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Note

Chromatographic separation of 2-phenylquinoline analogues

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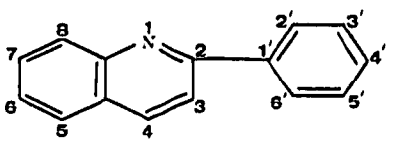
Recently, a series of new compounds, 2-phenylquinolines, were found to possess potent autonomic nervous system effects[1,2]. However, little or no information was available on the separation and quantitation of these particular compounds from biological material. As a result of this lack of information, the following study was performed to establish a sensitive and reproducible chromatographic procedure for the separation and quantitation of various 2-phenylquinoline analogues.

MATERIALS AND METHODS

Table I illustrates the various 2-phenylquinoline analogues utilized in the study. These compounds were synthesized by Dr. A. Gennaro (Philadelphia College of Pharmacy and Science).

TABLE I

2-PHENYLQUINOLINE ANALOGUES



Compound code letter	*Substituents and other chemical changes*
A	None
B	1-Methyl
C	1-Methyl; no 2-phenyl ring
D	1-Methyl; 3-hydroxy
E	1-Methyl; 4'-hydroxy
F	1-Methyl; 3',4'-dimethoxy
G	1-Methyl; 2',4'-dimethoxy
H	1-Methyl; 2',5'-dimethoxy
I	1-Methyl; 3',4',5'-trimethoxy
J	1-Methyl; 3',4'-methylenedioxy
K	2',4'-Dimethoxy
L	2',5'-Dimethoxy
M	3',4',5'-Trimethoxy
N	3-Hydroxy

For both the thin-layer (TLC) and gas–liquid (GLC) chromatographic procedures, the various compounds were dissolved in chloroform at a concentration of 1 mg/ml.

TLC was carried out on a silica gel thin-layer plate (Analtech, Newark, Del., U.S.A.). The two solvent systems utilized were: ethyl acetate–methanol–ammonium hydroxide (17:2:1) and methanol–ammonium hydroxide (19:1). Detection of the compounds was accomplished by utilizing a multiple spray system[3].

GLC was carried out on a Glowall (Willow Grove, Pa., U.S.A.), Model 310 instrument, equipped with a flame ionization detector. The chromatographic conditions were as follows: the temperatures of the injection block, the oven, and the detector were 275°, 255°, and 275°, respectively; the carrier gas was nitrogen at a flow-rate of 40 ml/min. The column employed was a 3% OV-17 on Chromosorb W HP 80–100 mesh (Supelco, Bellefonte, Pa., U.S.A.). One microgram of each of the compounds was injected into the column. The preparation of the bis(trimethylsilyl)acetamide (BSA) derivatives was carried out according to the method of Fish and Wilson[4].

RESULTS AND CONCLUSIONS

Table II shows the R_F values of the various 2-phenylquinoline compounds studied, utilizing two solvent systems and a multiple detection system. In solvent system S_1, all the quaternary compounds (B, C, D, E, F, H, I, and J) with the exception of compound G possessed relatively indistinguishably low R_F values. Similarly,

TABLE II

TLC SEPARATION OF PHENYLQUINOLINE ANALOGUES

Solvent systems: S_1 = ethyl acetate–methanol–ammonium hydroxide (17:2:1); S_2 = methanol–ammonium hydroxide (19:1). Detection: D_1 = UV light; D_2 = 0.1% diphenylcarbazone plus 0.25% mercuric sulfate; D_3 = iodoplatinate solution; D_4 = Dragendorff solution. Color code: Bl = blue; Br = brown; Or = orange; Pu = purple; R = red; W = white; Y = yellow; YPu = yellowish purple.

Compound	*R_F × 100 value*		*Detection*			
	S_1	*S_2*	*D_1*	*D_2*	*D_3*	*D_4*
A	99	87	W	—	Br	R-Pu
B	18	20	Pu	Pu	Br	R-Pu
C	14	70	Bl	—	Bl	Bl
D	38	83	Y	YPu	Br	R-Pu
E	8	13	Y	—	—	—
F	12	15	Y	YPu	Br	—
G	99	87	Or	YPu	Or	Or
H	14	17	Or	YPu	Br	R-Pu
I	11	13	Y	YPu	Br	R-Pu
J	17	19	Y	YPu	Br	R-Pu
K	99	87	Or	Y	Or	Or
L	99	87	Or	Y	Or	Or
M	99	87	Y	Y	Or	Or
N	90	94	Y	—	—	Or

all the tertiary compounds (A, K, L, M and N) were found to have very high R_F values. In an attempt to achieve a better separation, a second solvent system (S_2) was utilized. The results indicated that, although some of the closely related analogues separated, the majority of the R_F values still overlapped.

TABLE III

GLC SEPARATION OF 2-PHENYLQUINOLINE ANALOGUES

Optimum conditions as given in Materials and methods.

Compound	*Relative retention times*	
	*Free form**	*BSA derivatives**
A	1.00	1.00
B	1.00	ND
C	ND**	1.50
D	1.75	1.50
E	3.62	2.75
F	5.0	ND
G	5.75	3.00
H	3.62	3.75
I	7.25	ND
J	4.00	4.37
K	5.75	3.25
L	3.75	3.50
M	7.50	7.00
N	1.75	1.50

* Retention times are relative to compound A (2 min for both the free and the BSA derivatives).
** ND = Non-detectable.

As a result of the above findings, the compounds have been studied with the gas chromatograph. Table III shows the relative retention times to 2-phenylquinoline of the various compounds under study. The results indicate that utilizing the gas chromatograph, a separation and possibly a quantitation of the 2-phenylquinoline analogues could be accomplished with a high degree of accuracy.

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