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TECHNICAL NOTE

P. Daenens,[1] *D.Sc. and M. Van Boven,*[1] *D.Sc.*

The Identification of Quinazolinones on the Illicit Market

The abuse of hypnotics of the quinazolinone series is well known. Methaqualone [2-methyl-3-o-tolyl-4 (3H)-quinazolinone] in both licit and illicit tablets is encountered with increasing frequency. Several papers have discussed the identification of this drug in tablets and biological materials. Its metabolism has been studied in man [*1–4*] and animals [*5,6*]. Concentrations in urine, blood, and organs in cases of poisoning have been established [*7–11*].

The abuse of mecloqualone, a chlorinated homologue of methaqualone [2-methyl-3-(2′ chlorophenyl)-4 (3H)-quinazolinone] has been reported more recently [*12*]. The metabolism of mecloqualone in man has been established in our department [*13,14*].

A third drug of this series, nitromethaqualone [2-methyl-3-(2′ methoxy-4′ nitrophenyl)-4(3H)-quinazolinone] has been in use in Europe since 1967. When an overdose is taken in combination with alcohol, this much more active drug (a single therapeutic dose is 15 mg compared to 150 mg for methaqualone or mecloqualone) can provoke a toxic hallucinogenesis.

Pure methaqualone [melting point (MP) 120°C] and mecloqualone (MP 128°C) were kindly supplied by Merck (Darmstadt, Germany) through Diamond (France). Nitromethaqualone (MP 193°C) has been synthesized in our laboratory according to the method of Klosa and Starke [*15,16*]. The metabolism of the last compound in man is under study.

The present paper deals with the identification of all three commercially available quinazolinones by their ultraviolet (UV), infrared (IR), nuclear magnetic resonance (NMR), and mass spectra. Thin-layer (TLC) and gas-liquid (GLC) chromatographic data are also presented. The chemical structures together with common and trade names are listed in Table 1 and Fig. 1.

Experimental

Isolation of Quinazolinones from Illicit Seizures

Tablets are grinded and suspended in 0.1*N* sodium hydroxide solution. All three quinazolinones can be extracted quantitatively with chloroform or diethylether. The

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[1] Director and chemist, respectively, Laboratory of Toxicology, University of Louvain, Van Evenstraat, Leuven, Belgium.

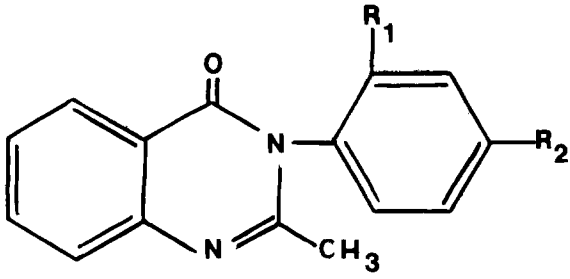

FIG. 1—*Chemical structure of the quinazolinone series.*

TABLE 1—*Chemical structures together with common and trade names for the quinazolinone series.*

R_1	R_2	Common Name	Trade Name
CH_3	H	methaqualone	Europe: Revonal, Cateudyl, Mandrax, Noxibel, Isonox, Toquilon, Hypnor, Mollinox, Somex, Noxal U.S.: Quaalude, Somnofac, Sopor
OCH_3	NO_2	nitromethaqualone	Europe: Parnox
Cl	H	mecloqualone	Europe: Nubarene

combined organic layers are filtered, dried on anhydrous sodium sulfate, and evaporated. Since the hydrochlorides are soluble in chloroform, a clean-up with 2*N* hydrochloric acid, when necessary, should be done on ethereal extracts.

Thin-Layer Chromatography

Standard techniques of ascending TLC were employed. Runs of 16 cm were made on silica gel G, type 60, (Merck, Darmstadt, art. 7731), 20 by 20-cm, 250-μm glass plates and on cellulose powder (Macherey-Nagel & Co., Düren) (MN-Polygram, CEL 300), 20 by 20-cm, 250-μm sheets. Numerous systems have been examined. A separation can be achieved by one of the three systems described in Table 2 which includes R_f data (Rf times 100) of codeine and cocaine as references. The R_f values of the compounds are the average values of several individual determinations. All mixtures were analytical grade and measured as v/v. The spots were located by iodoplatinate spray or by the reagent of Dragendorf-Meunier-Macheboeuf [*17*].

