# STUDIES OF MEDIUM-MEMBERED HETEROCYCLIC COMPOUNDS. II.[1] REACTION OF 5-BENZYL-4,6-DIHYDRO-3,7-DIARYL-1,2,5-TRIAZEPINES WITH HALOGENATION-REAGENTS

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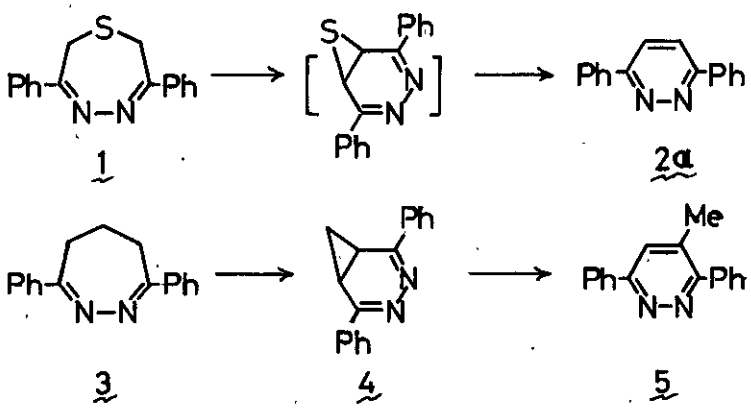
Treatment of 5-benzyl-4,6-dihydro-3,7-diaryl-1,2,5-triazepine (6a or 6b) with bromination-reagents afforded either 1-benzyl-4-arylimidazole (7a or 7b) or 3,6-diarylpyridazine (2a or 2b) as the main product, depending on the reaction conditions. On the other hand, 6a reacted with sulfuryl chloride to give 4-benzylamino-3,6-diphenylpyridazine (8), while the reaction of 6a with chlorine gas afforded 5-chloropyridazine derivative (9), which was easily obtained by further chlorination of 8. Although the reaction course for the formation of 2 is not clear, the products 7 and 8 can be accounted for by the pathway via triazanorcaradiene (10).

Loudon and Young[2] have demonstrated that in the treatment with NBS 2,7-

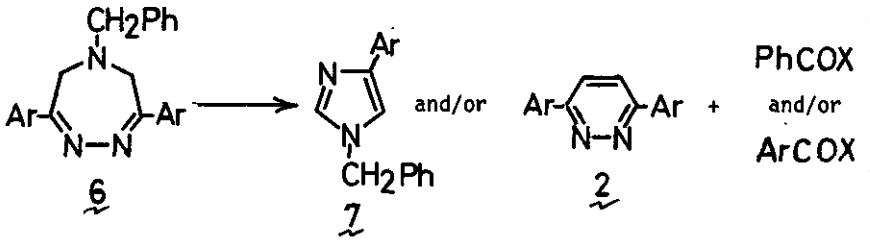
dihydro-3,6-diphenyl-1,4,5-thiadiazepine (1) was converted into 3,6-diphenylpyridazine (2a) via the episulfide intermediate. Recently, we found that the reaction of 4,6-dihydro-3,7-diphenyl-1,2-diazepine (3) with halogenation-reagents afforded 2,5-diphenyl-3,4-diaza-2,4-norcaradiene (4), which was easily converted into 4-methyl-3,6-diphenylpyridazine (5).[1]




On the basis of above observations, it might be expected that 4,6-dihydro-1,2,5-triazepine derivative would react with halogenation-reagents to give 3,4,7-triaza-2,4-norcaradiene derivative. In the present paper we report the reaction of 5-benzyl-4,6-dihydro-3,7-diphenyl- (6a)[3] and 5-benzyl-4,6-dihydro-3,7-di(p-tolyl)-1,2,5-triazepine (6b)[4] with halogenation-reagents under various conditions.

When a solution of dihydrotriazepine 6a and equimolar amount of bromine in methanol was refluxed for 30 min, 1-benzyl-4-phenylimidazole (7a) and methyl benzoate were obtained as major products, accompanied with trace of the pyridazine 2a. On the other hand, the reaction of 6a with bromine in methanol at room temperature for 2 hr afforded 2a and methyl benzoate, and no 7a was formed. The similar change was effected with bromine in refluxing diethyl ether, acetic

acid, dichloromethane, chloroform, and carbon tetrachloride, and with NBS in refluxing carbon tetrachloride. The results are summarized in Table 1.




a: Ar=Ph; b: Ar=p-tolyl

Table 1 Reaction of 6 with bromination-reagents

| 6 | Reaction conditions | Product, % 2 | 7 | PhCOX | ArCOX |
|---|---|---|---|---|---|
| a | $Br_2$, MeOH, reflux, 30 min | 1 | 49 | 38[a] | -- |
| b | $Br_2$, MeOH, reflux, 30 min | 0 | 36 | 5[b] | 33[c] |
| a | $Br_2$, MeOH, room temp., 2 hr | 53 | 0 | 65[a] | -- |
| b | $Br_2$, MeOH, room temp., 2 hr | 24 | 0 | 18[b] | 17[c] |
| a | $Br_2$, $Et_2O$, reflux, 1 hr | 52 | 0 | 33[b] | -- |
| a | $Br_2$, AcOH, reflux, 1 hr | 61 | 0 | 8.3[b] | -- |
| a | $Br_2$, $CH_2Cl_2$, reflux, 1 hr | 68 | 0 | 18[b] | -- |
| a | $Br_2$, $CHCl_3$, reflux, 1 hr | 66 | 0 | 25[b] | -- |
| a | $Br_2$, $CCl_4$, reflux, 1 hr | 73 | 0 | 19[b] | -- |
| b | $Br_2$, $CCl_4$, reflux, 1 hr | 62 | 0 | 12[b] | 0 |
| a | NBS, $CCl_4$, reflux, 2 hr | 48 | 0 | 0 | -- |

