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BENZODIAZEPINES. 2.[1]

PHOTOCHEMICAL TRANSFORMATION TO INDOLES

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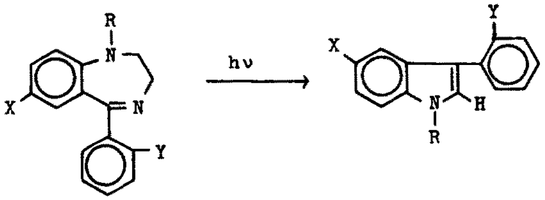
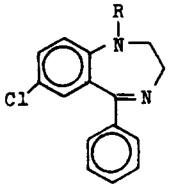
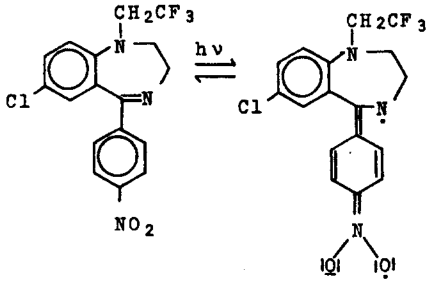
Irradiation of the 1-alkyl-2,3-dihydro-1,4-benzodiazepines 1a-d leads to the corresponding indoles 2a-d. This is a novel and preparatively useful phototransformation.[2] An alkyl group is required in the 1-position since 1e (R=H)[3,4] and 1f ($R=COCH_3$)[4] did not undergo this chemistry. Likewise a p-nitrophenyl group (1g) prevented the reaction, and starting material was recovered in these cases.



1	X	Y	R	2
a	Cl	F	CH_2CF_3	a
b	H	F	CH_2CF_3	b
c	Cl	H	CH_2CF_3	c
d	Br	F	CH_3	d



1e R=H
1f R=$COCH_3$



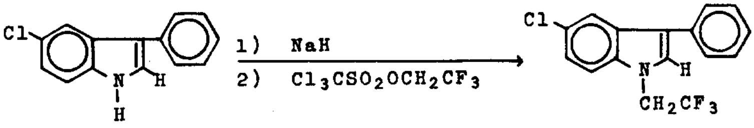
1g A

A large scale photolysis of 1a in methanol (5 g/250 ml) for 4 hours at room temperature led to an isolated yield of 70% of 2a. The irradiation was carried out under nitrogen in an immersion apparatus utilizing a Hanovia 450-watt medium-pressure quartz mercury-vapor lamp with a pyrex filter. Glacial acetic acid gave results comparable to methanol, but there was no reaction in dry acetonitrile. When benzene (dry, analytical reagent) was used as solvent, the reaction proceeded extremely slowly as judged by tlc, which indicated a trace of product after one week. No sensitization was observed upon photolysis in benzene with added benzophenone.

Photolysis of 1a in acetonitrile containing trifluoroacetic anhydride or in neat acetic anhydride resulted in formation of indole 2a.

The previously reported[1] benzodiazepines 1a,b,c as well as the new compounds 1d,g were prepared by Bischler-Napieralski reaction.[5]

Compound 2c, synthesized unambiguously by the alkylation of the anion of indole 3 with $Cl_3CSO_2OCH_2CF_3$, was identical with the photoproduct.[1,6]



3 2c

Some of the spectral and physical data for the indoles 2a-d are listed in the table.

SPECTRAL AND PHYSICAL DATA

	UV (MeOH)		NMR (60 MHz) CDCl$_3$			MS (m/e)*	M.p., °C†
	λ max	log ε	δ_{TMS}		J (Hz)		
2a	225 nm 260	4.53 4.12	4.64	(*q*, 2H)	9	327	80-83
2b	222 264	4.48 4.04	4.59	(*q*, 2H)	9	293	75-76
2c	225 261	4.46 4.18	4.60	(*q*, 2H)	9	309	129-130
2d	228 265	4.51 4.17	3.74	(*s*, 3H)		303	78-80

* In each case the molecular ion is the base peak.

† All compounds were recrystallized from ether-hexane; 2a,b, and d were first chromatographed on silica gel with ether-petroleum ether.

The mechanism of the reaction is currently under investigation. With the available evidence several possibilities are viable. A radical initiated process may be involved since addition of a catalytic amount of benzoyl peroxide to the solution of compound 1a in benzene resulted in the formation of a substantial amount of indole 2a in 4 hours. It was postulated that a nitro group in the position para to the imine bond (1g) would prevent reaction and this was found to be the case. Possibly a stable resonance form of an excited triplet state is involved, such as A.

REFERENCES

1. Part 1: M. Steinman, J.G. Topliss, R. Alekel, Y.S. Wong, and E.E. York, J. Med. Chem., **16**, 1354 (1973).
2. Although non-photochemical ring contractions of 3-substituted benzodiazepines, for example, have been reported, the chemistry of those reactions is quite different from the one reported herein. See W. Metlesics, G. Silverman, and L.H. Sternbach, J. Org. Chem., **29**, 1621 (1964).
3. T.S. Sulkowski and S.J. Childress, J. Org. Chem., **28**, 2150 (1963).
4. L.H. Sternbach, E. Reeder, and G.A. Archer, ibid., **28**, 2456 (1963).
5. Satisfactory analytical data were collected for all new compounds described herein.
6. P. Bravo, C. Guadiano, and A. Umani-Ronchi, Tetrahedron Letters, 679 (1969).