Tetrahedron, 1963, Vol. 19, pp. 1587 to 1589. Pergamon Press Ltd. Printed in Northern Ireland

HYDRAZONES—IV[1]

THE BROMINATION OF BENZYLIDENE 2-PYRIDYLHYDRAZONE

M. S. GIBSON
Chemistry Department, Faculty of Technology,
The University, Manchester

(*Received* 31 *May* 1963)

Abstract—Reaction of bromine (1 mole) with benzylidene 2-pyridylhydrazone in acetic acid gives benzylidene 2-(N-bromopyridylium)-hydrazone bromide, which has the properties of a typical N-bromo-compound. Bromination in the presence of sodium acetate, or treatment of the N-bromo-compound with bases, leads to 3-phenyl-s-triazolo[4,3-a] pyridine.

THE CHLORINATION and bromination of arylidene arylhydrazones have been extensively investigated, notably by Chattaway and co-workers;[2] these reactions, whose major features are now known, include substitution of the methine hydrogen by halogen and lead to the ω-halo-compounds, e.g.

$$\mathrm{PhCH{:}NNHC_6H_5} \xrightarrow{3\mathrm{Br_2}} \mathrm{PhCBr{:}NNHC_6H_3Br_2(2,4)}$$

Benzylidene 2-pyridylhydrazone provides an exception to this general behaviour. Addition of bromine (1 mole) to a solution of this hydrazone in acetic acid precipitates a deep yellow compound; though not obtainable in a pure condition by crystallization, this is quite stable, and analysis indicates it to be a 1:1 addition compound. The properties of the compound suggest that it is benzylidene 2-(N-bromopyridylium)-hydrazone bromide (I).

$$\mathrm{PhCH{:}NNHC_5H_4N} \longrightarrow \mathrm{PhCH{:}NNHC_5H_4\overset{+}{N}Br\ Br^-} \qquad \text{(I)}$$

Thus the compound liberates iodine from acidified potassium iodide solution. It is, further, an effective brominating agent, converting acetanilide to *p*-bromacetanilide, itself undergoing reduction to benzylidene 2-pyridylhydrazone. Boiling methanol also slowly reduces the compound to the parent hydrazone.

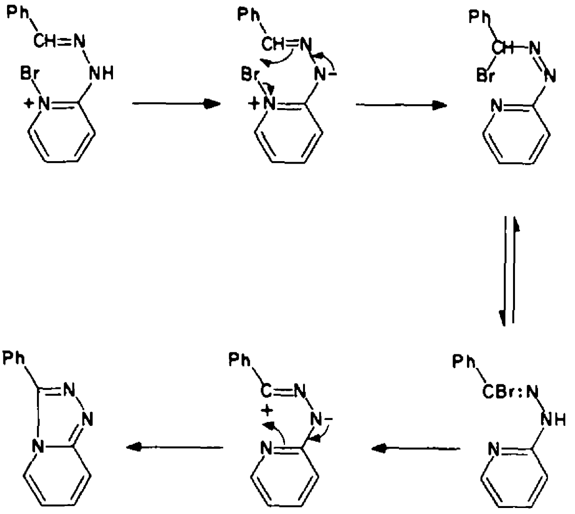
In the presence of bases, compound I undergoes an interesting reaction in which two molecules of hydrogen bromide are eliminated and 3-phenyl-s-triazolo[4,3-a]pyridine (II) is formed. Since I is a brominating agent, it seems likely that proton removal is followed by intramolecular bromination to give ω-bromobenzylidene 2-pyridylhydrazone. The latter would not survive under the reaction conditions, but would yield the triazolopyridine II, formally by isomerization of the intermediate nitrilimine.[1,3] Of interest in this connection is the report that ω-bromobenzylidene 5-tetrazolylhydrazone readily loses hydrogen bromide in ethanolic solution giving

---

[1] Part III; M. S. Gibson, *Tetrahedron* **18**, 1377 (1962).

[2] F. D. Chattaway and A. J. Walker, *J. Chem. Soc.* 975 (1925); and later papers.