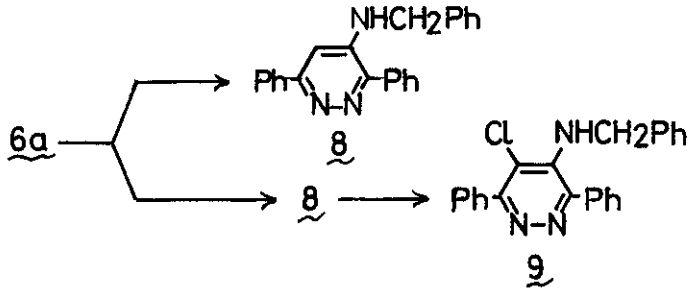
[a]Methyl benzoate, [b]Benzoic acid, [c]Methyl p-methylbenzoate

Similarly, dihydrotriazepine 6b reacted with bromine to give either 1-benzyl-4-p-tolylimidazole (7b) or 3,6-di(p-tolyl)pyridazine (2b), depending on

the reaction conditions. The results are also given in Table 1.

The structures of 7a, mp 102-103° (lit.,[5] mp 102-103°), and 7b, mp 150-151°, were confirmed by the microanalyses as well as by the spectral data. The quantitative estimation of benzoic acid, methyl benzoate, and methyl p-methylbenzoate was performed by gas-chromatography.

On the other hand, treatment of 6a with sulfuryl chloride in dichloromethane at 0-2° for 2 hr afforded 4-benzylamino-3,6-diphenylpyridazine (8), mp 137.5-138.5°, in a 72% yield. In the reaction with chlorine gas in dichloromethane, chloroform, and acetic acid at room temperature for 2 hr, 6a afforded 4-benzylamino-5-chloro-3,6-diphenylpyridazine (9), mp 160-161°, in 76, 62, and 22% yields respectively. The formation of 9 can be rationalized as arising from 8, because 9 was easily obtained by chlorination of 8 with chlorine gas.[6]



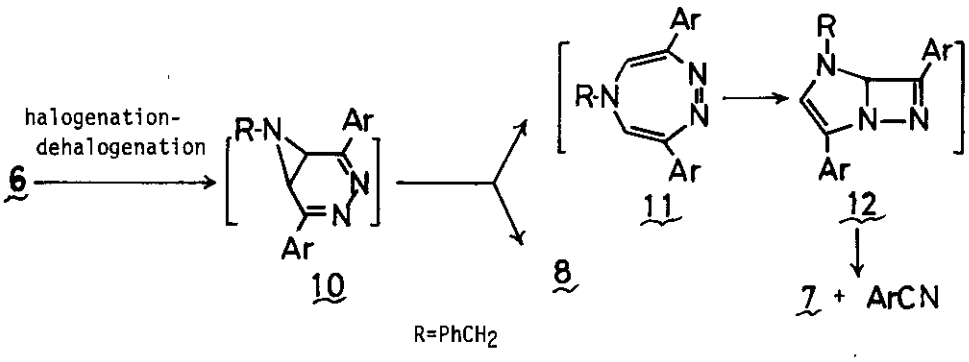

8: $\nu_{max}$ (KBr) 3420 $cm^{-1}$; δ ($CDCl_3$) 4.40 (2H, d, $CH_2$), 5.3 (1H, broad, NH), 6.88 (1H, s, pyridazine ring-H), 7.2-8.1 (15H, m, aromatic protons); m/e 337 ($M^+$). 9: $\nu_{max}$ (KBr) 3330 $cm^{-1}$; δ ($CDCl_3$) 4.05 (2H, d, $CH_2$), 5.1 (1H, broad, NH), 6.9-8.0 (15H, m, aromatic protons); m/e 371, 373 ($M^+$, rel. intensity 3:1).

Heine and Irving[7] found that brief heating of 7-benzyl-2,5-diphenyl-3,4,7-triaza-2,4-norcaradiene (10, Ar=Ph)[8] in benzene or ethanol formed benzonitrile and imidazole 7a. They also proposed the pathway via the valence tautomerization of 10 into triazacycloheptatriene 11, conversion of 11 into 12, followed by

fragmentayion of 12 into 7 and benzonitrile.

As reported previously,[1] dihydrodiazepine 3 afforded diazanorcaradiene 4 via a halogenation-dehalogenation process, and on treatment with hydrogen halide 4 was easily converted into pyridazine 5.

Consequently, the products 7 and 8 can be accounted for by the pathway via triazanorcaradiene 10 as depicted in the following scheme, although the reaction pathway for the formation of 2 is not clear.




REFERENCES AND NOTES

1 Part I of this series: O. Tsuge and K. Kamata, Heterocycles, 1975, 3, 15.

2 J. D. Loudon and L. B. Young, J. Chem. Soc., 1963, 5496.

3 O. Tsuge, M. Tashiro, K. Kamata, and K. Hokama, Org. Prep. & Proced. Int., 1971, 3, 289.

4 6a (mp 138-139°) was prepared by the reaction of p-methylphenacyl bromide ketazine which was obtained by bromination of p-methylacetophenone ketazine, with benzylamine in the presence of triethylamine.

5 H. Schubert, W. V. Berg, and H. Andrae, Wiss. Z. Martin-Luther Univ., Halle-Wittenberg, Math.-Nat. Reihe, 1962, 11, 603; Chem Abstr., 1964, 60, 14494.

6 Pyridazine 8 did not react with sulfuryl chloride.

7 H. W. Heine and J. Irving, Tetrahedron Letters, 1967, 4767.

8 A. B. Turner, H. W. Heine, J. Irving, and J. B. Bush, Jr., J. Amer. Chem. Soc., 1965, 87, 1050.

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