Gas-Liquid Chromatography

Determinations were carried out using a Varian Aerograph (Walnut Creek, Calif.)

TABLE 2—R_f *values and relative retention times* (RR_t) *of several quinazolinones.*[a]

Common Name	TLC ($R_f \times 100$)			GLC (RR_t, h)	
	A	B	C	OV-101	OV-17
Mecloqualone	25	39	81	0.67	0.77
Methaqualone	32	44	87	0.52	0.53
Nitromethaqualone	19	35	46	1.64	2.95
Codeine	6	16	77	1.00	1.00
Cocaine	40	51	91	0.57	0.53

[a] Silica gel plates: A=*iso*octane-benzene-acetone-diethylamine (25:5:5:2) (v/v), B=cyclohexane-dioxane-acetone-diethylamine (25:5:5:1) (v/v); cellulose sheets: C=hexane-diethylamine (98:2) (v/v).

gas chromatograph (model 1700). The operational conditions were as follows:

column: glass, 1.8 m, 2 mm inside diameter,

stationary phases: OV-101 2.5% on Gaschrom Q, 80–100 mesh and OV-17 3% on Gaschrom Q, 80–100 mesh,

carrier flow: 25 ml of nitrogen per minute,

flow of air and hydrogen: 300 ml per minute and 30 ml per minute, respectively,

temperature of column: 230°C isothermal for OV-101 and 250°C isothermal for OV-17, and

temperature of injector and detector: 270°C.

Retention times relative to codeine are listed in Table 2. A typical gas chromatogram on OV-101, 2.5% is shown in Fig. 2.

Infrared Spectra

Infrared spectra (KBr disks) were recorded on a Perkin-Elmer 257 spectrophotometer and are represented in Fig. 3. Nitromethaqualone can be easily distinguished from both mecloqualone and methaqualone by the presence of nitrophenyl peaks at 1515 and 1250 cm^{-1} and by a C-N stretching peak at 870 cm^{-1}. Other characteristic peaks are present at 800 and 740 cm^{-1}. The IR spectra of methaqualone and mecloqualone are quite similar except for the "fingerprint" region from 1300 to 625 cm^{-1}. Mecloqualone can be recognized by its strong absorption at 1275, 1115, and 720 cm^{-1}.

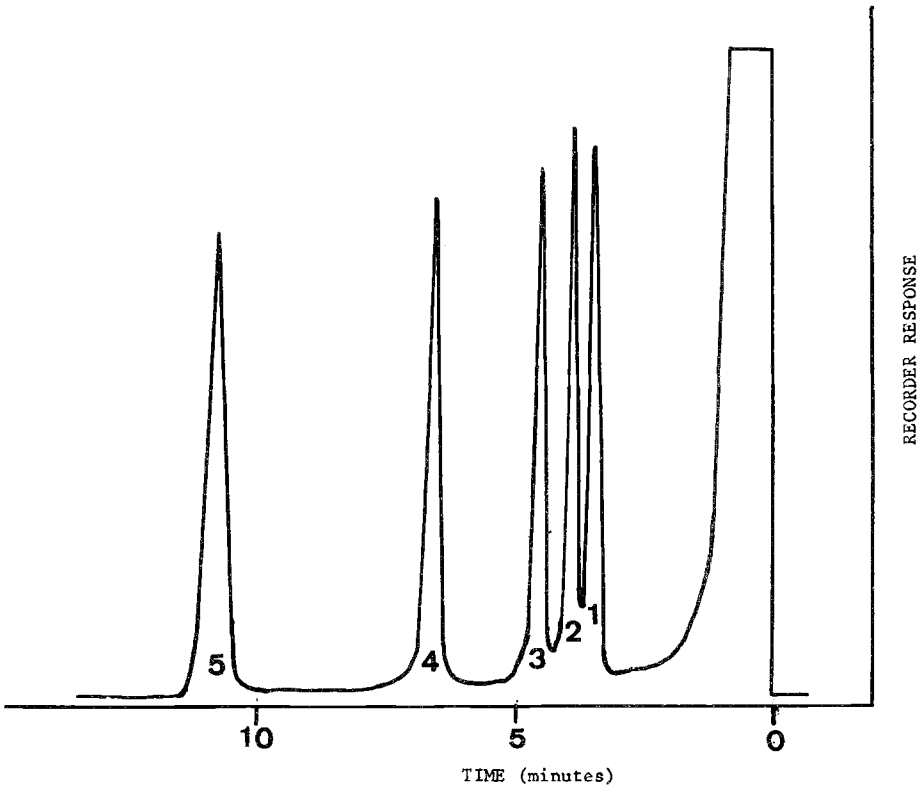

FIG. 2—*Typical gas chromatogram of different quinazolinones and two references on OV-101;* 1 = *methaqualone;* 2 = *cocaine;* 3 = *mecloqualone;* 4 = *codeine; and* 5 = *nitromethaqualone.*

