The Fragmentation of 7-(o- and p-R-Benzylidene)-3-(o- and p-R-Phenyl)-
2-methyl-3,3a,4,5,6,7-hexahydro-2H-indazoles
Under Electron Impact. II [1]

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The electron impact mass spectrometric fragmentation pathways for several 2-methylindazoles, II, were investigated. Our investigation of the mass spectra of these compounds revealed interesting relationships between the 2-N-methyl-substituent in the framework of II and the fragmentation patterns.

Following the research work on mass spectra of indazole compounds [1] we report here the electron impact mass spectra of twelve *ortho* and *para*-2-methyl-2H-indazoles II (Scheme 1) with the aim of comparing the fragments


R	
o-Br	p-Br
o-Cl	p-Cl
o-CH₃	p-CH₃
o-OCH₃	p-OCH₃
o-COOH	p-NO₂
H	p-NH₂
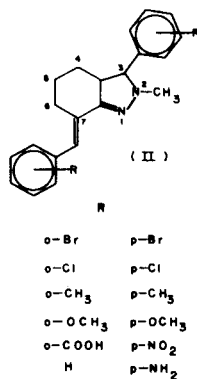
SCHEME 1

observed with those of the corresponding 2H-indazoles I [1]. For the compounds II the relative abundances of the ions are shown in the Table 1, and the proposed fragmentation patterns in Schemes 2 to 8. With few exceptions, the latter have been justified by the existence of metastable ions and by comparison with the fragmentation pattern of known-compounds.

The mass spectra of II and I [1] compounds show some common features. They exhibit an intense molecular ion, but contrary to what has been observed on I derivatives, it is the base peak with exception of *ortho*-carboxylic derivative. This probably reflects the stable nature of 2-methylindazole's ring under electron impact which has been obtained by the introduction of the methyl-substituent instead of an hydrogen on the 2 nitrogen atom of 2H-indazole ring.

The major fragmentation of the molecular ion proceeds along four pathways: (A) From $[M]^+$ to m/e (M^+ -1), 117, (M^+ -29). (B) From $[M]^+$ to m/e (M^+ -R), 182 and 128. (C) From $[M]^+$ to m/e (224 + R) and 223. (D) From $[M]^+$ to m/e (210 + R) and (90 + R).
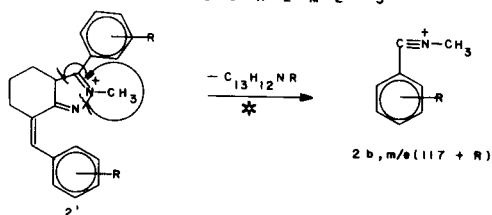
SCHEME 2
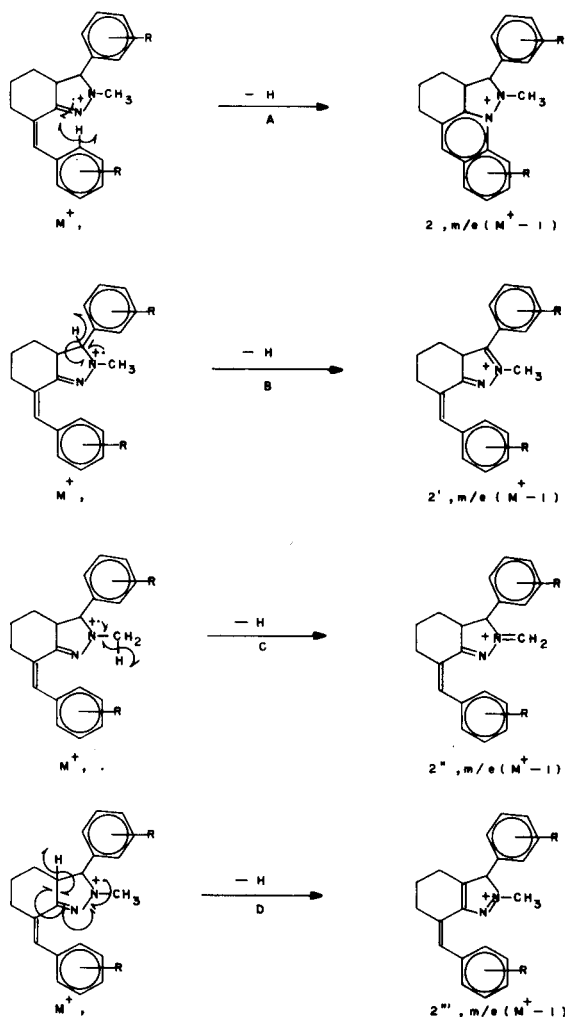
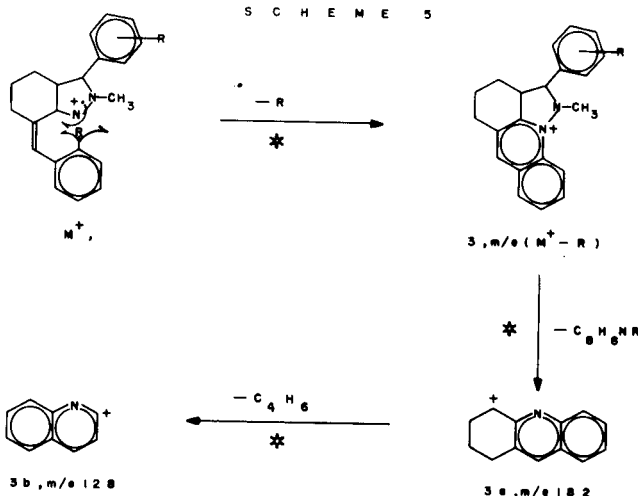
Pathway A.

