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THE PHOTOCONVERSION R-CH_3 → R-CHO IN INDAZOLE DERIVATIVES

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Abstract—The UV irradiation of 1-(*p*-nitrophenyl)-3-methyl-indazole leads to the formation of the corresponding 3-formyl derivative as product of the photooxidation R-CH_3 → R-CHO. This method was applied to a series of substituted indazoles and the same reaction was observed with methyl groups attached to the pyrazole and to the benzene ring of the indazole.

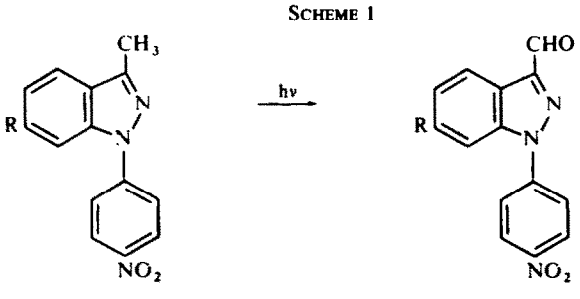
WE HAVE previously reported[1,2] that by UV irradiation of 1-(*p*-nitrophenyl)-3-methyl-indazole derivatives it was possible to obtain aldehydes as products of the photoconversion R-CH_3 → R-CHO.

This result is general for this type of substrate, since the same transformation occurs with methyl groups joined to the pyrazole as well as to the benzene ring of the indazole. Besides, the yields obtained make this reaction, at least in some instances, interesting as a preparative method.

Irradiations were performed in non-degassed acetic acid solutions in Pyrex glass containers, employing a high pressure Hg lamp (400 watts) as the luminous source. The formation of aldehydes was also observed using as solvents methanol, ethanol or benzene, but acetic acid was the most convenient medium for this reaction.

Formerly, we have irradiated the 1-(*p*-nitrophenyl)-3-methyl-indazole and its 6-chloro- and 6-methoxy- derivatives. In the first two cases, a carbonylic product was obtained (see Scheme 1, compounds **I** and **II**), together with a small amount of an acidic compound, however, with the 6-methoxy derivative no transformation was observed. The isolation of the carbonyl compound and the non-converted starting

SCHEME 1



R = H, Cl

I R = H
II R = Cl

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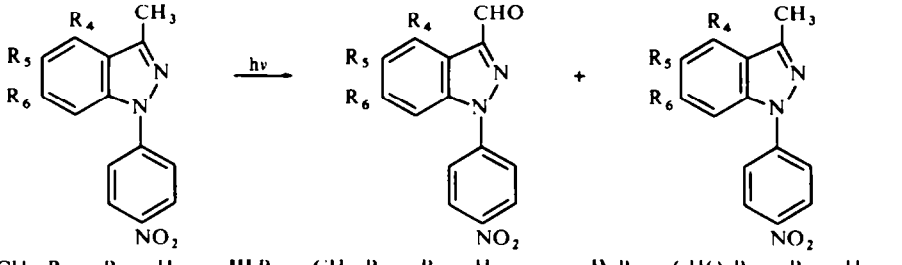
indazole was achieved by chromatography on silica-gel; the photo-product being contained in the second eluted fraction.

NMR spectra of compounds I and II (see Table 5) showed in each case the absence of the methyl group signal and the presence of an aldehydic proton. On the other hand, the aromatic region did not differ from that in the original indazole (see Table 4), with the exception of the shift of one proton (multiplet and doublet respectively) to lower field. This was interpreted as due to the anisotropic effect of the carbonyl group on H_4. UV spectra of both compounds (I and II) were similar to those of the starting substances and the IR spectra of I and II showed a typical carbonylic absorption at 1680 cm^{-1}.

The aldehydes I and II were then reduced with sodium borohydride in dioxane–water solution to the corresponding hydroxymethyl derivatives (XII and XIII). The spectroscopic properties of these substances agreed with an indazole structure (see Tables 3 and 6). Compounds XII and XIII were reconverted into the corresponding aldehydes (I and II) by UV irradiation of their acetic acid solutions. Moreover, the photoproduct II was oxidized with Ag_2O yielding a carboxylic acid (XXI) which was identified as the acidic compound obtained from the irradiation of the 1-(*p*-nitrophenyl)-3-methyl-6-chloro-indazole.

The same photooxidation was studied using as substrates several dimethyl, one methyl-ethyl and one trimethyl indazole derivative. The substrates and the photoproducts obtained (III–X) are represented in Scheme 2. Percentages of conversion and yields are given in Table 1; the physical properties and analytical data on the aldehydes are in Table 2.

