istered dose) at the 30-min observation point. This finding compares with an average of about 3% remaining in the blood at 30 min for palmitic acid. Heart–blood ratios for palmitic acid on a per gram basis were in the range of from a 30:1 to 40:1; for the metal chelates the concentration was always less than 3:1, thus making it impossible to differentiate myocardium from blood.

The high blood concentration may be due to the fact that these compounds are more tightly bound to serum albumin so that the transport of fatty acid derivatives across the cell membrane into the intracellular fluids is reduced. The greater difference in polarity between a simple fatty acid, *e.g.*, palmitic acid, and fatty acid derivatives (*i.e.*, IX) could affect the localization of the labeled compound. Compounds containing a diethylenetriamine chelating group also showed slow blood clearance.

The 30-min distribution was chosen to screen this series of compounds rapidly. Because the palmitic acid does not concentrate in an infarct but does concentrate in the normal myocardia, the 30-min myocardia to blood ratio is the important factor and should indicate if the compound may be useful.

The results of the distribution of the labeled IX in dogs with experimentally induced infarcts revealed that an average accumulation of 0.94% of the injected dose was localized in the heart, 16.6% was in the liver, and 2.7% was in the lungs and that 3.8% remained in the intravascular compartment at 30 min. The infarct contained less than half of the radioactivity found in adjacent normal myocardium.

The chemical analogs described here are not sufficient biological analogs to act as tracers for fatty acid metabolism in the myocardium. However, this approach of preparing drug derivatives should lead to more specific radiopharmaceuticals and will be pursued using other biologic molecules.

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Chemical Ionization Mass Spectra of Phenothiazine Derivatives and Their Oxygenated Analogs

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Abstract □ Twenty-nine derivatives of phenothiazine formed relatively stable ions by proton capture under conditions of chemical ionization, using methane or isobutane as reagent gas. Fragments of generally low abundance formed by simple bond cleavage in the trimethylene portion of the side chain and by loss of water or hydrogen halide. Mass spectra obtained from pyrolyzates of amine salts and from the corresponding free bases were essentially identical.

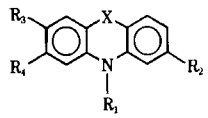
Keyphrases □ Chemical ionization mass spectrometry—various phenothiazines and oxygenated analogs □ Phenothiazines, various—and oxygenated analogs, chemical ionization mass spectra □ Mass spectrometry, chemical ionization—various phenothiazines and oxygenated analogs

Phenothiazines have dominated the interest of researchers in many diverse areas since the discovery that they exert profound effects upon the central nervous system, and a wealth of information pertaining to pharmacological action, therapeutic applications, and biotransformation pathways has been accumulated (1, 2). Some of the vicissitudes encountered in assaying phenothiazine compounds and their metabolites in biological fluids were summarized by Usdin (3).

Elucidation of the mechanisms of action and metabolic conversion and evaluation of the relationship of plasma concentrations of these drugs to their clinical efficacy became possible only after analytical procedures possessing adequate sensitivity and specificity had been developed. A recent monograph outlining many aspects of current research efforts in the area of phenothiazine derivatives describes three approaches to mass spectrometric identification of promazine, chlorpromazine, and several oxygenated homologs (4–6). Whereas electron-impact mass spectrometry has made significant contributions to the biomedical and pharmaceutical sciences over the years, application of chemical ionization mass spectrometry to these areas represents a fairly recent development (7). Finkle *et al.* (8) reported chemical ionization (methane) mass spectra of pharmaceutical agents, including some phenothiazines, and their metabolites as part of a broad program for rapid identification of the contents of body fluids in patients suspected to be intoxicated by a drug overdose.