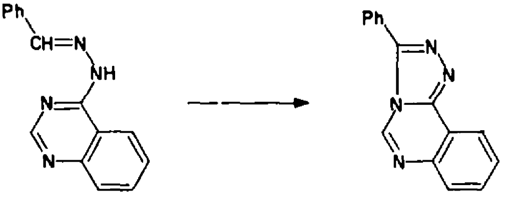
[3] cf. R. Huisgen, *Centenary Lecture, Proc. Chem. Soc.* 357 (1961).


I

II

3-azido-5-phenyl-1,2,4-triazole;[4] here the tetrazole ring functions as donor, and suffers rupture in the process.

Experimentally, the triazolopyridine II may be prepared directly from benzylidene 2-pyridylhydrazone by conducting the bromination in the presence of anhydrous sodium acetate (cf.[1]); the analogous reaction involving benzylidene 4-quinazolylhydrazone gives 3-phenyl-s-triazolo[4,3-c]quinazoline.



EXPERIMENTAL

Microanalyses were carried out by Mr. V. Manohin.

Benzylidene 2-pyridylhydrazone was prepared by the literature method[5] and formed needles (from ethanol), m.p. 148° (lit 148°); repeated crystallization from benzene raised this to 153–154°.

Bromination of benzylidene 2-pyridylhydrazone. Bromine (0·5 ml) in glacial acetic acid (1·5 ml) was added to a stirred solution of benzylidene 2-pyridylhydrazone (2 g) in acetic acid (18 ml). Immediately the solution became warm, turned orange, and a chrome-yellow precipitate of *benzylidene 2-(N-bromopyridylium)hydrazone bromide* (1·9 g) separated. This was collected, washed with glacial acetic acid, and dried *in vacuo*; the product had m.p. 131–135° to an opaque liquid, clearing at 152–155° (Found: C, 37·3; H, 2·9; N, 11·6; Br, 48·1. $C_{12}H_{11}Br_2N_3$ requires C, 40·3; H, 3·1; N, 11·8; Br, 44·8%). The compound was obtained crystalline, though not pure, by rapid chilling of a solution in hot acetonitrile, being obtained as slightly gummy yellow blades, m.p. 131–135° (opaque liquid, clearing at 152–155°). Spectroscopic results were: λ_{max} 240 (log ε 4·06), 286 (3·97) and 349·5 mμ (3·85), λ_{min} 232 (4·04), 256 (3·68) and 318 mμ (3·64); ν_{max} 3370, 3030, 1635,

[4] F. L. Scott and M. Holland, *Proc. Chem. Soc.* 106 (1962).

[5] R. G. Fargher and R. Furness, *J. Chem. Soc.* 688 (1915).

1590, 1555, 1440, 1265, 750 and 685 cm^{-1}. The compound may be kept indefinitely, dry, at room temperature.

The combined filtrate and washings from the reaction were basified with ammonia; the precipitated 3-phenyl-s-triazolo[4,3-a] pyridine (0·73 g) was collected, washed, dried and crystallized from benzene, forming plates, m.p. 172–173° (*lit*[6] 176°). A mixed m.p. with a sample prepared by conducting the above bromination in the presence of sodium acetate (see below) showed no depression.

Reactions of benzylidene 2-(*N-bromopyridylium*)*hydrazone bromide*

(a) *With acetanilide.* A slurry of powdered acetanilide (0·75 g) and benzylidene 2-(N-bromopyridylium)hydrazone bromide (2 g) in glacial acetic acid (5 ml) was warmed to 50°. The resulting orange solution remained hot for a few min, the colour fading to yellow. On cooling, a mass of colourless needles separated. Water (25 ml) was added with stirring, and, after 5 min, the colourless solid (1.2 g) was collected, washed with cold 2N hydrochloric acid and water, and dried; crystallization from methanol gave *p*-bromacetanilide as prisms, m.p. and mixed m.p. 167–168°.