SCHEME 2



$R_4 = CH_3, R_5 = R_6 = H$ III $R_4 = CH_3, R_5 = R_6 = H$ IV $R_4 = CHO, R_5 = R_6 = H$

$R_5 = CH_3, R_4 = R_6 = H$ V $R_5 = CH_3, R_4 = R_6 = H$ VI $R_5 = CHO, R_4 = R_6 = H$

$R_6 = CH_3, R_4 = R_5 = H$ VII $R_6 = CH_3, R_4 = R_5 = H$

$R_6 = C_2H_5, R_4 = R_5 = H$ VIII $R_6 = C_2H_5, R_4 = R_5 = H$

$R_5 = R_6 = CH_3, R_4 = H$ IX $R_5 = R_6 = CH_3, R_4 = H$ X $R_5 = CHO, R_6 = CH_3 R_4 = H$

As can be seen from Scheme 2, two isomeric aldehydes were always produced, but only one carbonylic compound was obtained from the 3,6-disubstituted indazoles. The photoproducts formed and the non-converted starting indazole were isolated by chromatography on silica gel. In some cases, together with the aldehydes, it was possible to isolate and identify small amounts of hydroxymethyl- derivatives. Thus, from the 3,4-dimethyl- and 3,5,6-trimethyl-indazole were obtained the hydroxymethyl- compounds XIV–XV and XIX–XX respectively. These substances were identified as the reduction products of the aldehydes III–IV and IX–X. By irradiation of 1-(*p*-nitrophenyl)-3-methyl-6-ethyl-indazole the 3-hydroxymethyl-indazole XVIII was formed, along with the normal compound VIII.

The acidic fractions represented a small percentage of the conversion and were not further investigated.

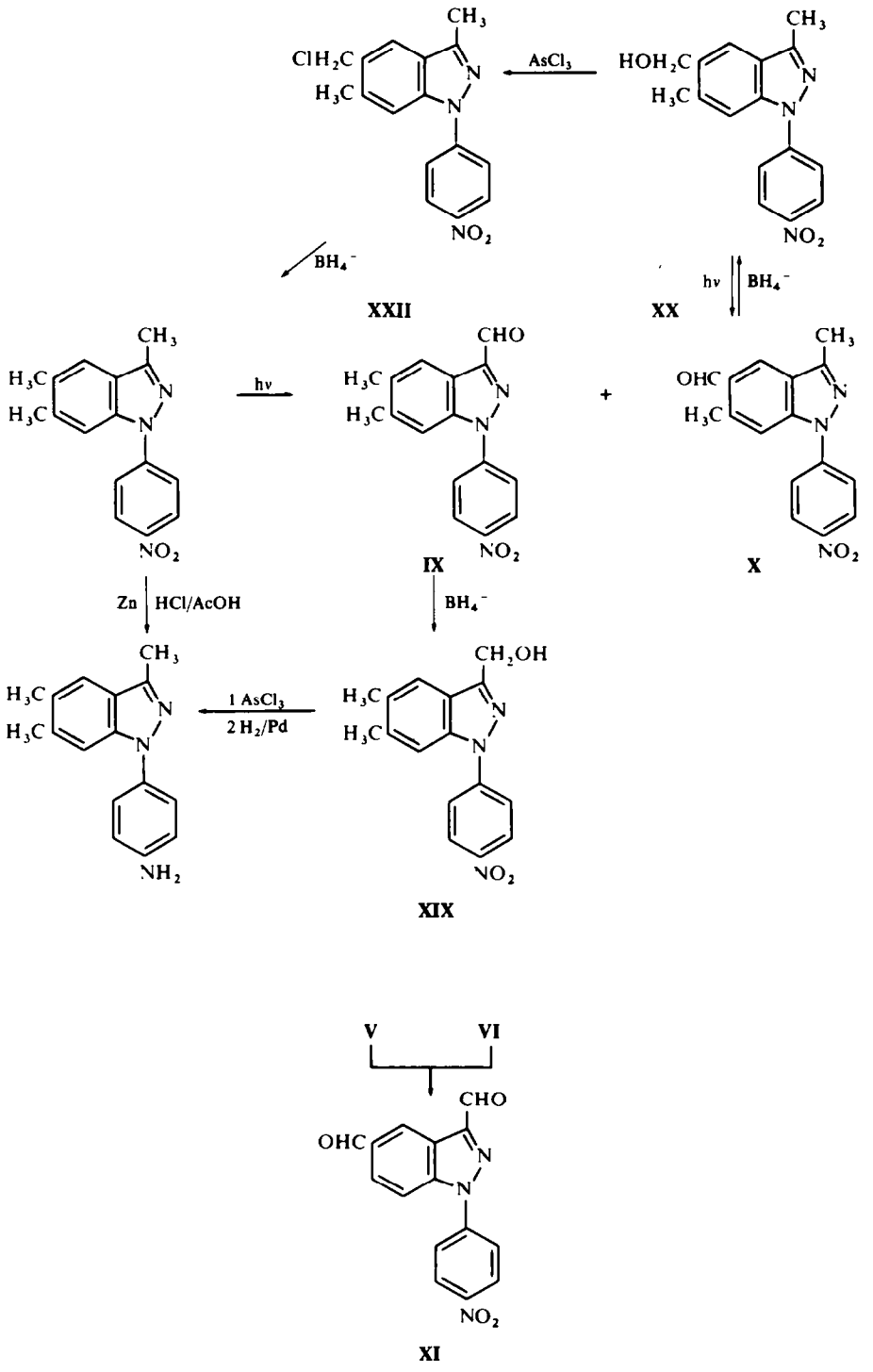
In all examples the NMR spectra showed that one of the methyl groups present in the starting indazole was transformed into a carbonyl group, whereas the UV spectra of all these products were similar to those of the original substances. A group of these carbonyl derivatives (higher R_f values, compounds **III**, **V**, **VII**, **VIII** and **IX**) had a chromatographic behaviour like that of the aldehydes previously mentioned (**I** and **II**) and thus we assumed that the formyl group was attached to position 3 of the indazole nucleus. This supposition was confirmed by interpretation of their NMR spectra (see Table 5). For example, in the NMR spectrum of **V**, the remaining methyl group appears at a δ value similar to that of the 5-CH_3 of 1-(*p*-nitrophenyl)-3,5-dimethyl-indazole (see Table 4). The spectrum of **V** also has a proton (singlet) deshielded 0·38 ppm with respect to the H_4 of the original indazole. Interpretation of the NMR spectra of **VII** and **IX** leads to the same conclusion. In the case of compound **III**, the position of the formyl group was assigned by considering the chemical shift value of its methyl group and that of the hydroxymethyl- derivative **XIV**. For the photoproduct **VIII** the conclusion was evident, since its NMR spectrum showed signals typical of the ethyl group, whereas the singlet of the 3-CH_3 of the original indazole had disappeared.