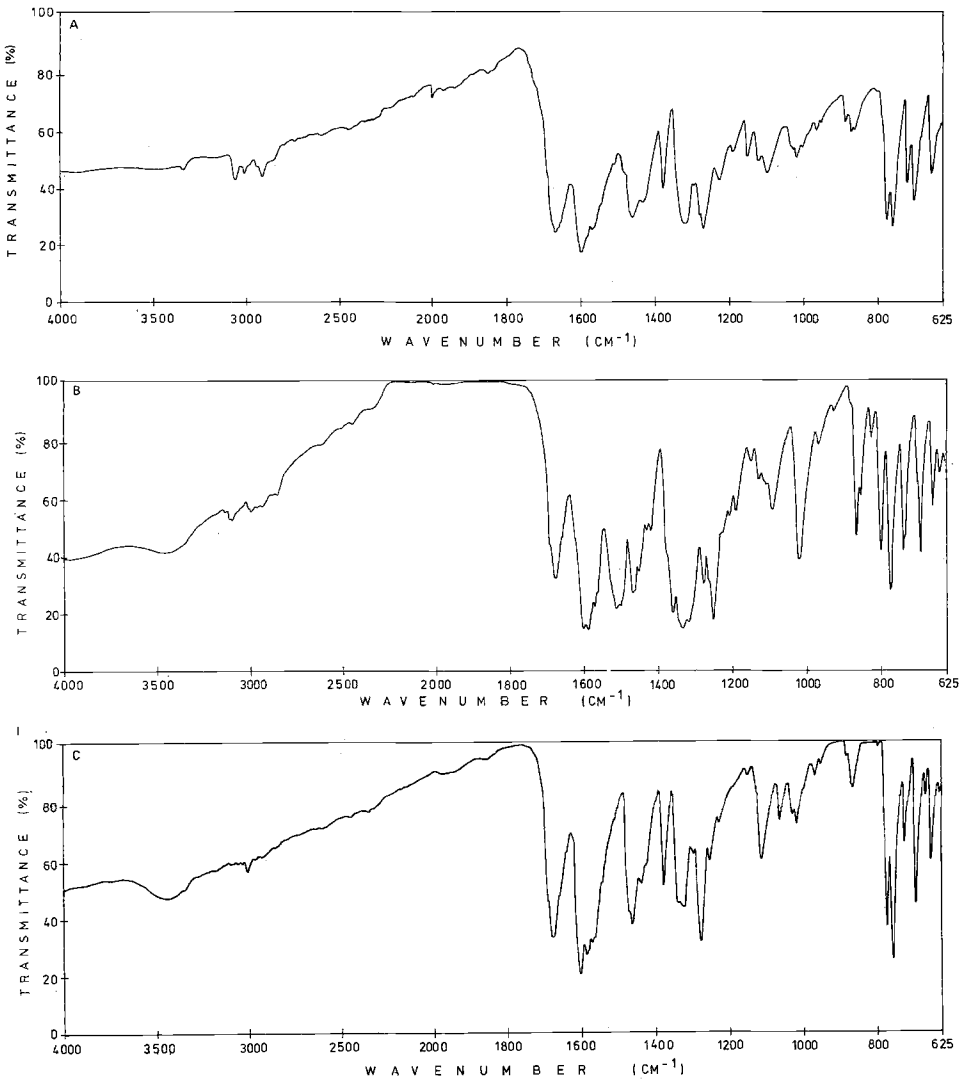

FIG. 3—*Infrared spectra of quinazolinones (KBr disk);* (a) *methaqualone;* (b) *nitromethaqualone; and* (c) *mecloqualone.*

Ultraviolet Spectra

In Fig. 4, UV spectra of all three compounds are shown. They were recorded on a Unicam SP 800 spectrophotometer after dissolving the materials in ethanol containing 1% ammonia (*continuous line*) and upon acidification with 6*N* sulfuric acid (*dotted line*). The absorbance values ($E^{1\%}_{1\,cm}$) in alkaline medium are the following: methaqualone 225 nm (1452), 264 nm (365), 304 nm (151), and 315 nm (132); mecloqualone 225 nm (1428), 265 nm (325), 304 nm (140), and 315 nm (112); nitromethaqualone 224 nm (2203), 265 nm (502), 304 nm (225), and 316 nm (217).

