Thin-layer chromatography of N-(*p*-toluenesulfonyl)-carbamates

In earlier studies we have described the chromatographic behavior (including thin-layer) of various classes of carbamates, *viz.*, 3,4-methylenedioxyphenyl- and 3,4-methylenedioxybenzyl esters[1], N-hydroxy-N-methyl-carbamate esters[2], the isomeric chlorophenyl-trichloroacetyl carbamates[3], and N-carbamoyl-aziridines[4], and by paper chromatography unsubstituted as well as N-hydroxy-carbamate esters[5].

Gas chromatography has been utilized for the evaluation of unsubstituted[6,8], N-substituted and N,N-disubstituted carbamate esters[7,8], N-hydroxymethyl-[9], chloroethyl-[10], bis(2-chloroethyl)-[10], trichloroacetyl-[11], *m*-fluorosulfonylphenyl-[12] and 3,4-methylenedioxyphenyl-[13] carbamic acid esters and N-carbamoyl-aziridines[14].

This study relates primarily to the chromatographic and chromogenic evaluation of a series of N-(*p*-tosyl) alkyl and aryl carbamate esters as well as a number of methyl (*p*-benzenesulfonyl)-carbamates. A variety of *p*-benzenesulfonamides have been included for chromatographic comparisons.

A number of *para*-substituted benzenesulfonyl carbamates have been recently reported to have utility as herbicides[15–17], while various benzenesulfonyl carbamate ethyl esters[18] as well as N-(*p*-tosyl)-urethans[19] have been used in the preparation of sulfonylureas which have recognized utility as oral hypoglycemia agents.

Experimental

Thin-layer chromatography. The silicic acid chromatoplates were prepared according to the method of MORLEY AND CHIBA[20]. Silica Gel DF-5* was applied on 8 × 8 in. plates to a thickness of 280 μ. After air-drying, the plates were activated in an oven for 30 min. Acetone solutions (1–2 μl containing 1–10 μg/μl) of test substance were applied along a line 2.5 cm from the lower end of the plate and developed by the ascending method (30 min, *ca.* 12 cm). After evaporation of the solvent, the spots were located by U.V. detection, then sprayed with one of the chromogenic reagents and the initial color development as well as subsequent color changes noted with the results described in Table I.

The developing solvent systems utilized in this work were:

(A) 2.5% acetone in benzene
(B) 2.0% ethanol in benzene
(C) Benzene–ethyl acetate (80:20)
(D) Acetone–benzene–water (65:30:5)[21]
(E) Chloroform–95% ethanol (9:1)[22]

Detecting reagents

(1) ***DDQ reagent.*** 2% 2,3-dichloro-5,6-dicyano-1,4-benzoquinoneimine in benzene.

(2) ***TCNE reagent.*** 2% tetracyanoethylene in benzene.

(3) ***Gibbs reagent.*** 2% 2,6-dibromo-N-chloro-*p*-benzoquinoneimine in benzene.

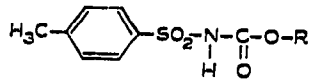
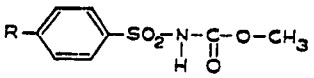
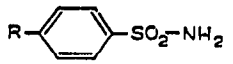
(4) ***FCNP reagent***[23,24]. Mixture of equal volumes of 10% sodium hydroxide, 10% sodium nitroprusside, 10% potassium ferricyanide diluted with 3 volumes of water, mixed in equal volumes with acetone, and the mixture left to stand 30 min prior to use.

* Obtained from Camag, Muttenz, Switzerland.

TABLE I

SPOT COLORS OF N-(*p*-TOSYL)-CARBAMATES ON SILICA GEL DF-5

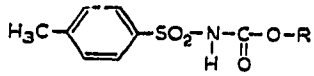
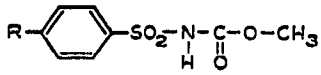
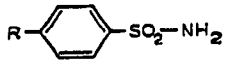
Colors developed at room temperature: B = blue; Bn = brown; C = crimson; Cr = cream; G = green; Gr = grey; L = lilac; Lav = lavendar; M = maroon; O = orange; Ol = olive; P = purple; Pk = pink; T = tan; V = violet; W = white; Y = yellow; wk = weak.