The filtrate and washings were basified with ammonia, and the solid (0·43 g) collected and dried. Crystallization from benzene gave benzylidene 2-pyridylhydrazone as needles, m.p. and mixed m.p. 149–151°.

(b) *With methanol.* The bromide (0·45 g) in methanol (15 ml) was boiled for 40 min, the solution becoming colourless. Solvent was then removed *in vacuo.* The syrupy residue was completely soluble in water, and the solution gave reactions for bromide ion. Basification with ammonia gave benzylidene 2-pyridylhydrazone (0·12 g); needles (from benzene), m.p. and mixed m.p. 149–151°.

(c) *With water.* The bromide (1·72 g) was dissolved in boiling water (35 ml), and the near-colourless solution was separated from a trace of tarry material. On cooling, and standing, colourless needles (0·15 g) slowly separated. These had m.p. 70–72° (opaque liquid), slowly resolidifying as plates and remelting at 167–172°. The substance was identified as benzylidene 2-pyridylhydrazone hydrobromide since its aqueous solution gave reactions for bromide ion, and basification liberated the hydrazone itself; needles (40 mg), m.p. and mixed m.p. 150–152°.

Basification of the reaction filtrate gave 3-phenyl-s-triazolo[4,3-a]pyridine (0·68 g); two crystallizations from benzene gave plates, m.p. and mixed m.p. 172–173°.

(d) *With ammonia.* The bromide (0·57 g) suspended in warm benzene (2 ml) was shaken with '880' ammonia (3 ml), the mixture becoming hot. When cool, the solid (0·27 g) was collected, washed and dried. Crystallization from benzene gave the triazolopyridine as plates, m.p. and mixed m.p. 172–173°.

Conversion of benzylidene 2-pyridylhydrazone to 3-phenyl-s-triazolo[4,3-*a*]*pyridine.* Bromine (0·5 ml) in glacial acetic acid (1·5 ml) was added to a suspension of powdered, anhydrous sodium acetate (2·7 g, 3 equiv) in acetic acid (18 ml) containing dissolved benzylidene 2-pyridylhydrazone (2 g). The slurry became golden, grew warm, and the solid rapidly passed into solution as the colour faded to pale pink. After 2–3 min, a white granular precipitate (sodium bromide) separated. After standing 30 min, the mixture was poured into ice-cold 2N sodium hydroxide solution (200 ml) with stirring; the crude triazolopyridine (1·88 g) separated as a cream solid, was collected, washed and dried *in vacuo.* Two crystallizations from benzene gave lustrous plates, m.p. 172–173° (Found: C, 73·5; H, 4·5; N, 21·3. Calc for $C_{12}H_9N_3$; C, 73·8; H, 4·6; N, 21·6%).

3-*Phenyl-s-triazolo*[4,3-c]*quinazoline.* Bromine (0·2 ml) in glacial acetic acid (0·8 ml) was added to a suspension of anhydrous sodium acetate (1·3 g) in acetic acid (9 ml) containing dissolved benzylidene 4-quinazolylhydrazone (1 g).[7] After a few moments, the mixture warmed slightly, the colour faded to yellow, and a solid separated. After 20 min, the mixture was poured into excess ice-cold 2N sodium hydroxide solution, and the product collected as in the previous case. Two crystallisations from ethanol gave 3-phenyl-s-triazolo[4,3-c]quinazoline (0·65 g) as needles, m.p. 202–203° (*lit*[8] 196–197°) (Found: C, 72·9; H, 4·1; N, 22·8. Calc for $C_{15}H_{10}N_4$; C, 73·15; H, 4·1; N, 22·75%).

---

[6] J. D. Bower and F. P. Doyle, *J. Chem. Soc.* 727 (1957).

[7] T. Higashino, *Nagasaki Yakugaku Zasshi* **80,** 245 (1960); *Chem. Abs.* **54,** 13126 (1960).

[8] R. Huisgen, H. J. Sturm and M. Seidel, *Ber. Dtsch. Chem. Ges.* **94,** 1555 (1961).