A second fragmentation pattern resembling that 2H-indazoles I [1] proceeds through the loss of a hydrogen atom from the molecular ion leading the ion **2** of m/e (M^+ -1).
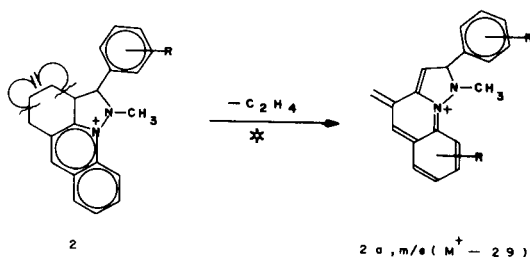
SCHEME 3

$2b, m/e(117 + R)$

SCHEME 4

$-C_2H_4$

$2, m/e(M^+ - 29)$

SCHEME 5

$3, m/e(M^+ - R)$

$-C_8H_6NR$

$3a, m/e 182$

$-C_4H_6$

$3b, m/e 128$

SCHEME 6

$-C_6H_4R$

$4, m/e(224 + R)$

$-HR$

$4a, m/e 223$

The intensities of **2** peak for II derivatives are lower than those of I compounds. Consistent with the behaviour of indazoles I, the relative abundances of **2** ion are more intense for *para*-derivatives than *ortho*-compounds. This indicates that the major part of (M⁺ -1) ion are due to the elimination of an *ortho*-hydrogen and support the fragmentation pattern proposed for this loss on the 2H-indazoles I [1] which invokes an *ortho* interaction of the o-R-substituent on the 7-benzylidene substituent with the 1 ring nitrogen atom of 2-methylindazoles II (Scheme 2, A).

Likewise, another three pathways are feasible for the formation of the ion **2** from [M]⁺. In the second pathway, elimination of one hydrogen atom from the molecular ion, involving the 3 ring hydrogen atom of indazoles II, affords
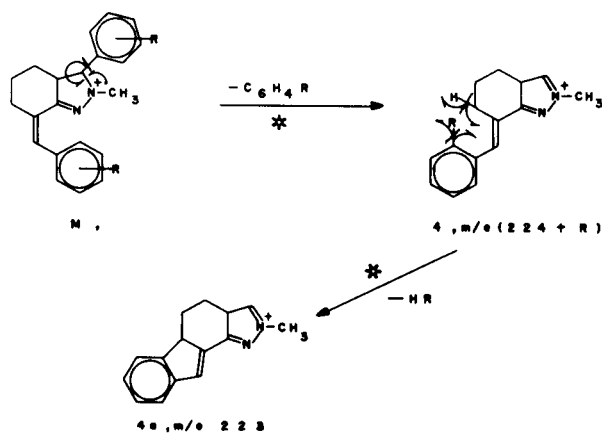
Table 1