Compound No.	*R*	*Detecting reagents*			
		1	*2*	*3*	*4*
					
1	Methyl	Cr	Y-G→T	Bn	B (wk)
2	Ethyl	Cr	Y-G→T	Bn	B (wk)
3	*n*-Propyl	Cr	Y-G→T	Bn	B (wk)
4	Isopropyl	Cr	Y-G→T	Bn	B (wk)
5	Allyl	Cr	Y-G	Bn	B (wk)
6	*tert.*-Butyl	Cr (wk)	Y-G→T	Bn (wk)	B (wk)
7	Amyl	Cr (wk)	Y-G→O	Bn (wk)	B (wk)
8	Octyl	Cr (wk)	Y-G→O	Bn (wk)	B (wk)
9	Cyclopentyl	Bn	T	Pk	T
10	Cyclohexyl	Bn	T	Pk	T
11	Phenyl	Y-G	Ol	O-Gn	Gr
12	Benzyl	Y	Ol	Bn	C
13	β-Phenethyl	O	Ol	Bn	L
14	Anisyl	B-Gr	Pk	Y-Pk	L
15	3,4-Methylenedioxyphenyl	B→G	V→O*	V→M*	V/B**
16	3,4-Methylenedioxybenzyl	G	B-V→L*	O	T
17	*o*-Chlorophenyl	Y	O-C	O	Y-O
18	*m*-Chlorophenyl	Y	O	O	B-G*
19	*p*-Chlorophenyl	Y	Bn	O-C	L*
20	2,3-Dichlorophenyl	V	Y-G	Y	L (wk)
21	2,4-Dichlorophenyl	B-G	Y-G	Pk-O	L (wk)
22	2,5-Dichlorophenyl	Pk-B	Y-G	Y-O	O
23	2,6-Dichlorophenyl	Lav/Bn**	Y-G	Y	O
24	3,4-Dichlorophenyl	B-Gr	Y-G	O-C	L (wk)
25	3,5-Dichlorophenyl	Pk	Y-G	Y-O	L (wk)
26	2,4,5-Trichlorophenyl	B-Gr	G	O	O
27	2,4,6-Trichlorophenyl	Gr	Y-G	C	O
28	2,3,4,6-Tetrachlorophenyl	Pk	Y-G	C	O
29	Pentachlorophenyl	Y	G	Y-O	O
					
30	Amino	P	B-Gr	O	L
31	Nitro	Pk	B-Gr	Pk (wk)	Pk (wk)
32	N-Acetyl	Pk	B-Gr	Y	Pk (wk)
					
33	Amino	P	W	O-C→M	V
34	Fluoro	Y-O	W	Cr	O-C
35	Chloro	Y-O	W	Cr	T
36	Nitro	Y-O	W	Y	T
37	Methoxy	Y-O	W	Y	Pk
38	Carboxy	Y-O	W	W	T
39	Tolyl	O-C	W	T	O

* Color development after 1 min at 90°.
** Fluorescence after spraying.

TABLE II

R_F VALUES × 100 OF ALKYL AND ARYL N-(*p*-TOSYL)-CARBAMATES

Compound No.	*R*	*M.p.* (°C)	*Solvent systems*				
			A	*B*	*C*	*D*	*E*
							
1	Methyl	106–107	11	18	22	37	31
2	Ethyl	82– 84	16	24	28	42	36
3	*n*-Propyl	64– 65	22	29	35	47	40
4	Isopropyl	79– 80	16	23	26	39	33
5	Allyl	68– 69	30	38	39	54	46
6	*tert.*-Butyl	115–117	21	28	35	46	40
7	Amyl	45– 46	27	35	44	56	48
8	Octyl	53– 54	33	47	55	67	59
9	Cyclopentyl	71– 72	17	27	29	47	42
10	Cyclohexyl	85– 86	23	32	34	52	48
11	Phenyl	116–118	25	34	34	54	50
12	Benzyl	98– 99	32	40	39	60	55
13	β-Phenethyl	93– 95	38	46	45	65	61
14	Anisyl	116–117	37	44	41	63	58
15	3,4-Methylenedioxyphenyl	133–135	26	28	30	52	41
16	3,4-Methylenedioxybenzyl	113–115	33	33	36	57	46
17	*o*-Chlorophenyl	119–120	33	40	44	61	55
18	*m*-Chlorophenyl	98– 99	20	34	32	50	43
19	*p*-Chlorophenyl	91– 92	11	28	24	42	36
20	2,3-Dichlorophenyl	112–113	29	38	41	57	53
21	2,4-Dichlorophenyl	113–114	30	37	43	56	52
22	2,5-Dichlorophenyl	132–133	23	31	34	50	46
23	2,6-Dichlorophenyl	113–114	17	35	27	42	40
24	3,4-Dichlorophenyl	117–118	6	21	19	35	32
25	3,5-Dichlorophenyl	129–130	11	29	22	30	26
26	2,4,5-Trichlorophenyl	125–127	30	36	40	58	50
27	2,4,6-Trichlorophenyl	138–139	37	42	48	65	60
28	2,3,4,6-Tetrachlorophenyl	119–121	40	44	57	71	66
29	Pentachlorophenyl	140–141	36	36	51	64	63
							