Nuclear Magnetic Resonance Spectra

The NMR spectra were recorded on a Hitachi Perkin-Elmer R24 apparatus. Tetramethylsilane was used as an internal standard for organic solvents. Chemical shifts are expressed in δ units.

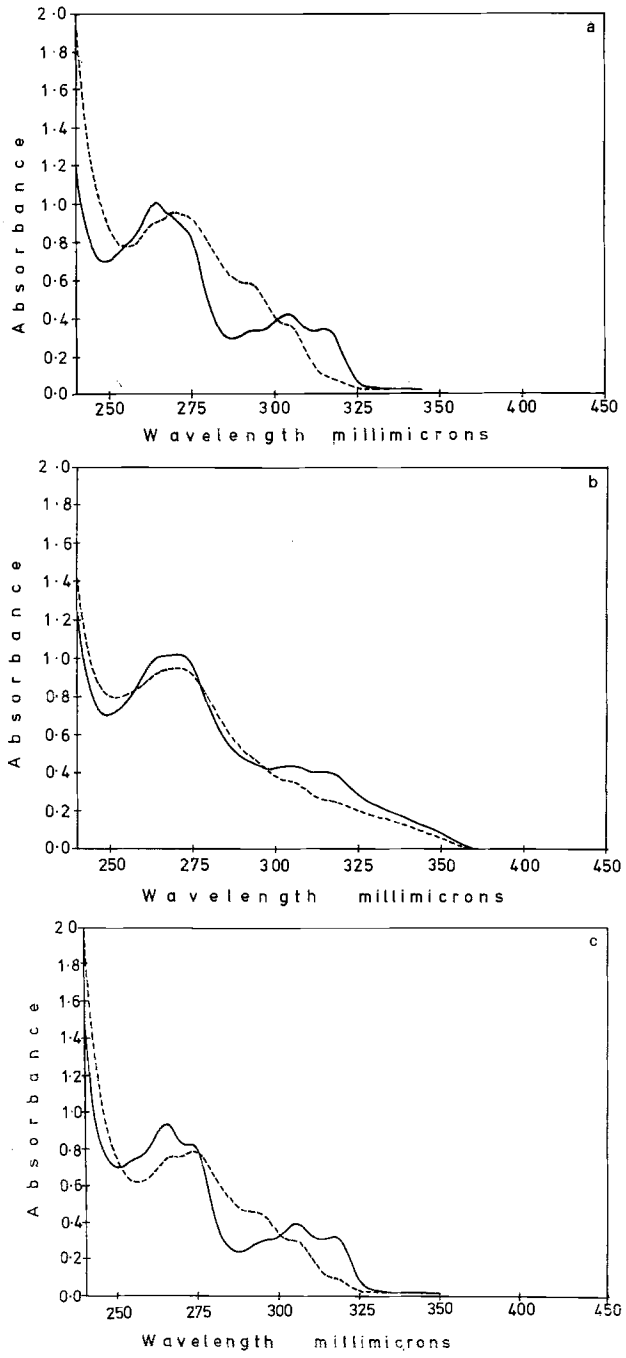

FIG. 4—*Ultraviolet spectra of quinazolinones;* (a) *methaqualone;* (b) *nitromethaqualone; and* (c) *mecloqualone.*

As can be seen from Fig. 5, the three products exhibit different spectra, allowing a facile identification by the presence of peaks at definite δ values. Methaqualone represents two singlets for the methyl groups at δ 2.1 and 2.18. Mecloqualone exhibits only one methyl group at δ 2.2. Nitromethaqualone shows one singlet at δ