The interpretation of the NMR spectra of the second group of aldehydic substances (lower R_f values, compounds **IV**, **VI** and **X**) suggested that the photooxidation took place on the methyl groups joined to the benzene ring. In the NMR spectrum of compound **VI**, the methyl group appears at a value similar to the signal from the 3-CH_3 of 1-(*p*-nitrophenyl)-3,5-dimethyl-indazole, and two aromatic protons are deshielded with respect to the identical protons from the parent indazole. When aldehyde **VI** was reduced to compound **XVI**, both protons moved again to higher field. The carbonyl group of compound **X** was assigned to position 5 (and not 6) by comparing the chemical shift of H_4 and H_7 in the original indazole, in compound **X** and in its hydroxymethyl- derivative **XX**. The resistance to oxidation showed by the alkyl groups at the position 6 is in agreement with this assignment.

In order to prove that the indazole structure has suffered no change during irradiation, we performed a series of reactions with compounds **IX** and **X** (see Scheme 3). Aldehydes **IX** and **X** were reduced to the hydroxymethyl- compounds **XIX** and **XX** respectively. When **XX** was treated with arsenic trichloride,[3] the chloromethyl derivative **XXII** was obtained. The reduction of this compound to the original indazole was easily accomplished with sodium borohydride in dioxane–water solution.[3] The same reduction method failed when it was applied to the product obtained from the treatment of **XIX** with arsenic trichloride, which was in turn hydrogenated employing Pd as catalyst to the 1-(*p*-aminophenyl)-3,5,6-trimethyl-indazole. Similar demonstrations were carried out in two other cases. From the aldehyde **VI** 1-(*p*-nitrophenyl)-3,5-dimethyl-indazole was obtained, whereas **VII** was transformed into 1-(*p*-aminophenyl)-3,6-dimethyl-indazole.

It was interesting to expose these aldehydes to UV radiation with the intention of producing a more intensive photooxidation. For this purpose we irradiated the aldehydes obtained from 1-(*p*-nitrophenyl)-3,5-dimethyl-indazole (compounds **V** and **VI**). From both reactions we isolated the same photoproduct which was identified as the dialdehydic compound **XI**.

SCHEME 3


CH3
ClH2C
H3C
N
N
NO2
AsCl3
HOH2C
BH4−
XXII
hv
XX
CHO
OHC
IX
X
Zn
HCl/AcOH
CH2OH
1 AsCl3
2 H2/Pd
NH2
XIX
V
VI
XI

The physical properties of the hydroxymethyl indazoles (compounds **XII-XX**) prepared during this work, are given in Table 3. These compounds were reconverted into the corresponding aldehydes by UV irradiation of their acetic acid solutions.

