85	98
IId	57	35	83	57	89
Ie	61	33	82	64	90
IIe	50	29	66	51	74
If	55	–	–	–	–
IIf	35	–	–	–	–

Palamareva *et al.*[4] reported that with 37 pairs of diastereoisomers, the *erythro* isomer invariably has the higher R_F value relative to the *threo* isomer and suggested that the relative configuration of such isomers could be assessed by TLC.

Phillipson and Shellard[5–8] have used TLC data as an aid to structural and configurational correlations in a series of closely related indole and oxindole alkaloids.

Cooper[9] found an R_F inversion among the related and relatively small series of some alicyclic analogues of mescaline. This observed inversion between his olefin and cyclopropane derivatives probably reflects differences in their mode of binding to the adsorbent. Our findings support those of Palamereva *et al.* in that among closely related analogues TLC can be used to assess configuration.

In the N-unsubstituted compounds the *cis* isomer (If) has a higher R_F value than the *trans* isomer (IIf), although both have much lower R_F values than their N-methyl analogues (Ia, IIa). This reflects the greater polarity of the amido group in If and IIf, which in turn causes an increase in their adsorption affinity for the silica gel.

REFERENCES

1 R. W. Daisley and J. Walker, *J. Chem. Soc., C*, (1971) 3357.
2 R. W. Daisley and C. J. Olliff, *J. Pharm. Pharmacol.*, 22 (1970) 202.
3 E. Stahl, *Pharmazie*, 11 (1956) 633.
4 M. Palamareva, M. Haimova, J. Stefanovsky, L. Viteva and B. Kurtev, *J. Chromatogr.*, 54 (1971) 383.
5 J. D. Phillipson and E. J. Shellard, *J. Chromatogr.*, 24 (1966) 84.
6 J. D. Phillipson and E. J. Shellard, *J. Chromatogr.*, 31 (1967) 427.
7 J. D. Phillipson and E. J. Shellard, *J. Chromatogr.*, 32 (1968) 692.
8 E. J. Shellard, J. D. Phillipson and D. Gupta, *J. Chromatogr.*, 32 (1968) 704.
9 P. D. Cooper, *J. Chromatogr.*, 67 (1972) 184.