As part of a continuing program of developing applications of chemical ionization GC–mass spectrometry in neurochemistry (9, 10), the chemical ionization mass spectra for 29 derivatives of phenothiazine were investigated including the tranquilizing agents chlorpromazine (VII), promazine (XV), promethazine (XVI), prochlorperazine (XVIII), trifluoperazine (XXII), perphenazine

Table I—Phenothiazine Derivatives



Compound	R_1[a]	R_2	R_3	R_4	X	Mol. Wt.
I	H	Cl	H	H	S	249
II	$(CH_2)_2CO_2H$	Cl	H	H	S	305
III	$(CH_2)_3NH_2$	Cl	H	H	S	290
IV	$(CH_2)_3NHCH_3$	Cl	H	H	S	304
V	$(CH_2)_3\overset{O}{\uparrow}NHCH_3$	Cl	OH	H	S	320
VI	$(CH_2)_3N(CH_3)_2$	Cl	H	H	S	334
VIa	$CH_2CH{=}CH_2$	Cl	H	H	S	273
VII	$(CH_2)_3N(CH_3)_2$	Cl	H	H	S	318
VIII	$(CH_2)_3N(CH_3)_2$	Cl	H	H	S→O	334
IX	$(CH_2)_3N(CH_3)_2$	Cl	OH	H	S	334
X	$(CH_2)_3N(CH_3)_2$	Cl	OH	H	S→O	350
XI	$(CH_2)_3N(CH_3)_2$	Cl	H	OH	S	334
XII	$(CH_2)_3N(CH_3)_2$	Cl	OH	OH	S	350
XIII	$(CH_2)_3N(CH_3)_2$	Cl	$OCOCH_3$	$OCOCH_3$	S	434
XIV	$(CH_2)_3N(CH_3)_2$	CF_3	OH	H	S	368
XV	$(CH_2)_3N(CH_3)_2$	H	H	H	S	284
XVI	$CH_2CH(CH_3)N(CH_3)_2$	H	H	H	S	284
XVII	$CH_2CH(CH_3)N(CH_3)_2$	H	H	H	S→O	300
XVIII	$(CH_2)_3C_4H_8N_2CH_3$	Cl	H	H	S	373
XIX	$(CH_2)_3C_4H_8N_2CH_3$	Cl	OH	H	S	389
XX	$(CH_2)_3C_4H_8N_2CH_3$	Cl	H	OH	S	389
XXI	$(CH_2)_3C_4H_8N_2CH_3$	Cl	OH	OH	S	405
XXII	$(CH_2)_3C_4H_8N_2CH_3$	CF_3	H	H	S	407
XXIII	$(CH_2)_3C_4H_8N_2CH_3$	CF_3	H	H	S→O	423
XXIV	$(CH_2)_3C_4H_8N_2(CH_2)_2OH$	Cl	H	H	S	403
XXV	$(CH_2)_3C_4H_8N_2(CH_2)_2OH$	Cl	OH	H	S	419
XXVI	$(CH_2)_3C_4H_8N_2(CH_2)_2OH$	Cl	OH	OH	S	435
XXVII	$(CH_2)_3C_4H_8N_2(CH_2)_2OH$	CF_3	H	H	S	437
XXVIII	$(CH_2)_3C_4H_8N_2(CH_2)_2OH$	CF_3	OH	H	S	453
XXIX	$(CH_2)_3C_4H_8N_2(CH_2)_2OH$	$COCH_3$	H	H	S	411

[a] $C_4H_8N_2$ is equivalent to —N⟨ ⟩N—.

(XXIV), fluphenazine (XXVII), and acetophenazine (XXIX), together with 21 possible or known (4, 6) metabolites (Table I) of these and related drugs.

EXPERIMENTAL

Chemical ionization mass spectra were obtained using a quadrupole mass spectrometer[1] interfaced to an interactive data system[2]. Source pressures were maintained at 1 (methane) or 0.8 (isobutane) Torr. These pressures were found, by observing the spectrum of the reagent gas, to afford optimal conditions for chemical ionization in the instrument. The source temperature was 110–130°. Samples (1 ± 0.5 μg) were placed in glass capillary tubes (5 mm long × 1 mm i.d.) and introduced through a vacuum lock into the source by a direct-insertion probe, which was then gradually heated above 300° to effect volatilization.