Relative Abundance of Principal Fragments
(Figures in parentheses indicate the nature of the ions)

| Compound No.	R	M⁺ (1)	M⁺ -1 (2)	M⁺ -29 (2a)	M⁺ -R (3)	224 + R (4)	223 (4a)	210 + R (5)	117 + R (2b)	90 + R (6)	182 (3a)	128 (3b)
1	H	100.0	62.0	5.4	62.0	28.0	2.0	5.4	14.0	26.0	15.0	12.0
2	o-Br	100.0	5.0	.	22.0	30.0	27.0	7.0	32.0	25.0	93.5	32.0
3	o-Cl	100.0	10.0	.	45.0	42.0	7.05	8.23	28.0	40.0	68.0	16.0
4	o-COOH	58.0	2.0	.	2.0	5.0	2.32	100.0	6.0	8.0	4.0	8.0
5	o-CH₃	100.0	15.0	.	80.5	30.7	2.32	11.63	18.0	35.7	28.0	22.0
6	o-OCH₃	100.0	10.0	.	80.0	20.0	2.32	14.0	15.0	28.0	26.0	12.0
7	p-Br	100.0	22.0	3.50	2.0	25.0	11.63	10.46	18.0	21.0	14.0	23.0
8	p-Cl	100.0	38.0	8.13	1.0	30.0	1.0	8.83	24.0	24.0	9.0	12.0
9	p-CH₃	100.0	50.0	6.97	1.0	19.0	.	8.13	12.0	18.0	4.0	12.0
10	p-OCH₃	100.0	32.0	10.46	1.0	5.0	.	15.5	10.0	12.0	.	6.0
11	pNO₂	100.0	19.4	1.0	4.0	43.9	4.65	4.65	12.0	2.0	5.0	14.0
12	p-NH₂	100.0	28.0	16.27	3.0	8.0	.	25.58	20.0	43.0	5.0	6.0

the ionic species **2′** consisting of a tetrahydroindazole cation (Scheme 2, B). On the other hand, elimination of one hydrogen atom of 2-methyl moiety (Scheme 2, C), or 4-hydrogen atom of indazole ring (Scheme 2, D) cannot be excluded.

Fragmentation of **2** then proceeds along two pathways. In one pathway, loss of an *R*-acridine unit from **2**, probably through the tetrahydroindazole cation **2′**, leads to the ion **2b** of m/e (117 + R) which is depicted as a protonated benzonitrile species (Scheme 3). In another pathway, expulsion of ethylene unit from **2**, leads to the formation of ion **2a** of m/e (M+ -29) (Scheme 4). This peak is absent on almost all of the *ortho* compounds analyzed II. On the other hand, 2*H*-Indazoles, I, have not been observed to undergo skeletal rearrangement of this sort. Therefore, this peak is characteristic of the *para*-R-compounds II.
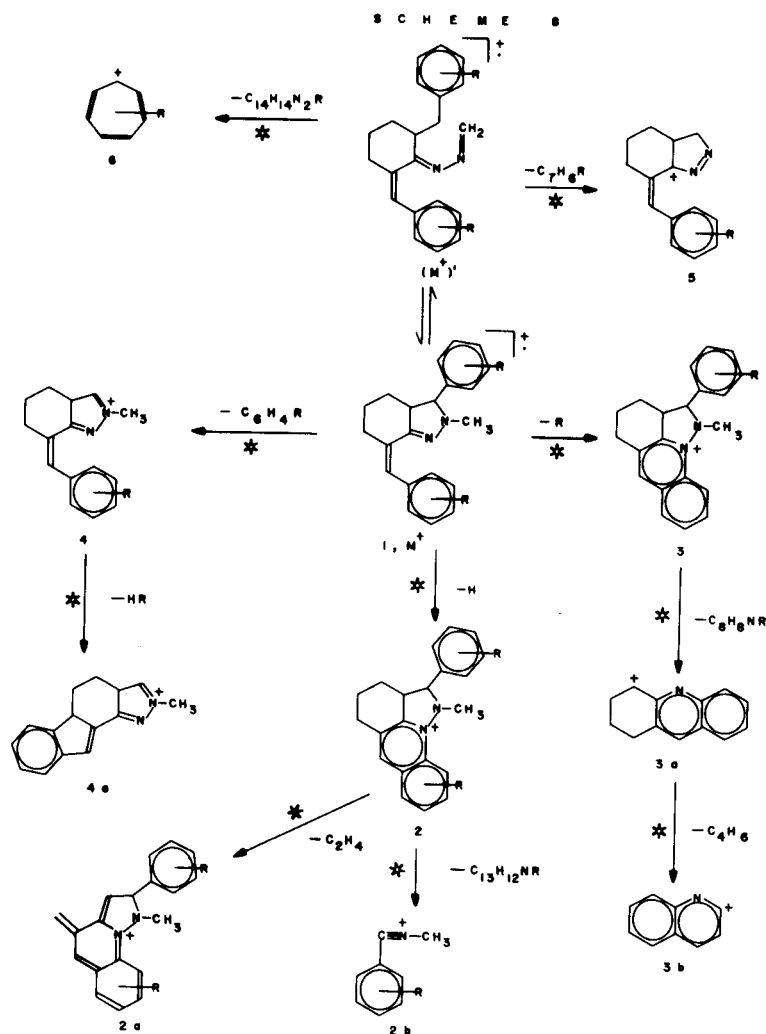
Pathway B.