DISCUSSION

The photooxidation of alkyl groups joined to an aromatic ring has many citations in the literature. It is probable that at some stage these reactions involve the formation of hydroperoxides. In some instances these intermediates can be isolated, but in other cases they are transformed to more stable products, depending upon the working conditions and on the structure of the initial compound. The preparation of hydroperoxides by irradiation of alkyl derivatives of aromatic hydrocarbons has been reported several times.[4,5,6] The phototransformation R-CH_3 → R-COOH has been observed in the benzene series[7] and with methyl derivatives of pyridine[8] and quinoline.[9] However, there are not many examples of the photoconversion R-CH_3 → R-CHO in the literature. Among the few, we must mention the photooxidation of toluene to benzaldehyde[10,11] and the recently published paper[12] on the irradiation of 1-methylanthraquinone to the corresponding aldehyde. In our case, the yields of the transformation R-CH_3 → R-CHO are, in most examples, good (see Table 1); one of the reasons could be the stability of the aldehydes formed.

Taking into account the photochemical rearrangements of indazoles previously described[13], we submitted to UV radiation both 1-(*p*-nitrophenyl)-3-formyl- and 1-(*p*-nitrophenyl)-3-formyl-6-chloro-indazole; in both cases we recovered unchanged most of the starting compound. Another experimental fact in accord with the proposed stability of the aldehydes, is the small amount of carboxylic acids that were obtained as by-products.

Probably, the primary photochemical process is the formation of a radical by abstraction of an hydrogen atom from the alkyl group:

$$\text{R-CH}_3 \rightarrow \text{R-CH}_2\cdot + \text{H}\cdot$$

The radical R-CH_2· could then react with oxygen as follows:

$$\text{R-CH}_2\cdot + \text{O}_2 \rightarrow \text{R-CH}_2\text{OO}\cdot$$

and the hydroperoxide radical could produce the hydroperoxide and a new radical R-CH_2· in the propagation step:

$$\text{R-CH}_2\text{OO}\cdot + \text{R-CH}_3 \rightarrow \text{R-CH}_2\text{OOH} + \text{R-CH}_2\cdot$$

The hydroperoxide could then be transformed photochemically to the radical R-CH_2O·, an intermediate for the formation of the aldehydes and the hydroxymethyl-compounds:

$$\text{R-CH}_2\text{OOH} \xrightarrow{h\nu} \text{R-CH}_2\text{O}\cdot + \text{HO}\cdot$$

$$\text{R-CH}_2\text{O}\cdot \xrightarrow{+\text{H}\cdot} \text{R-CH}_2\text{OH} \qquad \text{R-CH}_2\text{O}\cdot \xrightarrow{-\text{H}\cdot} \text{R-CHO}$$

As was previously mentioned, the presence of hydroxymethyl- derivatives was observed in some of our experiments, but always in small amounts. The formation

of these substances is not in line with their easy transformation into the respective aldehydes:

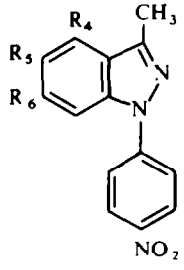
$$R\text{-}CH_2OH \xrightarrow{h\nu} R\text{-}CHO$$

To explain in another way how aldehydes and hydroxymethyl- compounds are obtained in the same reaction, we could postulate the decomposition of the hydroperoxide radical as follows: $2\ R\text{-}CH_2OO\cdot \rightarrow R\text{-}CHO + R\text{-}CH_2OH + O_2$ without forgetting that aldehydes can also be formed from hydroperoxides:

$$R\text{-}CH_2OOH \rightarrow R\text{-}CHO + H_2O$$

The latter transformation depends upon the reaction media and/or the temperature. The thermal and acid catalized decomposition of hydroperoxides has been mentioned in the literature.[14]

TABLE 1. PERCENTAGES OF CONVERSION AND YIELDS OF THE PHOTOOXIDATION OF 1-(*p*-NITROPHENYL)-3-METHYL INDAZOLES

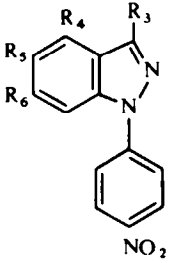


Substrate	Conversion (%)	Aldehydes obtained (yield %)	
$R_4 = R_5 = R_6 = H$	60	I (50)	
$R_6 = Cl, R_4 = R_5 = H$	94	II (77)	
$R_4 = CH_3, R_5 = R_6 = H$	48	III (13)	IV (34)
$R_5 = CH_3, R_4 = R_6 = H$	50	V (7)	VI (40)
$R_6 = CH_3, R_4 = R_5 = H$	60	VII (57)	
$R_6 = C_2H_5, R_4 = R_5 = H$	58	VIII (35)	
$R_5 = R_6 = CH_3\ R_4 = H$	83	IX (8)	X (70)

When 1-(*p*-nitrophenyl)-3-methyl-indazoles substituted with one or two methyl groups on the benzene ring are used, there exists the possibility of alternative or simultaneous oxidation of the methyl groups. In all examples, with the exception of the 3,6-dimethyl derivative, we obtained 3-formyl- and formyl(bz)indazoles simultaneously. However, considering the yields of each, it is possible to observe a greater facility for oxidation of the methyl groups joined to the benzene ring than those on the pyrazole nucleus, with the exception, mentioned before, of the 3,6-dimethyl-indazole. The difference in reactivity could be related to the ease of abstraction of a hydrogen atom in the first step of the reaction. The resistance to oxidation showed by the alkyl groups at position 6 of the indazole, could also be observed in the case of the 3-methyl-6-ethyl-indazole, from which only the 3-formyl derivative was isolated.