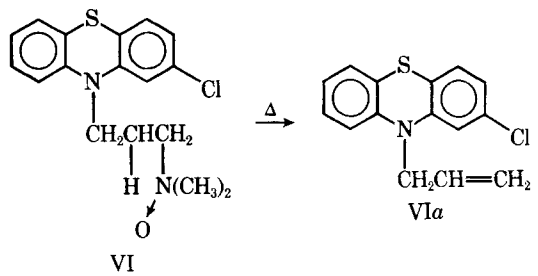
Tabulated intensities are expressed as the percent of the intensity of the base peak; satellite peaks due to isotopes present in natural abundance are not included, although characteristic satellite clusters facilitated the identification of some ions at unit resolution. Compounds XIII, XVIII, and XXIX were introduced into the mass spectrometer as bimaleate salts; the remainder of the compounds were examined as hydrochlorides.

RESULTS AND DISCUSSION

Relative intensities of prominent peaks larger than *m/e* 100 in the chemical ionization mass spectra of I–XXIX are given in Table II; separate determinations are presented using methane or isobutane as the reactant gas. Although these values were obtained for the hydrochloride or bimaleate salts of amines subjected to pyrolysis in the region proximate to the source of the mass spectrometer, essentially identical results were found using the free bases of VII, VIII, XVIII, XXII, XXIII, XXVII, and XXIX; an intense peak at *m/e* 117 (MH^+ of maleic acid) was observed for derivatives (XIII, XVIII, and XXIX) introduced as bimaleate salts.

In all chemical ionization (isobutane) spectra and in all but a few of the chemical ionization (methane) spectra, the base peak was the intact, protonated molecular ion (MH^+); intensity of the MH^+ ion exceeded 50% of the base peak in the spectra of XX and XXI. The failure of VI to afford a prominent MH^+ ion is a consequence of spontaneous degradation of VI (prior to ionization) by the Cope-elimination process (11) illustrated in Scheme I. The MH^+ ion of the resulting *N*-allyl derivative (VIa) was the base peak in the spectrum under both chemical ionization conditions. In general, the usual satellite pattern of hydrocarbon-capture ions [M + $C_2H_5^+$ and M + $C_3H_5^+$ for chemical ionization (methane) and M + $C_4H_9^+$ for chemical ionization (isobutane)] was present to confirm the molecular weight indicated by the MH^+ ion.

Apparent molecular ions (M^+) were found one mass number below the MH^+ ion in these spectra. Although the precise abundance of the M^+ ion varied somewhat between determinations for a given compound, the value was generally >30% of the base peak for all derivatives except the sul-



Scheme I

[1] Model 3200, Finnigan Corp., Sunnyvale, Calif.
[2] Model 6000, Finnigan Corp., Sunnyvale, Calif.

Table II—The *m/e* and Relative Intensity Values of Characteristic Ions in the Chemical Ionization (Methane and Isobutane) Mass Spectra of Phenothiazine Derivatives I–XXIX

