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The Reaction of 1,2,4,5-Tetrazines with 2-Phenyl-1-azirine. The Synthesis of 2*H*-1,2,4-Triazepine Derivatives

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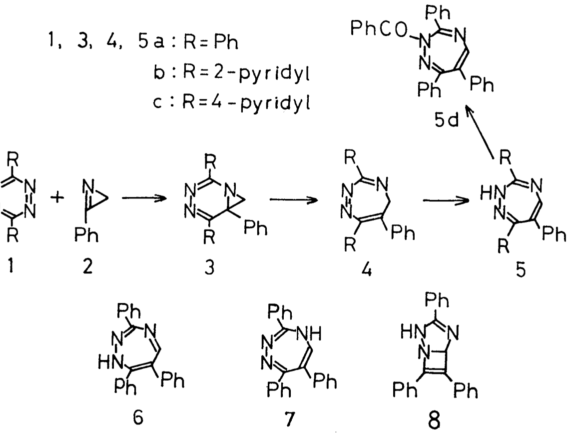
Synopsis. The Reaction of 3,6-disubstituted 1,2,4,5-tetrazines (**1a**—**c**) with 2-phenyl-1-azirine (**2**) afforded 3,7-disubstituted 6-phenyl-2*H*-1,2,4-triazepines (**5a**—**c**) in good yields.

The thermal and photochemical reactions of 1-azirines have been extensively investigated in recent years. Some examples of the Diels-Alder reaction of 1-azirines with cyclic dienes have been reported to yield cycloadducts or their ring-expanded products. The reaction of 1-azirines with cyclopentadienones[1,2] gives strained cycloadducts, which undergo a loss of carbon monooxide to yield azanorcaradienes, followed by ring enlargement to form 3*H*-azepine derivatives. The reaction of the benzo analogue of cyclopentadienones[3] has also been reported to form condensed azepine derivatives. The reaction of diphenylisobenzofuran[4,5] has been reported to yield cycloadducts and to be subjected to subsequent ring expansion to isoquinoline and azanorcarane derivatives.

The reaction of 1,2,4,5-tetrazines with cyclopropenes is a simple and convenient diene synthesis of substituted 5*H*-1,2-diazepines.[6] A similar reaction of 1,2,4,5-tetrazine with 1-azirine suggests a useful method for the synthesis of 1,2,4-triazepines. As an extension of our studies of the synthesis of triazepine derivatives,[7] we examined this reaction. Recently, Anderson *et al.*[8] and Johnson *et al.*[9] have reported that the same cycloaddition reaction gives 2*H*-1,2,4-triazepines. We wish to report our independent results[10] on the sunthesis of 2*H*-1,2,4-triazepines.

A toluene solution of 3,6-diphenyl-1,2,4,5-tetrazine (**1a**) and 2-phenyl-1-azirine (**2**) was refluxed for 26 hr. A product was obtained in a 58% yield as orange needles. The IR spectrum of the product showed a NH absorption at 3320 cm^{-1} and a C=N absorption at 1635 cm^{-1}. The mass spectrum of the product showed the following significant peaks: *m/e* 323 (M$^+$, 41%), 322 (M$^+$−1, 52%), 296 (M$^+$−HCN, 42%), 220 (M$^+$−PhCN, 100%), and 178 (PhC≡CPh$^+$, 19%). From the above data and the elemental analysis, the structure of the product was considered not to be triazanorcaradiene (**3a**) or its [3,3]sigmatropically rearranged product (**4a**), but rather the 2*H*-1,2,4-triazepine derivative (**5a**) or its 1*H* isomer (**6**), which seemed to be the result of the [1,5]sigmatropical shift of the C-5 hydrogen of **4a**. However, it was thought that **6** was more unstable than **5a** because of the sterical crowding of the C-6 and C-7 phenyl groups. Similar examples have been described in the case of the isomerization of 2*H*-azepines to 3*H*-azepines.[1,2] The possibility of the 4*H*-1,2,4-triazepine structure (**7**) is small, because **7** seemed to be the product of the 1,5-hydrogen shift of **6**. The signal of the vinyl proton resonance is probably contained in the region of aromatic protons at δ7.0—8.1 ppm, as is observed in the case of azepines.[1,2] Although 5*H*-1,2-diazepine derivatives were thermally isomerized into diazabicyclo[3,2,0]heptadiene,[6] another possibility of a bicyclic structure (**8**) of the present product was eliminated on the basis of the absence of bridgehead methine proton resonance at *ca.* δ 3.1—4.1 ppm such as observed for the photoisomers of azepines and oxepines.[11] The results cited above indicate that the structure of the product is probably 3,6,7-triphenyl-2*H*-1,2,4-triazepine, **5a**. Other derivatives, **5b** and **5c**, were similarly obtained in good yields.

The reaction **5a** with benzoyl chloride afforded a bezoate (**5d**) in a 35% yield. The IR spectrum of **5d** showed no NH absorption, but it did show a C=O absorption at 1685 cm^{-1}. Although the parent peak at *m/e* 427 was not observed in the mass spectrum, the other peaks were analogous to those of **5a**.