From the irradiation of mono- and dimethyl- derivatives of 1-(*p*-nitrophenyl)-3-methyl-indazole, we could not isolate dialdehydic compounds. However, when the 3-formyl-methyl(bz)indazole **V** and the 3-methyl-formyl(bz)indazole **VI** were irradiated, the dialdehyde **XI** was obtained.

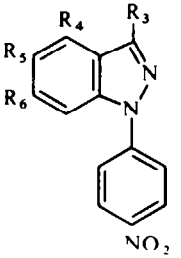
TABLE 2. ALDEHYDES OBTAINED BY UV IRRADIATION OF 1-(*p*-NITROPHENYL)-3-METHYL-INDAZOLES



Compound	m.p.	Formula	Analysis Required/Found C	H	N	λ_{max} nm (log ε) (solvent–chloroform)
I R_3 = CHO, R_4 = R_5 = R_6 = H	223–25°[a]	$C_{14}H_9N_3O_3$	62·92	3·39	15·73	346 (4·53); sh 291 (4·09)
			63·10	3·67	16·00	
II R_3 = CHO, R_6 = Cl, R_4 = R_5 = H	264–67°[b]	$C_{14}H_8ClN_3O_3$	55·74	2·65	13·93	378 (4·32); 347 (4·00); sh 304 (3·85)
			55·61	2·82	13·90	
III R_3 = CHO, R_4 = CH_3, R_5 = R_6 = H	207–08°[c]	$C_{15}H_{11}N_3O_3$	64·04	3·94	14·94	351 (4·33); sh 250 (4·19)
			63·84	4·10	15·10	
IV R_3 = CH_3, R_4 = CHO, R_5 = R_6 = H	214–16°[a]	$C_{15}H_{11}N_3O_3$	64·04	3·94	14·94	357 (4.31); sh 301 (3·99)
			64·27	4·22	15·09	
V R_3 = CHO, R_5 = CH_3, R_4 = R_6 = H	227–28°[c]	$C_{15}H_{11}N_3O_3$	64·04	3·94	14·94	354 (4.54); 298 (3·74)
			64·03	4·04	15·03	
VI R_3 = CH_3, R_5 = CHO, R_4 = R_6 = H	260–65°[a]	$C_{15}H_{11}N_3O_3$	64·04	3·94	14·94	350 (4·41); sh 301 (4·08); 252 (4·50)
			63·91	4·05	15·10	
VII R_3 = CHO, R_6 = CH_3, R_4 = R_5 = H	258–60°[a]	$C_{15}H_{11}N_3O_3$	64·04	3·94	14·94	348 (4·21); sh 295 (3·86)
			64·30	4·19	14·86	
VIII R_3 = CHO, R_6 = C_2H_5, R_4 = R_5 = H	170–72°[c]	$C_{16}H_{13}N_3O_3$	65·08	4·44	14·23	347 (4.32); sh 297 (3·99)
			64·95	4·37	14·30	
IX R_3 = CHO, R_5 = R_6 = CH_3, R_4 = H	244–45°[a]	$C_{16}H_{13}N_3O_3$	65·08	4·44	14·23	355 (4·38); 305 (4·15); sh 250 (4·29)
			64·94	4·59	14·07	
X R_3 = R_6 = CH_3, R_5 = CHO, R_4 = H	278–80°[a]	$C_{16}H_{13}N_3O_3$	65·08	4·44	14·23	355 (4·40); 307 (4·14); 254 (4·56)
			64·84	4·26	14·42	
XI R_3 = R_5 = CHO, R_4 = R_6 = H	241 43°[a]	$C_{15}H_9N_3O_4$	61·02	3·07	14·23	330 (4·28); sh 295 (4·22); sh 248 (4·45)
			61·15	3·19	14·38	