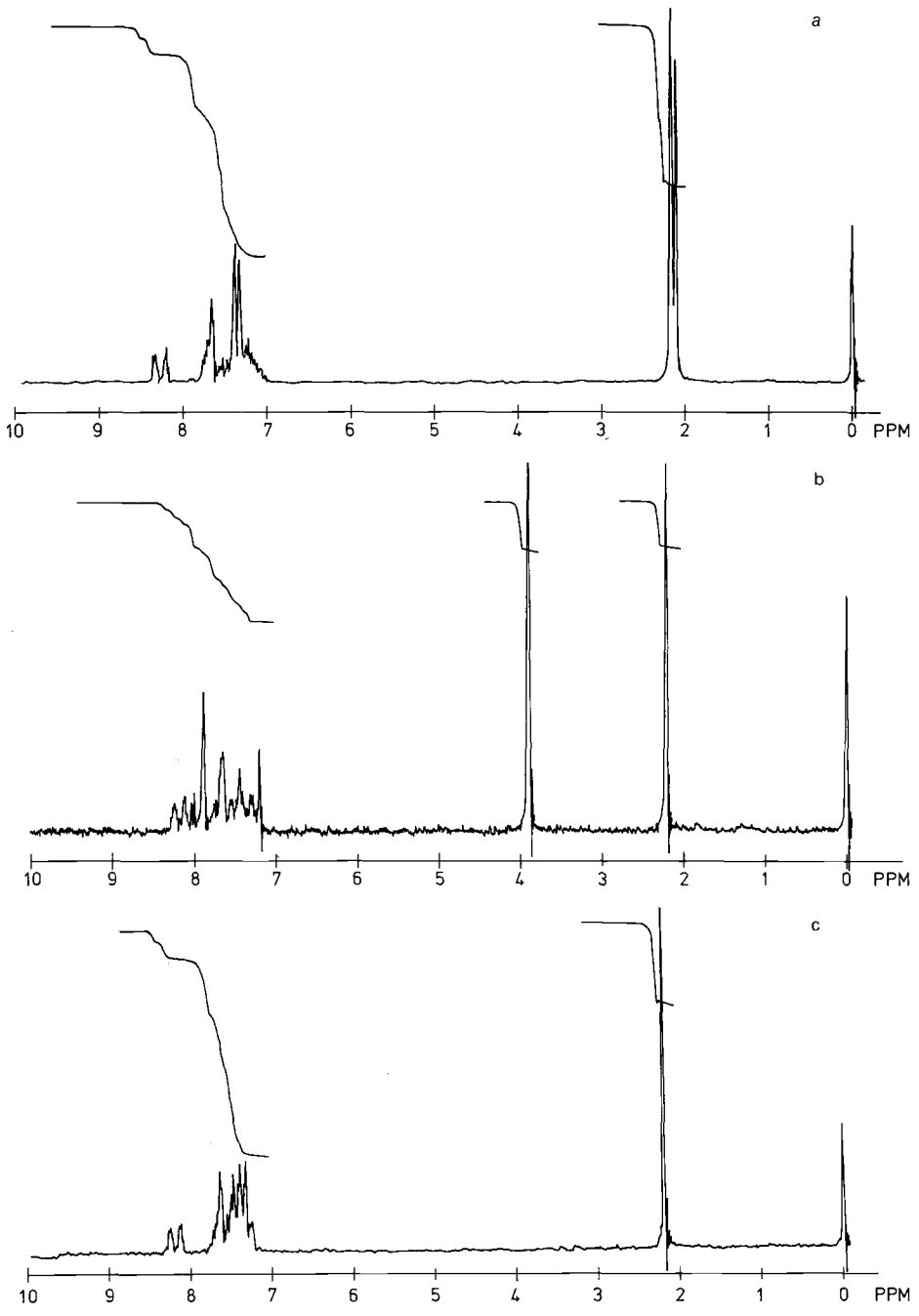

FIG. 5—*Nuclear magnetic resonance spectra of quinazolinones;* (a) *methaqualone;* (b) *nitromethaqualone; and* (c) *mecloqualone.*

2.22 integrating for three protons from the methyl group and one singlet integrating for three protons at $\delta = 3.93$, as can be expected for a methoxy group. The protons in the range 7 to 8.4 exhibit a rather complicated pattern, resulting from overlapping of the protons of the two phenyl rings.

Mass Spectra

The mass spectra were recorded on a single-focusing AEI-MS 12 mass spectrometer, operated at 8 kV accelerating voltage, 100 μA trap current, and 70 eV ionization energy. The source temperature was 130 to 150°C, and the direct insertion technique was used. The mass spectra are represented in Fig. 6.

