

A SIMPLE METHOD FOR THE SYNTHESIS OF SOME 1,2-DIAZOCINES

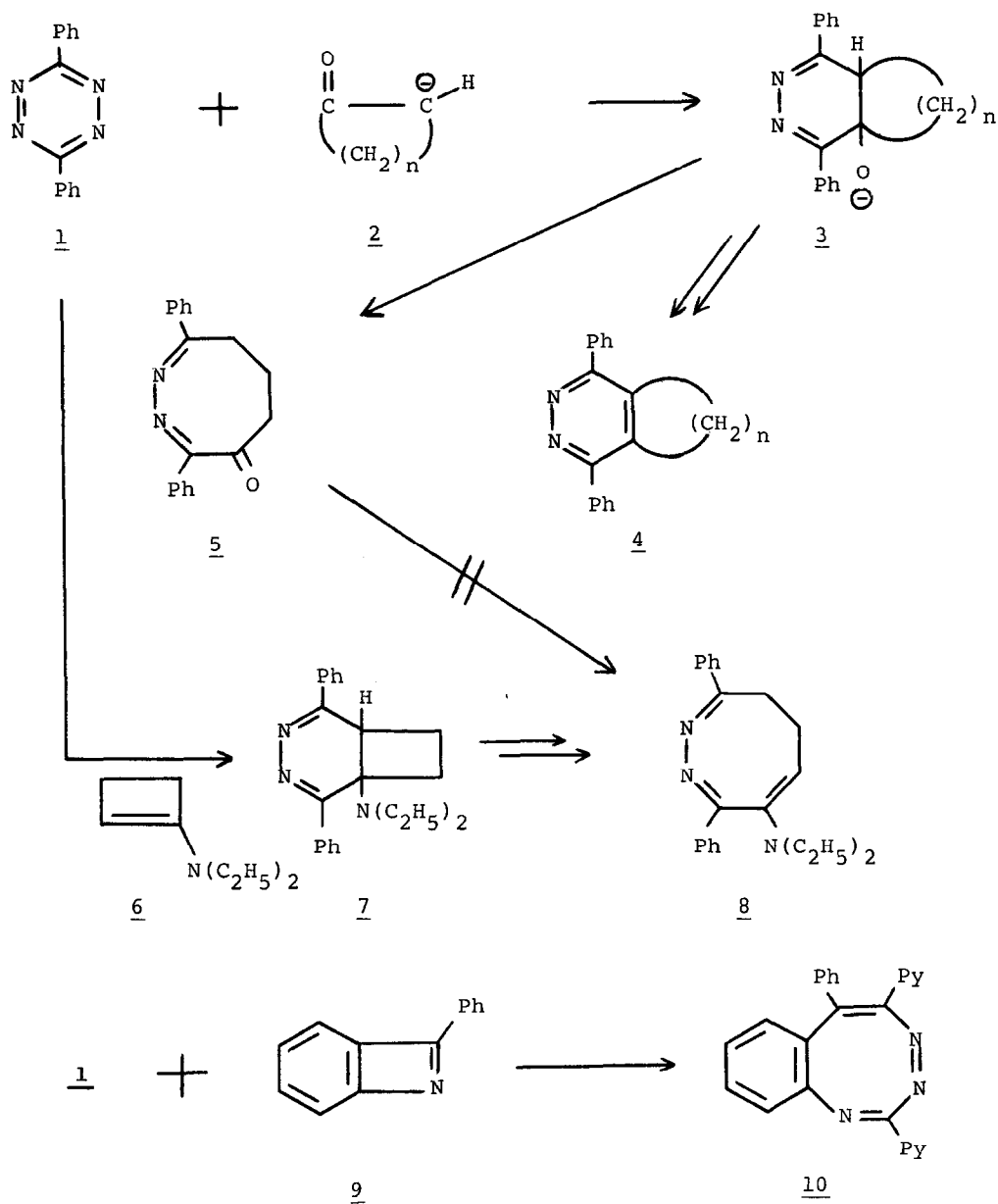
Makhluf J. Haddadin*, Bushra J. Agha, and M. Samer Salka
Department of Chemistry, American University of Beirut, Beirut,
Lebanon.

Summary - Cyclobutanone reacts with diphenyl-1,2,4,5-tetrazine, in alcoholic base and in diethylamine, to give 3,8-diphenyl-6,7-dihydro-1,2-diazocin-4(5H)-one (5) and 4-diethylamino-3,8-diphenyl-6,7-dihydro-1,2-diazocine (8) respectively. With diethylamine the tetrazine yields 3,6-diphenylpyridazine.