Recrystallization solvents: [a] chf-EtOH; [b] chf; [c] EtOH

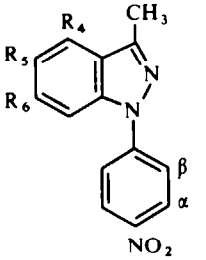
TABLE 3. HYDROXYMETHYL DERIVATIVES PREPARED DURING THIS WORK



Compound	m.p.	Formula	Analysis Required/Found C	H	N	λ_{max} nm (log ε) (solvent–chloroform)
XII $R_3 = CH_2OH, R_4 = R_5 = R_6 = H$	185–87 [a]	$C_{14}H_{11}N_3O_3$	62·45	4·12	15·61	354 (4·26); sh 260 (3·89)
			62·27	4·23	15·74	
XIII $R_3 = CH_2OH, R_6 = Cl, R_4 = R_5 = H$	234–36 [a]	$C_{14}H_{10}ClN_3O_3$	55·34	3·32	13·83	345 (4·24); sh 270 (3·86)
			55·22	3·37	13·76	
XIV $R_3 = CH_2OH, R_4 = CH_3, R_5 = R_6 = H$	147 153 [c]	$C_{15}H_{13}N_3O_3$	63·59	4·63	14·83	355 (4·15); sh 260 (3·82)
			63·75	4·69	14·65	
XV $R_3 = CH_3, R_4 = CH_2OH, R_5 = R_6 = H$	164–68 [a]	$C_{15}H_{13}N_3O_3$	63·59	4·63	14·83	358 (4·45); sh 260 (3·81)
			63·54	4·80	14·78	
XVI $R_3 = CH_3, R_5 = CH_2OH, R_4 = R_6 = H$	169 76 [a]	$C_{15}H_{13}N_3O_3$	63·59	4·63	14·83	360 (4·52); sh 310 (3·77)
			63·47	4·75	14·86	
XVII $R_3 = CH_2OH, R_6 = CH_3, R_4 = R_5 = H$	209–10 [a]	$C_{15}H_{13}N_3O_3$	63·59	4·63	14·83	355 (4·30); sh 265 (3·97)
			63·68	4·93	15·15	
XVIII $R_3 = CH_2OH, R_6 = C_2H_5, R_4 = R_5 = H$	182–84 [a]	$C_{16}H_{15}N_3O_3$	64·63	5·09	14·14	354 (4.23); sh 265 (3·89)
			64·83	5·20	14·29	
XIX $R_3 = CH_2OH, R_5 = R_6 = CH_3, R_4 = H$	221–23 [b]	$C_{16}H_{15}N_3O_3$	64·63	5·09	14·14	361 (4·27); sh 265 (4·03)
			64·50	4·96	14·31	
XX $R_3 = R_6 = CH_3, R_5 = CH_2OH, R_4 = H$	218–21 [b]	$C_{16}H_{15}N_3O_3$	64·63	5·09	14·14	363 (4·29); sh 270 (3·81)
			64·43	5·03	14·13	

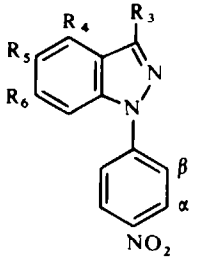
Recrystallization solvents: [a] benzene; [b] EtOH; [c] EtOH–H_2O

TABLE 4. NMR SPECTRA OF 1-(*p*-NITROPHENYL)-3-METHYL-INDAZOLES (δ VALUES, SOLVENT $AsCl_3$)



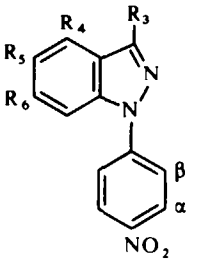
Compound	3-CH_3	Alkyl substituents	H_4	H_5	H_6	H_7	H_α	H_β
$R_4 = R_5 = R_6 = H$	2·97			7·50–8·17			8·53	8·03
$R_6 = Cl, R_4 = R_5 = H$	2·87		7·90	7·47		7·78	8·51	7·97
$R_4 = CH_3, R_5 = R_6 = H$	3·13	2·83		7·33–8·00			8·55	8·00
$R_5 = CH_3, R_4 = R_6 = H$	2·97	2·60		7·75			8·53	8·00
$R_6 = CH_3, R_4 = R_5 = H$	3·00	2·63	7·97	7·48		7·57	8·60	8·03
$R_6 = C_2H_5, R_4 = R_5 = H$	3·05	1·33 (CH_3) 2·95 (CH_2)		7·25–7·75			8·68	8·08
$R_5 = R_6 = CH_3, R_4 = H$	2·97	2·50 (5) 2·47 (6)	7·71			7·48	8·47	7·91

TABLE 5. NMR SPECTRA OF 1-(*p*-NITROPHENYL)-FORMYL-INDAZOLES.
(δ values, solvent $AsCl_3$)