Compounds II give rise to [M+ -R] peaks, **3**, which in *ortho*-R-compounds are more intense than those of *para*-R-derivatives. An explanation of this difference can be found in the different structures of the (M+ -R) ion. For *ortho* isomers it is stabilized by cyclization, which is quite impossible, however, for *para*-isomers (Scheme 5). A similar *o*-R interaction has been reported for 2*H*-indazoles I [3]. The **3** ion subsequently undergoes decomposition by loss
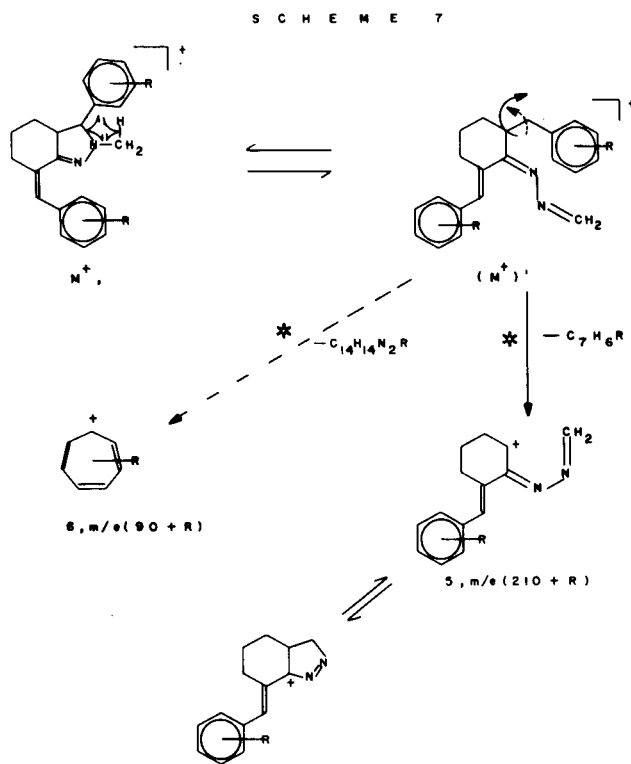
S C H E M E 7

of a C_8H_8NR unit to yield **3a** (m/e 182), which is depicted as a tetrahydroacridinium cation (Scheme 5). The **3a** ion

Table 2

Analytical and Physical Data for Compounds II

Compound No.	R	Mp °C	Yield	Molecular Formula	C	Analysis H	N
1 [5]	H	109-111	62.25	$C_{21}H_{22}N_2$	83.40 (83.37)	7.33 (7.33)	9.26 (9.21)
2	*o*-Br	87-90	54.4	$C_{21}H_{20}Br_2N_2$	54.80 (54.78)	4.38 (4.34)	6.08 (6.00)
3	*o*-Cl	74-76	48.7	$C_{21}H_{20}Cl_2N_2$	67.92 (67.90)	5.43 (5.42)	7.54 (7.60)
4	*o*-COOH	108-110	43.0	$C_{23}H_{22}N_2O_4$	70.75 (70.71)	5.68 (5.70)	7.17 (7.21)
5	*o*-CH₃	103-105	52.90	$C_{23}H_{26}N_2$	83.59 (83.62)	7.93 (7.97)	8.48 (8.55)
6	*o*-OCH₃	88-91	44.60	$C_{23}H_{26}N_2O_2$	76.20 (76.21)	7.23 (7.23)	7.73 (7.77)
7	*p*-Br	164-166	42.90	$C_{21}H_{20}Br_2N_2$	54.80 (54.82)	4.38 (4.36)	6.08 (6.13)
8	*p*-Cl	155-157	60.90	$C_{21}H_{20}Cl_2N_2$	67.92 (67.95)	5.43 (5.43)	7.54 (7.60)
9	*p*-CH₃	145-147	71.59	$C_{23}H_{26}N_2$	83.59 (83.61)	7.93 (7.98)	8.48 (8.50)
10	*p*-OCH₃	91-93	49.50	$C_{23}H_{26}N_2O_2$	76.20 (76.22)	7.23 (7.21)	7.73 (7.80)
11	*p*-NO₂	186-188	45.72	$C_{21}H_{20}N_4O_4$	64.27 (64.30)	5.13 (5.13)	14.28 (14.30)
12	*p*-NH₂	177-179	30.00	$C_{21}H_{24}N_3$	79.20 (79.23)	7.60 (7.60)	13.19 (13.22)