Each product is characterized by a different molecular ion: methaqualone (250) and mecloqualone (270) have an even molecular ion resulting from the presence of two nitrogens. Nitromethaqualone (311) has an odd molecular ion because of the presence of three nitrogens. The presence of one chlorine in both molecular ion and fragment ions of mecloqualone can easily be recognized by the presence of the chlorine and its isotope at mass to charge ratio (*m/e*) 270 and 272, *m/e* 255 and 257, *m/e* 152 and 154, and *m/e* 111 and 113. The respective fragmentations can be explained by the fragmentation pattern as represented in Fig. 7. These different characteristic spectra allow a very easy identification. A mass spectrometric analysis in mixtures of drugs is also possible after collecting individual products by preparative gas chromatography on a OV-101, 10% column at 270°C.

Conclusions

Following extraction with chloroform from alkaline medium, identification of different quinazolinone hypnotics can best be done by combined GC-MS. The UV data only show the presence of a quinazolinone nucleus but make identification of the individual products impossible. The IR spectra are very similar, as can be expected from the structure of the quinazolinones examined. However, they provide sufficient details for individual identification. Gas chromatographic and thin-layer chromatographic determinations can only give useful indication of probable identity, especially when different systems are used. However, both techniques are of potential interest when it is necessary to isolate and purify quinazolinones from mixtures before any further analysis. If sufficient pure product is available (about 15 mg), NMR spectra also allow a quick identification.

Summary

This paper describes the analytical data for the identification of three commercially available hypnotics of the quinazolinone series (methaqualone, mecloqualone, and nitromethaqualone) which are encountered on the illicit market with increasing frequency.

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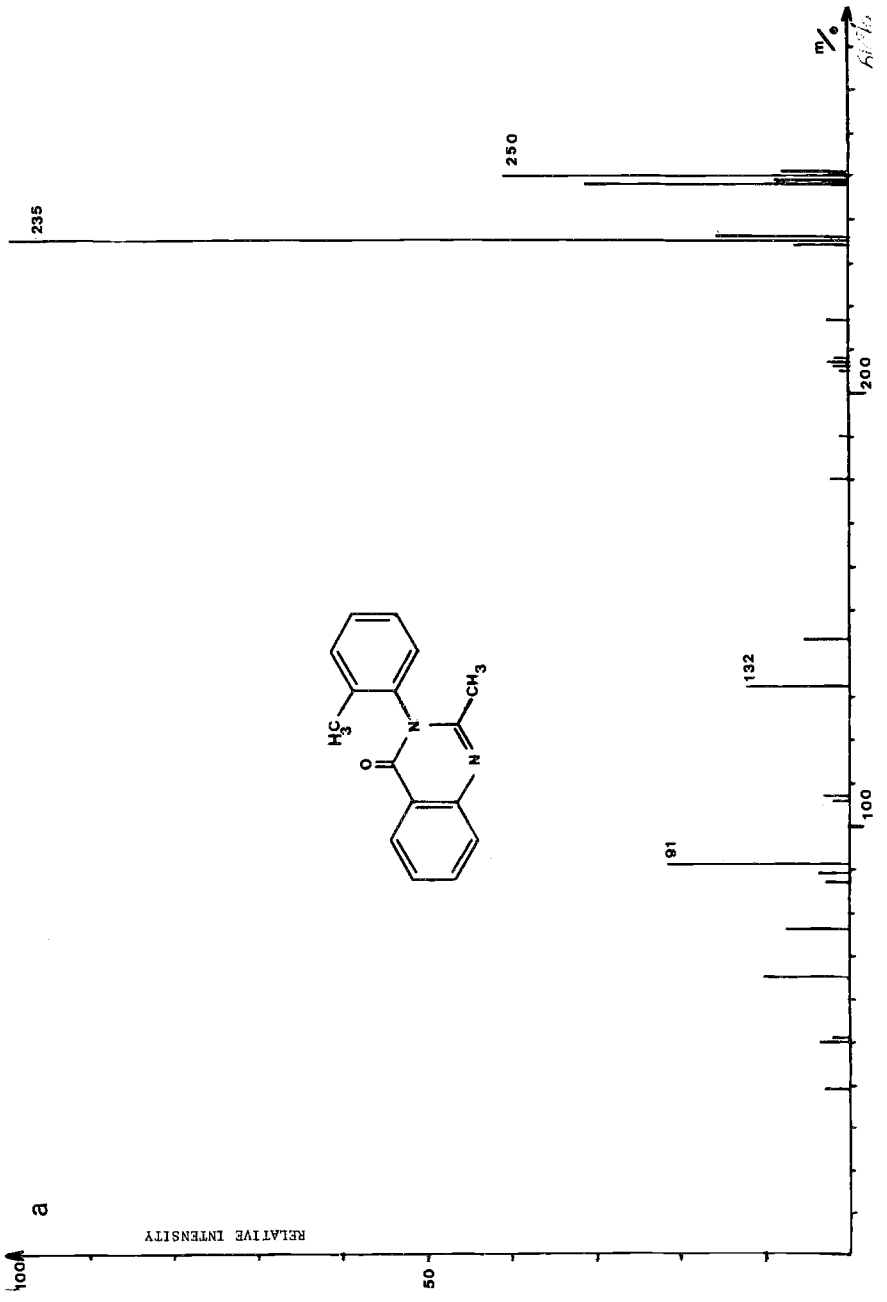