Compound	Alkyl substituents	H_4	H_5	H_6	H_7	H_α	H_β	CHO
I R_3 = CHO, R_4 = R_5 = R_6 = H		8·50		7·50–8·25		8·51	8·08	10·38
II R_3 = CHO, R_6 = Cl, R_4 = R_5 = H		8·37	7·48		7·88	8·53	8·05	10·33
III R_3 = CHO, R_4 = CH_3, R_5 = R_6 = H	2·90		7·17–7·83			8·41	7·98	10·25
IV R_3 = CH_3, R_4 = CHO, R_5 = R_6 = H	3·12		7·70–8·08			8·47	7·90	10·28
V R_3 = CHO, R_5 = CH_3, R_4 = R_6 = H	2·58	8 13		7·45	7·75	8·43	8·00	10·26
VI R_3 = CH_3, R_5 = CHO, R_4 = R_6 = H	2·83	8·38		8·11	7·83	8·38	7·91	10·03
VII R_3 = CHO, R_6 = CH_3, R_4 = R_5 = H	2·60	8·30	7·40		7·70	8·53	8·06	10·33
VIII R_3 = CHO, R_6 = C_2H_5, R_4 = R_5 = H	1·35 (CH_3) 2·91 (CH_2)	8·33	7·53		7·78	8·51	8·01	10·40
IX R_3 = CHO, R_5 = R_6 = CH_3, R_4 = H	2·43 (5 and 6)	8·05			7·60	8·41	7·98	10·20
X R_3 = R_6 = CH_3, R_5 = CHO, R_4 = H	2·88 (3) 2·85 (6)	8·37			7 53	8·41	7·90	10·20

TABLE 6. NMR SPECTRA OF 1-(*p*-NITROPHENYL)-HYDROXYMETHYL-INDAZOLES.
(δ values, solvent $AsCl_3$)



Compound	CH_2OH	Alkyl substituents	H_4	H_5	H_6	H_7	H_α	H_β
XII $R_3 = CH_2OH, R_4 = R_5 = R_6 = H$	5·55			7·41–8·00			8·48	8·00
XIII $R_3 = CH_2OH, R_6 = Cl, R_4 = R_5 = H$	5·55		7·90	7·37		7·51	8·57	8·01
XIV $R_3 = CH_2OH, R_4 = CH_3, R_5 = R_6 = H$	5·61	2·77		7·17 7·83			8·45	7·88
XV $R_3 = CH_3, R_4 = CH_2OH, R_5 = R_6 = H$	5·45	3·13		7·17–7·83			8·47	7·91
XVI $R_3 = CH_3, R_5 = CH_2OH, R_4 = R_6 = H$	5·28	3·01		8·00			8·47	7·93
XVII $R_3 = CH_2OH, R_6 = CH_3, R_4 = R_5 = H$	5·57	2·60	7·97	7·41		7·61	8·51	7·98
XVIII $R_3 = CH_2OH, R_6 = C_2H_5, R_4 = R_5 = H$	5·65	1·33 (CH_3) 2·91 (CH_2)	8·05	7·50		7·65	8·70	8·05
XIX $R_3 = CH_2OH, R_5 = R_6 = CH_3, R_4 = H$	5·53	2·47 (5) 2·43 (6)	7·71			7·50	8·45	7·90
XX $R_3 = R_6 = CH_3, R_5 = CH_2OH, R_4 = H$	5·23	3·00 (3) 2·57 (6)	7·81			7·50	8·48	7·91

The photoconversion of alcohols in carbonyl compounds has been studied by several authors. Schenck[15] irradiated secondary aliphatic alcohols and obtained hydroxy-hydroperoxides which were decomposed by water into the corresponding ketones. If we consider that in our case the reaction $R\text{-}CH_2OH \xrightarrow{h\nu} R\text{-}CHO$ is easier than $R\text{-}CH_3 \xrightarrow{h\nu} R\text{-}CHO$, it is probable that the reaction sequence could begin with: $R\text{-}CH_2OH \xrightarrow{h\nu} R\text{-}CH_2\cdot + HO\cdot$, and the $R\text{-}CH_2\cdot$ radical could continue the course indicated for the formation of aldehydes.

EXPERIMENTAL

Melting points are uncorrected. The UV spectra were determined on a Beckman DK-2A spectrophotometer. The NMR spectra were recorded on a Varian A-60 spectrometer using TMS as internal standard.

Indazoles used in this work. The 1-(*p*-nitrophenyl)-3-methyl-indazoles used for the photochemical reactions, and the 1-(*p*-aminophenyl)-3-methyl-indazoles mentioned in this work, were prepared as previously described.[16,17]

General method of irradiation

The indazoles (200 mg) were irradiated in AcOH solns (100 ml) with magnetic stirring. Pyrex flasks fitted with a condenser were used. The light source was a Hg high pressure lamp (Philips, 400 watts) which was placed 10 cm from the middle of the flask. Irradiation times were of 7–8 h and the progress of the reaction was followed by TLC (solvent, ethyl acetate-ligroin 10:100). The soln was then diluted with water and the reaction product extracted with $CHCl_3$. The organic layer was separated and washed with water and then with $NaHCO_3$ soln in order to extract the acid compounds. The residue obtained by evaporation of the $CHCl_3$ was chromatographed on a silica-gel column. $CHCl_3$, CH_2Cl_2 were used as eluents or a mixture of ethyl acetate-ligroin (2:100 for the elution of the non-converted starting material and the first eluted aldehyde and 20:100 for the remaining products). In all cases, the first eluted fraction contained the non-converted starting compound; the products eluted in the following order: first the 3-formyl-indazoles and then the formyl(bz)indazoles. The best eluent for the isolation of the hydroxymethyl derivatives was found to be CH_2Cl_2. These substances eluted after the carbonyl compds. The bands on the column and the spots on the TLC plates were made visible by UV light. The aldehydes were revealed by spraying the plates with an alcoholic soln of 2,4-dinitrophenylhydrazine acidified with H_2SO_4.