Compound	Chemical Ionization Condition	MH^+	M^+	$M+C_2H_5^+$	$M+C_3H_5^+$	$M+C_4H_9^+$	MH^+-H_2O	MH^+-34	MH^+-HX	Ion B	Ion A	Ion D	Ion C	Other
I	CH_4[a]	250 (100)[b]	249 (55)	278 (1)	—	—	232 (12)	216 (7)[c]	214 (40)	—	—	—	—	—
	C_4H_{10}	(100)	(75)	—	—	306 (2)	(<1)	(1)	(<1)	—	—	—	—	—
II	CH_4	306 (100)	305 (85)	334 (8)	—	—	288(<1)	272 (5)	270 (10)	246 (45)	232 (36)	—	—	—
	C_4H_{10}	(100)	(85)	—	—	362 (11)	(<1)	(10)	—	(8)	(11)	—	—	—
III	CH_4	291 (100)	290 (90)	319 (11)	331 (2)	—	—	257(<1)	255 (32)	246 (12)	232 (5)	—	—	274 (10)
	C_4H_{10}	(100)	(35)	—	—	347 (10)	—	—	—	(2)	(2)	—	—	—
IV	CH_4	305 (100)	304 (65)	333 (9)	345(<1)	—	—	271 (8)	269 (6)	246 (5)	232 (3)	—	—	—
	C_4H_{10}	(100)	(35)	—	—	361 (9)	—	(9)	—	(<1)	(<1)	—	—	—
V	CH_4	321 (100)	320 (75)	349 (9)	361 (1)	—	303 (8)	287 (1)	285 (10)	262 (6)	248 (6)	—	—	—
	C_4H_{10}	(100)	(35)	—	—	377 (12)	—	(<1)	—	(1)	(2)	—	—	—
VI	CH_4	335 (<1)	—	—	—	—	—	—	—	—	—	—	—	—
		274[d] (100)	273 (70)	302 (11)	314 (1)	—	—	240 (6)	238 (70)	246 (4)	232 (40)	—	—	233 (45)[e]
	C_4H_{10}	335 (1)	—	—	—	—	—	—	—	—	—	—	—	—
		274[d] (100)	273 (65)	—	—	330 (20)	—	(1)	(<1)	(2)	(12)	—	—	233 (45)[e]
VII	CH_4	319 (100)	318 (90)	347 (8)	359 (4)	—	—	285 (4)	283 (3)	246 (2)	232 (5)	—	—	—
	C_4H_{10}	(100)	(20)	—	—	375 (7)	—	(11)	—	(<1)	(<1)	—	—	—
VIII	CH_4	335 (100)	334 (15)	363 (12)	375 (3)	—	—	301 (1)	299 (7)	262 (<1)	248 (1)	—	—	—[f]
	C_4H_{10}	(100)	(9)	—	—	391 (2)	—	(1)	—	—	—	—	—	—[f]
IX	CH_4	335 (100)	334 (60)	363 (8)	375 (1)	—	317 (8)	301 (<1)	299 (5)	262 (3)	248 (1)	—	—	—
	C_4H_{10}	(100)	(40)	—	—	391 (13)	—	(<1)	—	(<1)	(<1)	—	—	—
X	CH_4	351 (100)	350 (15)	379 (10)	391 (3)	—	333 (5)	317 (2)	315 (8)	278 (<1)	264 (1)	—	—	—[g]
	C_4H_{10}	(100)	(5)	—	—	407 (3)	(3)	(5)	(<1)	(<1)	(1)	—	—	—[g]
XI	CH_4	335 (100)	334 (65)	363 (10)	375 (2)	—	—	301 (1)	299 (8)	262 (2)	248 (2)	—	—	—
	C_4H_{10}	(100)	(40)	—	—	391 (16)	—	(<1)	(<1)	(<1)	(<1)	—	—	—
XII	CH_4	351 (100)	350 (80)	379 (15)	—	—	—	318 (<1)	316 (5)	278 (4)	264 (3)	—	—	—
	C_4H_{10}	(100)	(45)	—	—	407 (8)	—	(<1)	—	(<1)	(<1)	—	—	—
XIII	CH_4	435 (100)	434 (80)	463 (7)	—	—	—	—	—	—	—	—	—	—[h]
	C_4H_{10}	(100)	(35)	—	—	491 (1)	—	—	—	—	—	—	—	—[h]
XIV	CH_4	369 (100)	368 (80)	397 (3)	—	—	351 (3)	—	349 (14)	296 (3)	282 (2)	—	—	—
	C_4H_{10}	(100)	(55)	—	—	425 (2)	—	—	—	(2)	(1)	—	—	—
XV	CH_4	285 (100)	284 (80)	313 (4)	—	—	—	—	—	212 (8)	198 (7)	—	—	—
	C_4H_{10}	(100)	(35)	—	—	341 (5)	—	—	—	(1)	(1)	—	—	—
XVI	CH_4	285 (100)	284 (90)	313 (7)	—	—	—	—	—	212 (9)	198 (57)	—	—	240 (30)
	C_4H_{10}	(100)	(20)	—	—	341 (5)	—	—	—	(4)	(2)	—	—	—
XVII	CH_4	301 (100)	300 (5)	329 (3)	341 (1)	—	—	—	—	—	214 (1)	—	—	285 (2)
		—	—	—	—	—	—	—	—	—	—	—	—	256 (8)
		—	—	—	—	—	—	—	—	—	—	—	—	212 (2)
		—	—	—	—	—	—	—	—	—	—	—	—	198 (2)[i]
	C_4H_{10}	301 (100)	300 (15)	—	—	357 (2)	—	—	—	—	214 (3)	—	—	341 (1)
		—	—	—	—	—	—	—	—	—	—	—	—	285 (7)
		—	—	—	—	—	—	—	—	—	—	—	—	256 (7)
		—	—	—	—	—	—	—	—	—	—	—	—	212 (2)
		—	—	—	—	—	—	—	—	—	—	—	—	198 (2)[i]

