

Novel Syntheses of 5-Chloro-2-(4*H*-1,2,4-triazol-4-yl)benzophenone

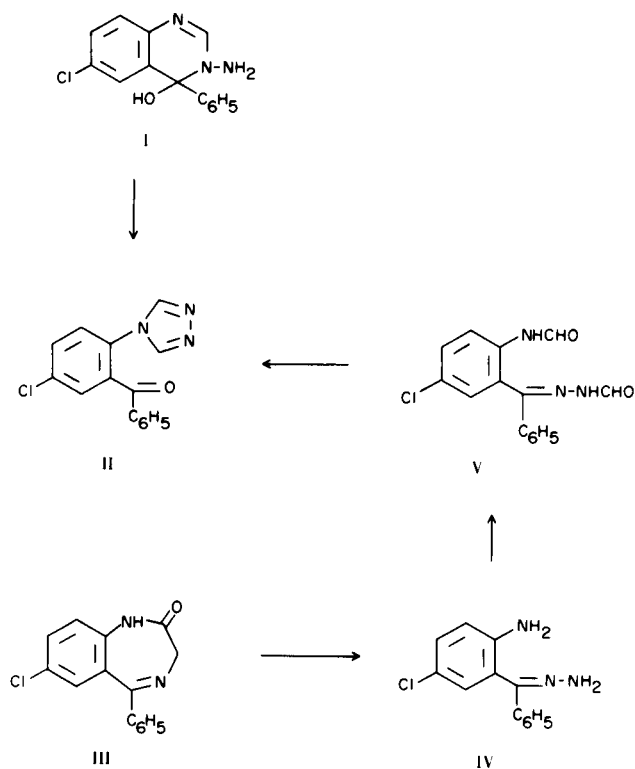
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Sir:

Recently we discussed the structure elucidation of 3-amino-6-chloro-3,4-dihydro-4-hydroxy-4-phenylquinazoline (I) from both physical and chemical points of view (1,2). We would now like to report an unusual transformation of compound I in formic acid. The same product was obtained by the treatment of 5-chloro-2-formamidobenzophenone formylhydrazone (V) under similar conditions.



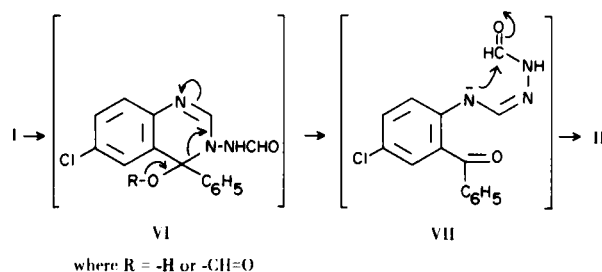
When compound I was dissolved in formic acid and heated at reflux overnight, a multicomponent mixture resulted from which a 40% yield of a new compound was isolated. The product was recrystallized from benzene to give colorless needles, m.p. 184-186° (3). The ir spectrum (Chloroform) was distinguished by a strong absorption at 1670 cm^{-1} which was interpreted as an unbonded benzophenone carbonyl. The nmr spectrum (deuteriochloroform) exhibited a singlet (2H) at δ 8.21 and a multiplet

(8 aromatic H) at 7.33-7.79 and the mass spectrum exhibited major fragment ions at m/e 283, 255, 254, 227 and 105 (4).

On the basis of these data, structure II was assigned. The same product was obtained in a 27% yield when compound V was heated at the reflux temperature in a formic acid solution.

The starting material for V was the known 2-amino-5-chlorobenzophenone hydrazone (IV) (5). The obvious synthetic route to IV by way of 2-amino-5-chlorobenzophenone is not attractive from the point of yield or work-up and an alternate method was devised. Thus, when the known benzodiazepine III (6) was heated for 18 hours at reflux in ethanol containing a large excess of hydrazine, removal of the solvent *in vacuo* and recrystallization of the product from an ethanol-hexane solution gave compound IV in 56% yield, spectrally identical with an authentic sample. Treatment of a solution of IV (10 g., 41 mmoles) in benzene (350 ml.) with formic acid (98-100%, 25 ml.) gave, after 18 hours at reflux, followed by removal of the solvent *in vacuo* and washing of the residue with hot benzene and hot ethanol, 7.0 g. (57%) of crystalline V, m.p. 226-228°. An analytical sample, m.p. 228.5-230° (3) was prepared by recrystallization from DMF-water.

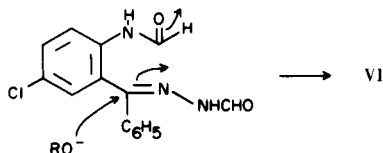
The reaction of I with formic acid is envisaged as proceeding *via* formylation to an intermediate such as VI (in analogy to the acetylation of I (2)), followed by ring fission to give VII.



The intermediate VII would then dehydrate to give the observed product (II). Although refluxing formic acid might well effect the intramolecular dehydration of VI

where R = H to give the appropriate *N*-formylidiaziridine (7), such a product would be expected then to be attacked by formic acid to give VI where R = formyl.

It is also plausible to view VI as an intermediate in the conversion of V to II. The attack of formyl ion at the imine bond (8) concomitant with cyclization and dehydration would yield the intermediate VI which would then proceed to II as shown (9).



Acknowledgment.

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- (2) M. E. Derieg, R. I. Fryer, S. Hillery, W. Metlesics and G. Silverman, *J. Org. Chem.*, **36**, 000 (1971).
- (3) A satisfactory elemental analysis was obtained for C, H, and N. Melting points were determined microscopically on a hot stage and are corrected.
- (4) The nmr spectra were determined on a Varian A-60 instrument, the ir spectra were determined on a Beckmann IR-9 spectrophotometer and the mass spectra were determined on a CEC-21-110B instrument at 70eV by direct insertion.
- (5) G. N. Walker, *J. Org. Chem.*, **27**, 1929 (1962).
- (6) L. H. Sternbach and E. Reeder, *ibid.*, **26**, 4936 (1961).
- (7) Similar diaziridines are discussed by E. Schmitz, *Angew. Chem.*, **71**, 127 (1959).
- (8) The susceptibility of imines to attack by acids is discussed by K. Harada in "The Chemistry of the Carbon-Nitrogen Double Bond", Saul Patai, Ed., John Wiley & Sons, N. Y., 1970, p. 264. The reaction of anhydrides with imines is discussed by G. N. Walker and M. A. Moore, *J. Org. Chem.*, **26**, 432 (1961).
- (9) Although intramolecular mechanisms may be envisaged for the conversion of V to II, the apparent necessity of the presence of formic acid leads us to prefer the intermediate mechanism shown.