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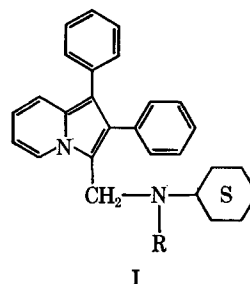
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TLC Analysis of Mannich Bases Derived from Indolizines

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Abstract □ Seven Mannich bases derived from indolizines were studied using TLC procedures. Alumina, cellulose, and silica gel plates and a number of solvent systems were employed.

Keyphrases □ Mannich bases, from indolizines—TLC studies □ TLC—characterization, Mannich bases derived from indolizines □ Indolizine Mannich base derivatives—TLC requirements, characterization



It was established in previous work that certain indolizines with dialkylaminomethyl side chains at the C-3 position exhibit pronounced CNS depression (1, 2). As part of a continuing exploration of indolizines with potential biological activity, a series of Mannich bases with *N*-substituted cyclohexylaminomethyl groupings were synthesized using 1,2-diphenylindolizine as the starting compound. The chemistry and biological activities of these compounds are reported elsewhere (3). In the present investigation, the characterization of these compounds is attempted using TLC procedures.

EXPERIMENTAL

Materials—3-Cyclohexylaminomethyl derivatives of 1,2-diphenylindolizine (Structure I) were used, where R was substituted as indicated in Table I. These compounds were prepared according to the methods described by Harrell *et al.* (3).

Developing Systems—Nineteen different solvent systems, indicated in Table II, were employed.

Table I—Compounds Used

Compound Number	R =	Melting Point
I		182–183°
II	—C ₆ H ₅	123–124°
III	—CH ₃	112–113°
IV	(CH ₃) ₂ CH—	127–128°
V	NC—CH ₂ —CH ₂ —	152–153°
VI	HO—CH ₂ —CH ₂ —	138–139°
VII		137–138°

Detection—In most cases the spots were observed visually, giving a characteristic green color. The color was developed immediately after the plates were removed from the tank. A UV lamp¹ was also used. All compounds appeared to fluoresce under the longwave UV light.

Preparation of Plates—The plates (20 × 20 cm.) were coated with alumina², cellulose³, or silica gel⁴, 250 nm. thick, according to Stahl (4).

General Procedure—Solutions of the compounds were prepared by dissolving 10-mg. quantities into 3 ml. of acetone, chloroform, dioxane, or dimethylformamide (DMF). Samples of the solutions were applied 1.5 cm. from the bottom edges of the alumina, cellulose, or silica gel plates, and the ascending chromatograms were allowed to travel 10 cm. at room temperature. All experiments were repeated in a dark room at the same temperature (21°).

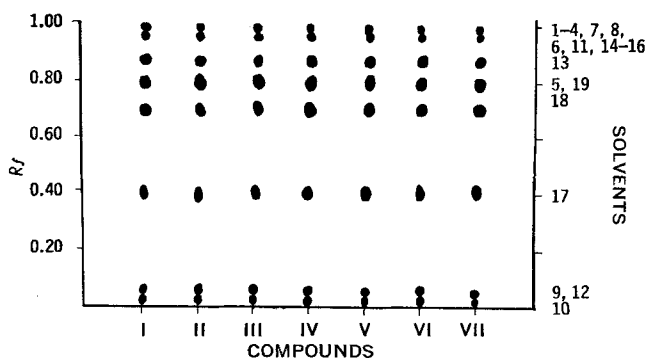


Figure 1—Spot detection on silica gel plates. Left: R_f values. Right: solvent systems used (Table II). Compounds I–VII are those listed in Table I.

¹ B. L. E. Spectroline, model C-3F.

² Aluminum Oxide G, Merck Co.

³ MN-Cellulose Powder 300, Macherey, Nagel and Co.

⁴ Silica gel G, Merck Co.

Table II—Solvent Systems Used

System Number	Composition
1	Chloroform-methanol (90:10)
2	Chloroform-methanol (90:10) (saturated with 10% ammonia)
3	Benzene-acetone (90:10)
4	Benzene-ethanol (90:10)
5	Acetone-chloroform-acetic acid-water (40:40:20:5)
6	Acetone-chloroform-acetic acid-water (30:30:30:10)
7	Chloroform-ethanol (99:1)
8	Acetone
9	n-Hexane
10	Water
11	Benzene
12	Cyclohexane
13	Methanol
14	Dichloromethane
15	n-Butanol saturated with water
16	n-Butanol-acetic acid-water (30:50:20)
17	n-Hexane-benzene (70:30)
18	n-Hexane-benzene (50:50)
19	Methanol-cyclohexane-acetone (60:40:20)

After development, the chromatoplates were removed, air dried, and visualized. All experiments were performed in triplicate.