Table II—*Continued*

Compound	Chemical Ionization Condition	MH^+	M^+	$M + C_2H_5^+$	$M + C_3H_5^+$	$M + C_4H_9^+$	$MH^+ - H_2O$	$MH^+ - 34$	$MH^+ - HX$	Ion B	Ion A	Ion D	Ion C	Other
XVIII	CH_4	374 (100)	373 (70)	402 (8)	414 (<1)	—	—	340 (5)	338 (9)	246 (2)	232 (1)	141 (9)	113 (17)	—
	C_4H_{10}	(100)	(20)	—	—	430 (6)	—	(10)	(<1)	(1)	(<1)	(6)	(10)	—
XIX	CH_4	390 (100)	389 (45)	418 (12)	430 (1)	—	—	356 (1)	354 (16)	262 (2)	248 (2)	141 (22)	113 (37)	—
	C_4H_{10}	(100)	(40)	—	—	446 (11)	—	(1)	(<1)	(<1)	(<1)	(7)	(9)	—
XX	CH_4	390 (100)	389 (90)	418 (4)	—	—	—	—	354 (9)	262 (1)	248 (1)	141 (100)	113 (160)	—
	C_4H_{10}	(100)	(45)	—	—	446 (8)	—	356 (2)	(<1)	(<1)	(<1)	(20)	(27)	—
XXI	CH_4	406 (100)	405 (25)	—	—	—	—	372 (5)	370 (3)	278 (2)	264 (3)	141 (140)	113 (170)	—
	C_4H_{10}	(100)	(40)	—	—	462 (6)	—	(1)	—	(<1)	(2)	(14)	(22)	—
XXII	CH_4	408 (100)	407 (75)	436 (9)	448 (2)	—	—	—	388 (35)	280 (2)	266 (3)	141 (5)	113 (12)	—
	C_4H_{10}	(100)	(20)	—	—	464 (3)	—	—	—	(1)	(12)	(7)	(9)	—
XXIII	CH_4	424 (100)	423 (10)	452 (17)	464 (4)	—	—	—	404 (25)	296 (<1)	282 (<1)	141 (10)	113 (18)	436 (2)
		—	—	—	—	—	—	—	—	—	—	—	—	408 (23)
		—	—	—	—	—	—	—	—	—	—	—	—	388 (7)
		—	—	—	—	—	—	—	—	—	—	—	—	280 (4)
		—	—	—	—	—	—	—	—	—	—	—	—	266 (2)[i]
	C_4H_{10}	424 (100)	423 (5)	—	—	480 (2)	—	—	—	—	—	141 (4)	113 (6)	464 (2)
		—	—	—	—	—	—	—	—	—	—	—	—	408 (11)
		—	—	—	—	—	—	—	—	—	—	—	—	280 (1)
		—	—	—	—	—	—	—	—	—	—	—	—	266 (<1)[i]
XXIV	CH_4	404 (100)	403 (50)	432 (8)	444 (2)	—	386 (6)	370 (2)	368 (5)	246 (5)	232 (2)	171 (7)	143 (9)	—
	C_4H_{10}	(100)	(15)	—	—	460 (14)	(1)	(2)	(<1)	(1)	(<1)	(1)	(2)	—
XXV	CH_4	420 (100)	419 (80)	448 (7)	—	—	402 (6)	386 (1)	384 (4)	262 (15)	248 (9)	171 (31)	143 (40)	—
	C_4H_{10}	(100)	(35)	—	—	476 (7)	(1)	—	—	(2)	(1)	(11)	(12)	—
XXVI	CH_4	436 (100)	435 (30)	464 (12)	478 (2)	—	418 (7)	402 (20)	400 (10)	278 (3)	264 (10)	171 (27)	143 (37)	430 (2)
		—	—	—	—	—	—	—	—	—	—	—	—	131 (100)