30	Amino	146–147	10	20	23	33	25
31	Nitro	147–149	34	44	48	58	52
32	N-Acetyl	212–214	18	28	31	45	35
							
33	Amino	164–166	10	13	23	35	21
34	Fluoro	126–128	15	20	29	40	29
35	Chloro	145–146	26	34	43	54	43
36	Nitro	175–177	39	48	56	65	63
37	Methoxy	113–115	32	40	50	60	52
38	Carboxy	294–296	7	8	17	28	12
39	Methyl	136–138	20	27	36	48	36

Materials

p-Toluenesulfonyl isocyanate (*p*-tosyl isocyanate) was obtained from the Upjohn Co., Carwin Research Labs, North Haven, Conn., U.S.A. *p*-Fluoro-, *p*-chloro-, *p*-nitro- and *p*-carboxysulfonamide were obtained from Aldrich Chemical Co., Milwaukee, Wisc., U.S.A.; *p*-amino- and *p*-tolylsulfonamide from J. T. Baker Chemical Co., Phillipsburg, N.J., U.S.A.; and *p*-methoxysulfonamide from K & K Labs Inc., Plainview, N.Y., U.S.A. N-(*p*-Tosyl)-carbamates were prepared via the reaction of *p*-tosyl isocyanate with the appropriate alcohol or phenol according to the procedure of McFARLAND AND HOWARD[25], and the products recrystallized from benzene–petroleum ether. Compounds 30–32 (methyl benzenesulfonyl-carbamates) were furnished by Dr. H. J. COTTRELL, May & Baker Ltd., Dagenham, Great Britain.

Results and discussion

Table I depicts the spot colors of alkyl and aryl N-(*p*-tosyl)-carbamates, methyl *p*-substituted N-benzenesulfonyl-carbamates and *p*-substituted sulfonamides on Silica Gel DF-5 plates obtained with four detecting reagents. Table II depicts the R_F values of the above classes of compounds obtained with five solvent systems.

It is possible to distinguish the monochlorophenyl derivatives (compounds 17–19) from one another utilizing the FCNP reagent. The isomeric dichlorophenyl derivatives (compounds 20–25) can best be distinguished from one another with the aid of the DDQ reagent.

The isomeric monochlorophenyl carbamate esters have been found to be best separated utilizing solvent system A (2.5 % acetone–benzene). The order of R_F values for the monochlorophenyl derivatives (compounds 17–19) in all solvent systems tested was *o* > *m* > *p*.

Separation of isomeric dichlorophenyl derivatives has best been accomplished utilizing solvent system C (benzene–ethyl acetate). It has not been possible to effect the separation of 2,3- from 2,4-dichlorophenyl N-(*p*-tosyl)-carbamates with any of the solvent systems employed. For all the solvent systems studied the following order prevails: 2,3; 2,4 > 2,5 > 2,6 > 3,5 > 3,4.

This same order of separation was previously observed for the chromatography of N-trichloroacetyl-carbamates[3].

The isomeric trichlorophenyl derivatives, *viz.*, 2,4,5 and 2,4,6 have been best separated utilizing solvent E (chloroform–ethanol) with the order being 2,4,6 > 2,4,5 for all solvent systems employed.

In regard to the methyl N-(benzenesulfonyl)-carbamates (compounds 30–32) the order of separation achieved in all solvent systems was NO_2 > N-acetyl > amino.

The influence of functionality in the *para* position of *p*-benzenesulfonamides is shown in the following order of R_F values:

$$NO_2 > OCH_3 > Cl > CH_3 > F > NH_2 > COOH$$

in all the solvent systems tested, with solvent system E (chloroform–ethanol) being the most efficient.

The efficacy of this solvent system has been previously noted[22] for the separation of ten medicinal sulfonamides on polyamide layers.

In results to be published separately, it was observed that aryl N-(*p*-tosyl)-

carbamates underwent thermal cleavage to *p*-toluenesulfonamide and the respective phenol during gas chromatographic analysis. This present study has indicated the feasibility of separating the alkyl and aryl N-(*p*-tosyl)-carbamates intact by thin-layer chromatographic techniques.

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