[5] Prepared by Krapcho and Turk.

SCHEME 8

further suffers the loss of a C_4H_6 unit to yield the ion **3b** (m/e 128). It is interesting to note that we observed the formation of $(M^+ \text{-R})$ and acridinium ions in the mass spectra of 2H-indazoles, therefore they are characteristics of the indazoles of type I and II.

Pathway C.

Unlike their 2H-analogues, all 2-methylindazoles II have a most abundant peak in their spectra corresponding to the ion **4** [m/e (224 + R)]. This is formed by the loss of an C_6H_4R radical from the molecular ion by a simple β-cleavage as shown in Scheme 6. The loss of a HR molecule from **4** leads the **4a** ion of m/e 223.

Pathway D.

Another interesting difference between I and II derivatives appear when we compare their mass spectra. The first compounds present an ion at m/e (90 + R), **6**, with a

middle relative abundance; in the case of II compounds together with this ion, appear another ion at m/e (210 + R), **5**. We proposed that both ions arising from the molecular ion via an $(M^+)'$ intermediate (Scheme 7), and that, the stability of **5** ion, is due to the presence of methyl-substituent on the 2-ring nitrogen-atom of indazole framework.

In summary, it can be said that the mass spectra of substituted 2-methylindazoles II indicate very selective breakdown patterns upon electron impact. It is note worthy that the mechanisms shown in Schemes 3, 4, 6 and 7 are useful to distinguish the compounds I and II. In fact, the spectrum of compounds I do not show peaks at m/e $(M^+ \text{-29})$, (224 + R), 223, (210 + R), (117 + R) and 128. It is therefore, conceivable that the fragmentation pattern of II compounds investigated is largely dependent on the methyl-substituent present in the 2 ring nitrogen atom of indazole moiety.

EXPERIMENTAL

The compounds were synthesized following reported procedures [5] with some modifications. The structures of compounds 1 to 12 were supported by ir and ¹H-nmr spectral data. The ir spectra (chloroform) for all compounds showed very characteristic bands at 1610, 1590, 1500, 1450, 1350, 1100-1010, 990 and 880 cm⁻¹. Besides these, bands for the R substituents are also shown.

The ¹H-nmr spectra (deuteriochloroform) of compound 1 (R = H) had signals at 7.5-7.1 ppm (11H, m, Ar, and -C = CH-), 3.65 (1H, d, J = 13 Hz, N-CH-), 3.2-1.2 (7H, bm, aliphatic), 2.8 (3H, S, -N-CH₃). The ¹H-nmr spectra of the other compounds analyzed also showed these characteristic signals with modifications on their chemical shifts due to the *ortho* and *p*-substituent.

Melting points are uncorrected. The ir spectra were recorded on a Perkin-Elmer 283-B spectrophotometer. The ¹H-nmr spectra were recorded on a Varian FT-80A spectrometer operating at 80 MHz in deuteriochloroform solution containing tetramethylsilane as an internal standard with chemical shifts (δ) expressed in ppm downfield from TMS. Mass spectra were obtained with a Perkin-Elmer RMU-7H double focusing mass spectrometer and a Hewlett Packard 59854-A quadropole mass spectrometer using the direct inlet system.

The samples were recorded at an ionization chamber temperature of 210° and operating at 70 eV. Analytical and physical data on the new compounds are given in Table 2.

REFERENCES AND NOTES

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[2] To whom correspondence should be addressed.

[3] Contribution No. 761 from Instituto de Química, UNAM.

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