RESULTS AND DISCUSSION

The results (Table III and Fig. 1) indicate that although a number of solvent systems (Table II) were employed, using layers of alumina, cellulose, and silica gel, all seven compounds (I-VII, Table I) gave the same R_f value, although different for the various solvent systems and layers (Table III).

Two main possibilities should be examined for the explanation of these results. First, the steric effects of the introduced (at the position R of the ring) groups are not profound enough to overcome the effect of the bulky main component on the adsorption properties of the various compounds in the series.

Martin (5) stated that a dependence between chemical structure and chromatographic behavior exists (6, 7) and that R_f values are affected by the substitution on the ring. However, deviations from the rule have also been observed (8). Here, the contribution of the introduced group to the R_m value ($R_m = \log 1/R_f$) is probably dependent on the total molecule, on the position of this group in the

Table III— $R_f \times 100$ Values of 1,2-Diphenylindolizine Derivatives*

Com- pounds	Solvents																		
	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19
Silica Gel Plates																			
I	100	100	100	100	80	95	100	100	5	0	100	4	85	98	100	100	40	70	80
II	100	100	100	100	80	95	100	100	5	0	100	4	85	98	100	100	40	70	80
III	100	100	100	100	80	95	100	100	5	0	100	4	85	98	100	100	40	70	80
IV	100	100	100	100	80	95	100	100	5	0	100	4	85	98	100	100	40	70	80
V	100	100	100	100	80	95	100	100	5	0	100	4	85	98	100	100	40	70	80
VI	100	100	100	100	80	95	100	100	5	0	100	4	85	98	100	100	40	70	80
VII	100	100	100	100	80	95	100	100	5	0	100	4	85	98	100	100	40	70	80
Alumina Plates																			
I	98	—	100	—	—	95	—	—	—	0	—	—	—	—	—	86	60	—	—
II	98	—	100	—	—	95	—	—	—	0	—	—	—	—	—	86	60	—	—
III	98	—	100	—	—	95	—	—	—	0	—	—	—	—	—	86	60	—	—
IV	98	—	100	—	—	95	—	—	—	0	—	—	—	—	—	86	60	—	—
V	98	—	100	—	—	95	—	—	—	0	—	—	—	—	—	86	60	—	—
VI	98	—	100	—	—	95	—	—	—	0	—	—	—	—	—	86	60	—	—
VII	98	—	100	—	—	95	—	—	—	0	—	—	—	—	—	86	60	—	—
Cellulose Plates																			
I	99	—	100	—	—	99	—	—	—	0	—	—	—	—	—	—	100	—	—
II	99	—	100	—	—	99	—	—	—	0	—	—	—	—	—	—	100	—	—
III	99	—	100	—	—	99	—	—	—	0	—	—	—	—	—	—	100	—	—
IV	99	—	100	—	—	99	—	—	—	0	—	—	—	—	—	—	100	—	—
V	99	—	100	—	—	99	—	—	—	0	—	—	—	—	—	—	100	—	—
VI	99	—	100	—	—	99	—	—	—	0	—	—	—	—	—	—	100	—	—
VII	99	—	100	—	—	99	—	—	—	0	—	—	—	—	—	—	100	—	—

* Compounds I-VII are the ones depicted in Table I; Solvents 1-19 are the ones depicted in Table II.

molecule, and upon the rest of the molecule. Moreover, the adsorbents and solvents used may have suppressed possible R_f deviations due to chain substitutes. As a result, all compounds traveled the same distance, producing the same R_f .

Studies of the separation of the compounds between the liquid phase of the support system and that of the moving solvent (partition coefficient) did not produce any valid information. The use of cellulose layers (where partition is predominant) as well as silica gel and alumina layers left no doubt that differences in partition will not be conclusive, since all seven compounds produced the same R_f value whether on cellulose, alumina, or silica gel layers (although different for the various solvent systems and/or layers, Table III).

Moreover, to avoid any changes in the stationary phase, the plates were equilibrated with the vapor of the developing solvent mixture, and the chromatograms were run in a solvent-saturated tank.

Second, although stability studies indicated that all seven compounds remained unchanged under normal conditions (3), some chemical changes may have occurred. These changes probably occurred after the compounds were dissolved in the solvents or were applied on the plates, resulting in the formation of a common compound, which gave the same R_f value in any given solvent system or layer for all seven compounds.

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