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Note

Gas chromatographic data of 31 benzodiazepines and metabolites

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Since the discovery of chlordiazepoxide in 1957, the benzodiazepines have had a tremendous impact on the treatment of disorders of nervous origin. These drugs have become among the most widely prescribed in medicine and referred to in the analytical literature[1–20,26].

Many other benzodiazepine derivatives have also been introduced. In this work we have determined the gas chromatographic properties of 31 important benzodiazepine compounds and metabolites.

EXPERIMENTAL AND RESULTS

The gas chromatograph was a Varian Aerograph Series 2100 with a flame-ionization detector, integrator, a 1.5 m × 2 mm I.D. glass column packed with 3% OV-17 or 3% SE-30 on Chromosorb G AW DMCS (80–100 mesh), using nitrogen as the carrier gas at a flow-rate of *ca.* 15 ml·min^{-1}.

Retention indices were calculated according to the literature[21–25]. When the gas chromatographic data are discussed, it must be considered that rearrangements and thermolysis are possible, especially with 3-hydroxybenzodiazepines[27,28].

TABLE I

GAS CHROMATOGRAPHIC DATA FOR BENZODIAZEPINES

No.	*Benzodiazepine*	*250°*				*280°*			
		Retention time (sec)		*Retention index*		*Retention time (sec)*		*Retention index*	
		SE-30	*OV-17*	*SE-30*	*OV-17*	*SE-30*	*OV-17*	*SE-30*	*OV-17*
1	Chlordiazepoxide	134	435	2570	3070	65	180	2660	3160
		+266	+671	2845	3220	+114	+520	2910	3595
2	Demoxepam (nordiazepam N-oxide)	135	420	2575	3060	—	169	—	3140
3	Desmethylchlordiazepoxide base	279	1234	2885	3485	114	474	2930	3590
4	Diazepam	102	297	2490	2950	48	127	2510	3020
5	Nordiazepam	120	403	2555	3060	57	162	2585	3125
6	3-Hydroxydiazepam (temazepam)	152	472	2630	3125	70	194	2675	3002

(Continued on p. 410)

TABLE 1 *(continued)*

No.	Benzodiazepine	200°				280°			
		Retention time (sec)		Retention index		Retention time (sec)		Retention index	
		SE-30	OV-17	SE-30	OV-17	SE-30	OV-17	SE-30	OV-17
7	Oxazepam	73	198	2380	2830	40	93	2425	2890
8	Nitrazepam	—	—	—	—	96	335	2830	3455
9	7-Aminonitrazepam	215	—	2785	—	104	369	2870	3475
10	7-Acetamidonitrazepam	—	—	—	—	210	823	3205	3815
11	Medazepam base	66	146	2285	2710	34	71	2360	2775
12	Chlorazepate	—	377	—	3070	65	163	2655	3125
13	Lorazepam	86	255	2440	2925	48	115	2515	2980
14	Prazepam	—	—	—	—	81	230	2715	3180
15	3-Hydroxyprazepam	—	—	—	—	110	358	2860	3375
16	Clonazepam	—	—	—	—	140	435	2965	3520
17	7-Aminoclonazepam	—	—	—	—	115	470	2905	3560
18	7-Acetamidoclonazepam	—	—	—	—	246	1200	3270	3970
19	Flurazepam	—	—	—	—	91	219	2800	3275
20	N-1-Desalkylflurazepam	110	359	2500	3020	47	134	2510	3060
21	N-1-Hydroxyethylflurazepam	189	638	2715	3235	74	210	2730	3255
22	Bromazepam	170	695	2670	3260	85	364	2700	3355
23	3-Hydroxybromazepam	121	359	2540	3020	61	150	2570	3070
24	Flunitrazepam	162	484	2645	3170	66	181	2680	3195
25	Norflunitrazepam	203	737	2735	3320	77	264	2745	3350
26	7-Aminoflunitrazepam	198	654	2725	3280	72	236	2720	3305
27	7-Acetamidoflunitrazepam	—	—	—	—	178	713	3115	3750
28	7-Aminonorflunitrazepam	—	—	—	—	94	425	2825	3550
29	Clobazam	153	482	2660	3170	75	232	2645	3170
30	Norclobazam	225	705	2815	3315	84	316	2695	3295
31	Fosazepam	146	—	2605	—	57	164	2615	3155

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