		—	—	—	—	—	—	—	—	—	—	—	—	113 (42)
	C_4H_{10}	436 (18)	435 (40)	—	—	492 (2)	—	402 (3)	—	278 (1)	264 (29)	171 (13)	143 (15)	—
XXVII	CH_4	438 (100)	437 (35)	466 (14)	478 (2)	—	—	—	418 (27)	280 (6)	266 (3)	171 (7)	143 (16)	420 (9)
		—	—	—	—	—	—	—	—	—	—	—	—	258 (12)
	C_4H_{10}	438 (100)	437 (15)	—	—	494 (14)	—	—	—	280 (3)	266 (1)	171 (3)	143 (5)	420 (2)
		—	—	—	—	—	—	—	—	—	—	—	—	258 (3)
XXVIII	CH_4	454 (100)	453 (50)	482 (7)	494 (1)	—	436 (8)	—	434 (15)	296 (9)	282 (3)	171 (5)	143 (4)	414 (6)
	C_4H_{10}	(100)	(35)	—	—	—	(2)	—	—	(5)	(2)	(7)	(13)	422 (3)
XXIX	CH_4	412 (100)	411 (20)	430 (8)	442 (1)	—	394 (4)	—	—	254 (2)	240 (1)	171 (4)	143 (9)	—
	C_4H_{10}	(100)	(15)	—	—	468 (10)	(1)	—	—	(2)	(<1)	(3)	(5)	—

[a] CH_4 = chemical ionization (methane), and C_4H_{10} = chemical ionization (isobutane). [b] The *m/e* ratio of the ion (intensity of the ion expressed as the percent of the intensity of the MH^+ ion). [c] Possibly due to unchlorinated contaminants. [d] The tertiary *N*-oxide VI undergoes virtually complete degradation by a Cope reaction (Scheme I) preceding or concurrent with vaporization, affording the *N*-allyl derivative VI*a*. [e] Probably arising by loss of C_3H_4 from the allyl substituent. [f] Compound VII is present as a contaminant. [g] Compound IX is present as a contaminant. [h] Compound XII and its monoacetate appear to be present as contaminants. [i] Compound XVI is present as a contaminant. [j] Compound XXII is present as a contaminant.

foxides VIII, X, XVII, and XXIII, the latter affording M^+ ions having <15% relative abundance. The variations in the abundance of this ion are not surprising because plausible processes leading to its formation (including charge transfer to M, loss of H· from MH^+, and direct ionization by electron impact) are sensitive to slight variations in temperature, pressure, and chemical entities in and near the source.