The hydroxymethyl compds were reconverted into the aldehydes by UV irradiation under the same conditions. The irradiation times varied between 45 min and 4 h. The aldehydes were isolated and purified as indicated before.

Preparation of the hydroxymethyl derivatives by reduction of aldehydes

In a typical example, the aldehyde was dissolved in a soln of dioxane-water (100:4) and at room temp $NaBH_4$ was slowly added. The reaction was followed by TLC and when the aldehyde disappeared the addition of $NaBH_4$ was stopped. The soln was diluted with water and extracted with $CHCl_3$. The purification of the hydroxymethyl- compds was achieved by filtration of the concentrated extracts through a short silica-gel column, using $CHCl_3$ as eluent.

1-(*p-Nitrophenyl*)-6-*chloro-indazole* 3-*carboxylic acid* (XXI). A soln of aldehyde II (90 mg) in EtOH (60 ml) was treated with $AgNO_3$ (120 mg) and KOH (53 mg) dissolved in water. The mixture was heated under reflux for 7 h. After dilution with water, the solid was collected and the filtrate acidified and extracted with $CHCl_3$. The residue obtained by evaporation of the solvent was recrystallized from EtOH giving colourless needles, m.p. 272–275° (68 mg). (Found: C, 53·13; H, 2·67; N, 13·24. $C_{14}H_8ClN_3O_4$ requires: 52·93; H, 2·54; N, 13·23%).

Preparation of 1-(*p-aminophenyl*)-3,5,6-*trimethyl-indazole from* XIX. The hydroxymethyl- compd XIX (23 mg) was dissolved in $AsCl_3$ (3 ml), and the soln was heated at 70° for 3 h. After dilution with water, the product was extracted with $CHCl_3$. The residue obtained by evaporation of the solvent was dissolved in MeOH and hydrogenated at room temp for 3 h in a Parr apparatus at 34 psi the catalyst being Pd on $CaCO_3$. The catalyst was separated by filtration and the solvent evaporated. The product was chromatographed through a silica-gel column using benzene as eluent. The evaporated residue of the principal fraction was sublimated in high vacuum and was identified as 1-(*p*-aminophenyl)-3,5,6-trimethyl-indazole[17] by m.p. and IR.

1-(p-Nitrophenyl)-3-chloromethyl-6-methyl-indazole (XXIII). This was obtained from XVII in a similar manner to that described for compound XXII.[3] In this case, the heating period was 8 h. Yellow needles from benzene, m.p. 216–219°. (Found: C, 59·50; H, 4·16; N, 14·13. $C_{15}H_{12}ClN_3O_2$ requires: C, 59·70; H, 4·01; N, 13·93%). UV ($CHCl_3$) λ_{max} 353 nm (log ε 4·26); sh 270 (3·92). NMR ($AsCl_3$) 6-CH_3 2·60; CH_2 5·11; H_5 (d) 7·36; H_7 (s) 7·71; H_4 (d) 7·95; $H_{2',6'}$ (d) 8·03; $H_{3',5'}$ (d) 8·61.

Preparation of 1-(*p-aminophenyl*)-3,6-dimethyl-indazole from XXIII. This was obtained by a similar method to that used for the amino compound described above. The product, isolated by chromatography, was recrystallized from benzene-ligroin giving colourless needles, m.p. 109–111° (lit[16] 114–115°) and a IR spectrum identical with that of 1-(*p*-aminophenyl)-3,6-dimethyl-indazole.

Preparation of 1-(*p-nitrophenyl*)-3,5-*dimethyl-indazole from* XVI. The hydroxymethyl- compound **XVI** (66 mg) was dissolved in $AsCl_3$ (3ml) and the soln heated at 70° for 30 min. After dilution with water, the reaction product was extracted with $CHCl_3$. Evaporation of the solvent gave a residue that was dissolved in a mixture of dioxane–water (50:2) and to which an excess of $NaBH_4$ was added. The mixture was heated for 2 h at 70° and then extracted with $CHCl_3$. The evaporated residue was chromatographed on a silica-gel column using as eluent ethyl acetate–ligroin (2:100). From the principal fraction (the first), 1-(*p*-nitrophenyl)-3,5-dimethyl-indazole (47 mg) was obtained and identified by m.p. and IR.

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