FIG. 6—(a) *Mass spectrum of methaqualone.*

FIG. 6—(b) *Mass spectrum of nitromethaqualone.*

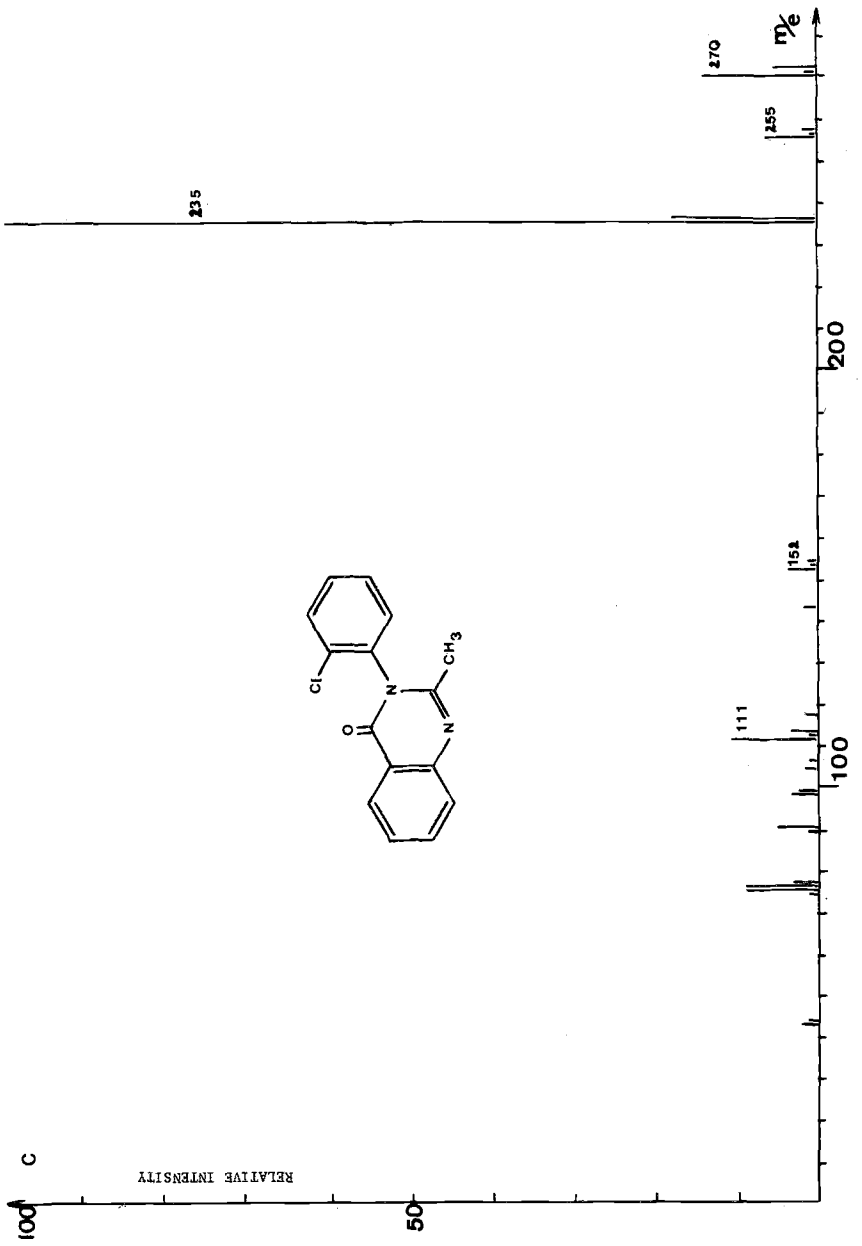

FIG. 6—(c) *Mass spectrum of mecloqualone.*

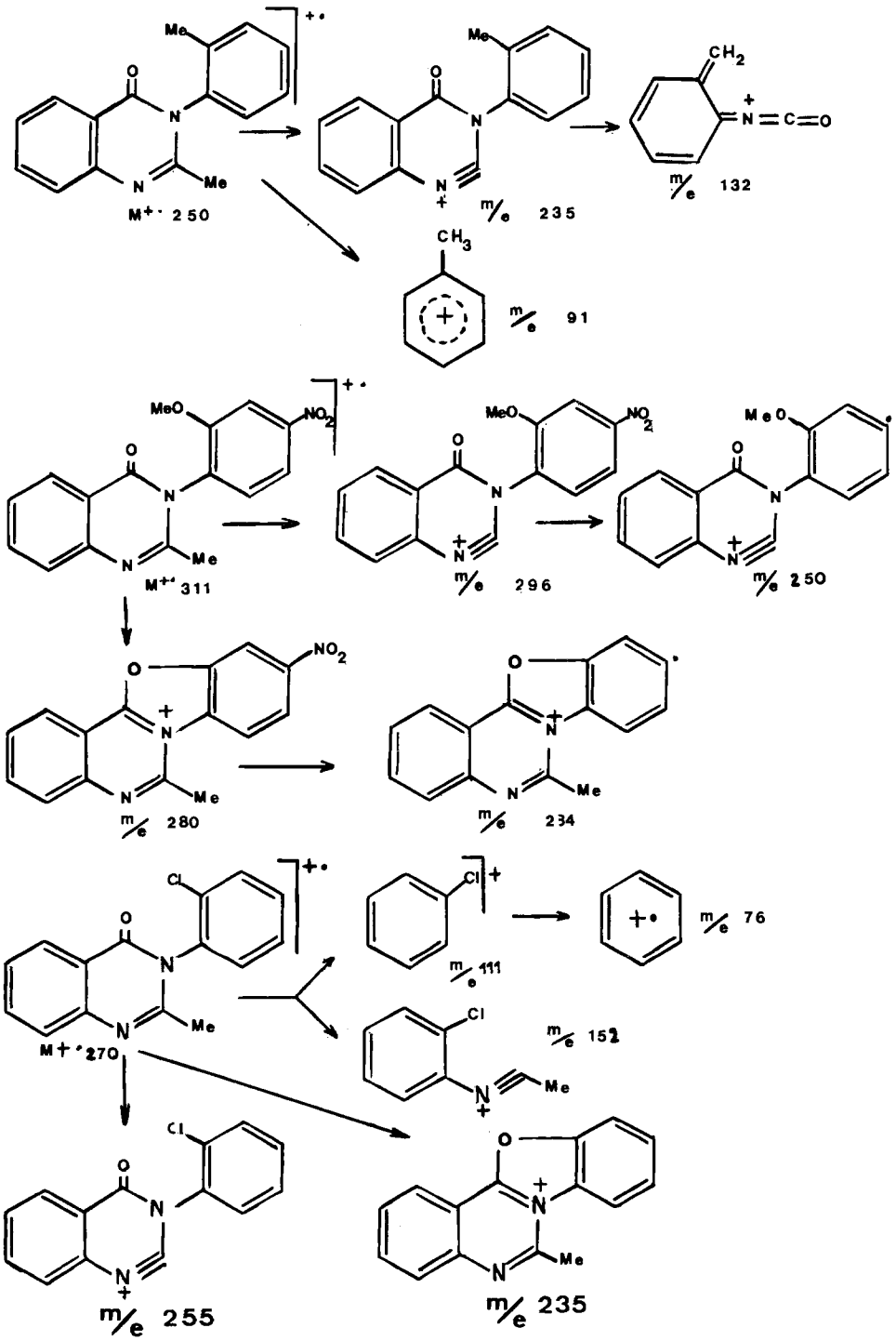

FIG. 7—*Fragmentation pattern of quinazolinones.*

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University Louvain
Laboratory of Toxicology
Director, Prof. Daenens
Van Evenstraat 4, Leuven, Belgium