The reaction of diphenyl-1,2,4,5-tetrazine (1) with some acyclic and cyclic (2) enolate anions has been shown to give pyridazine derivatives 4¹. We find that this reaction takes a different course in the case of cyclobutanone (2, n = 2) in methanolic base, at the reflux temperature. The reaction proceeded smoothly, as evidenced by the evolution of nitrogen and the gradual discharge of the purple color of tetrazine 1, to yield 3,8-diphenyl-6,7-dihydro-1,2-diazocin-4(5H)-one (5) and not the expected pyridazine 4 (n = 2). The structural evidence for 5 (mp 156-158°C, 40%) is based on its spectroscopic properties: a strong i.r. carbonyl band at 1695 cm⁻¹, and a broad detailed multiplet extending from 1-3.1 δ (6H) and two multiplets centered at 7.3 δ (6H) and 7.7 δ (4H) in the pmr. It is known that enamines react with tetrazine 1 to give pyridazine derivatives², so the above reaction was repeated in refluxing diethylamine as solvent. 4-Diethylamino-3,8-diphenyl-6,7-dihydro-1,2-diazocine (8) was isolated (mp 121°C, 50%; ir: strong enamine band at 1620 cm⁻¹; pmr: 1 δ (t, 6H), 2.7 δ (m, 8H), 4.6 δ (m, 1H), 7.4, 7.9 δ (m, 6H, 4H each)). The reaction involved the formation of enamine 6 which in turn reacted with 1. Reaction of 5 with diethylamine, under similar conditions, failed to give 8 and starting material 5 was recovered. The formation of diazocines 5 and 8, through an electrocyclic ring-opening reaction of intermediates 3 (n = 2) and 7 respectively, seems to be preferred to an elimination reaction which would have resulted in angular strain in the expected

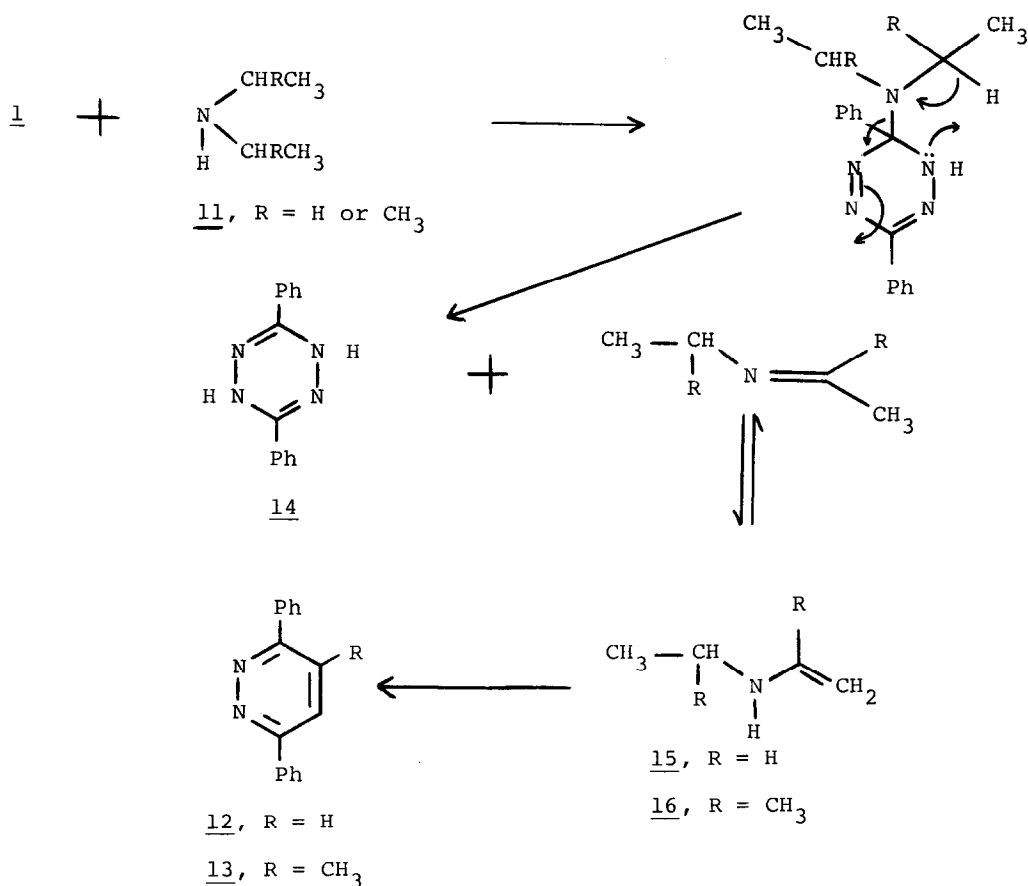
pyridazine 4 ($n = 2$). The reported reaction³ of 2-phenylbenzazete (9) with di-2'-pyridyl-1,2,4,5-tetrazine to give 6-phenyl-2,5-di(2-pyridyl)-1,3,4,-benzotriazocine (10) which involves a ring enlargement to the eight-membered triazocine, is a close analogy to the above described reactions.

Scheme I



The residue from the evaporation of the amine mother liquor of the reaction of 1 + 6 was subjected to TLC which gave, in addition to more of 7, another white solid which was identified as 3,6-diphenylpyridazine¹ (12). Pyridazine 12 was obtained in 15% yield upon reaction of 1 with diethylamine at reflux temperature for a week. Similarly, triethylamine and diisopropylamine reacted with 1 to give 12 and 3,6-diphenyl-4-methylpyridazine¹ (13) respectively. These reactions are slower and give lower yields than the reaction of 1 with diethylamine. The reactions of 1 with amines 11 were monitored by TLC which showed the formation of 3,6-diphenyl-1,4-dihydro-1,2,4,5-tetrazine (14) in traces. It is likely that the latter, upon prolonged heating, is air-oxidized to 1. These results are related to the recent findings of Hunter and Neilson⁴ who showed that lithium diethylamide or LDA reacted with 1 to give pyridazines 12 and 13 respectively. It is proposed that both 12 and 13 result from the reaction of 1 with enamine 15 and 16 (Scheme II).

Scheme II



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REFERENCES AND NOTES

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5. Diazocines 5 and 8 gave satisfactory elemental analyses.

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