Fragmentation processes involving the trimethylene bridge appeared to be common to the spectra of II–V, VII–XV, and XVIII–XXIX (phenothiazine–$CH_2CH_2CH_2$–base) and to XVI and XVII, producing weak ions that corresponded in mass to the (substituted) phenothiazin-10-yl nucleus (Ion A) and to its methylene homolog (Ion B). Generally more abundant ions, corresponding in mass to the terminal methylene unit plus the attached aliphatic nitrogen atom and its substituents (Ion C, CH_2–base or CH_3CH–base) and to the ethylene homolog (Ion D, C_3H_6–base), were observed at *m/e* 113 and 141 (XVIII–XXIII) or 143 and 171 (XXIV–XXIX), respectively. Although the corresponding ions in the spectra of III–XVIII had *m/e* values <100 and were, therefore, not measured in this study, the chemical ionization (methane) mass spectra of XII and two other hydroxylated homologs of XII were found (6) to exhibit prominent ions at *m/e* 58 and 86, corresponding to $[CH_2N(CH_3)_2]^+$ and $[C_3H_6N(CH_3)_2]^+$, respectively, in accord with the idea that these form by processes general for compounds of this type.

Molecules in this study having polar substituents (halogen or hydroxyl groups) also generally appeared to undergo loss of a hydrogen atom plus the substituent from the MH^+ species. Fragments resulting from such processes were relatively abundant in the chemical ionization (methane) spectra but minor or not observed in the corresponding chemical ionization (isobutane) spectra. The derivatives of 2-chlorophenothiazine (I–XII, XVIII–XXI, and XXIV–XXVI) also exhibited an $MH^+ - 34$ ion that did not have a satellite ion heavier by two mass numbers; this resulted from contamination by the respective halogen-free homologs.

In summary, derivatives of phenothiazine generally form very stable MH^+ and M^+ ions under conditions of chemical ionization. Although no simple correlation is obvious to account for the variations in relative intensity of fragment ions formed by different compounds in this study, decomposition appears to be limited mainly to cleavage of exocyclic carbon–carbon single bonds, plus loss of water or hydrogen halide in appropriately substituted derivatives. The prominence of these stable proton-capture ions in the chemical ionization spectra affords a measurable property that is not only characteristic of a given drug or metabolite but also exquisitely sensitive for its detection. These two conditions suggest that selective ion monitoring techniques (12) in conjunction with chemical ionization are potentially useful for bioanalytical studies of phenothiazines.

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Possible Antineoplastic Agents II

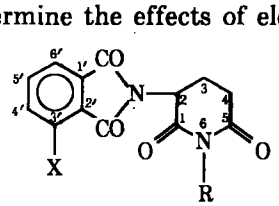
A. U. DE ˣ and D. PAL

Abstract □ Various glutarimide derivatives were synthesized, and some showed significant activity against Ehrlich ascites carcinoma in Swiss albino mice.

Keyphrases □ Glutarimides, substituted—various derivatives synthesized, antineoplastic activity evaluated, mice □ Antineoplastic activity, potential—substituted glutarimides synthesized and screened, mice □ Structure–activity relationships—various substituted glutarimides synthesized and screened for antineoplastic activity in mice

Synthesis of a few glutarimide analogs of the types 2-phthalimidoglutarimide (thalidomide) (I) and 3-phenylglutarimide (II) and their biological evaluation in Ehrlich ascites carcinoma were reported previously (1). Meanwhile, more derivatives of I and II were synthesized and evaluated biologically according to the same procedures (1) (Table I).

In the previous article (1), the rationale behind the projected synthesis of these glutarimides (I and II) and others with some structural variations (II*a*–II*l*, III, and IV) was discussed. These structural changes were designed to determine the effects of electron-repelling or electron-



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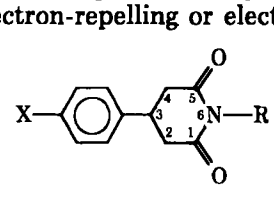

II