Experimental

All the melting points are uncorrected. The IR, UV, and NMR spectra were measured with a JASCO Model IRA-2 spectrometer, a Shimadzu Model MPS-501 spectrometer, and a Hitachi Model R-20 spectrometer respectively. A Shimadzu Model UM-3B apparatus was used for the elemental analysis.

*3,6,7-Triphenyl-2*H*-1,2,4-triazepine (5a).* A mixture of 0.80 g (3.4 mmol) of 3,6-diphenyl-1,2,4,5-tetrazine[12], **1a**, and 0.90 g (7.7 mmol) of **2**[13] in 60 ml of toluene was refluxed for 26 hr. After the subsequent concentration of the solution *in vacuo* and cooling, the resulting precipitates were filtered to afford 0.65 g (58% yield) of **5a**. It was recrystallized from ethanol to give orange needles; mp 208—210 °C. Found: C, 81.43; H, 5.24%. Calcd for $C_{22}H_{17}N_3$: C, 81.71; H, 5.30%. IR (KBr): 3320, 3050, 3020, 1635 cm^{-1}. UV $\lambda_{\max}^{\mathrm{MeOH}}$ nm (log ε): 234 (4.59), 271 (4.67), 360 sh (3.50). NMR (DMSO-d_6): δ 7.00—8.10 (m, aromatic and olefinic H). Mass *m/e* (%): 323 (41), 322 (52), 297 (10), 296 (42), 295 (18), 221 (18), 220 (100), 219 (20), 191 (17), 189 (17), 178 (19), 165 (17), 118 (8.3), 104 (11), 90 (13), 77 (17).

*3,7-Bis(2-pyridyl)-6-phenyl-2*H-*1,2,4-triazepine (5b).* A mixture of 2.58 g (11 mmol) of 3,6-bis(2-pyridyl)-1,2,4,5-tetrazine,[14] **1b**, and 2.11 g (18 mmol) of **2** in 140 ml of toluene was refluxed for 16 hr. A treatment of the mixture similar to that described for **5a** afforded 2.25 g (63% yield) of **5b**. It was recrystallized from methanol to give orange needles; mp 190—192 °C. Found: C, 73.97; H, 4.62%. Calcd for $C_{20}H_{15}N_5$: C, 73.83; H, 4.65%. IR (KBr): 3330 (NH), 3042, 1640 (C=N) cm^{-1}. UV $\lambda_{\max}^{\mathrm{MeOH}}$ nm (log ε): 232 (4.21), 281 (4.34), 383 sh (3.34). NMR (CDCl$_3$): δ 6.90—8.70 (aromatic and olefinic H).

*3,7-Bis(4-pyridyl)-6-phenyl-2*H-*1,2,4-triazepine (5c).* A mixture of 710 mg (3.0 mmol) of 3,6-bis(4-pyridyl)-1,2,4,5-tetrazine,[15] **1c**, and 420 mg (4.2 mmol) of **2** was refluxed for 20 hr. After the evaporation of the solvent *in vacuo*, the solid residue was washed with a small amount of methanol to afford 812 mg (83% yield) of **5c**. It was recrystallized from methanol to give orange needles; mp 218—219 °C. Found: C, 73.27; H, 4.58%. Calcd for $C_{20}H_{15}N_5$: C, 73.83; H, 4.65%. IR (KBr): 3320 (NH), 3050, 3020, 1626 (C=N) cm^{-1}. UV $\lambda_{\max}^{\mathrm{MeOH}}$ nm (log ε): 232 (4.44), 268 (4.42). 385 sh (3.07).

*2-Benzoyl-3,6,7-triphenyl-2*H-*1,2,4-triazepine (5d).* A solution of 407 mg (1.3 mmol) of **5a** and 247 mg (1.8 mmol) of benzoyl chloride in 10 ml of tetrahydrofuran was refluxed for 21 hr. The solvent was removed *in vacuo* to give an oily residue, which was then dissolved into 10 ml of methanol and crystallized by cooling. The precipitates were filtered to afford 190 mg (35% yield) of **5d**. It was recrystallized from the mixed solvent of benzene and methanol to give white needles; mp 145—146 °C. Found: C, 81.55; H, 4.99%. Calcd for $C_{29}H_{21}ON_3$: C, 81.48; H, 4.95%. IR (KBr): 3040, 3020, 1685, 1595 cm^{-1}. UV $\lambda_{\max}^{\mathrm{MeOH}}$ nm (log ε): 228 (4.58), 282 sh (4.02). NMR (CDCl$_3$): δ 7.20—8.60 (m, aromatic and olefinic H). Mass *m/e* (%): 323 (43), 322 (6.3), 296 (6.3), 295 (8.0), 221 (3.6), 220 (2.7), 219 (3.6), 191 (8.0), 189 (13), 165 (5.4), 105 (100), 77 (72).

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References

1) D. J. Anderson and A. Hassner, *J. Amer. Chem. Soc.*, **93**, 4339 (1971).
2) V. Nair, *J. Org. Chem.*, **37**, 802 (1972).
3) A. Hassner and D. J. Anderson, *J. Amer. Chem. Soc.*, **94**, 8225 (1972).
4) V. Nair, *J. Org. Chem.*, **37**, 2508 (1972).
5) A. Hassner and D. J. Anderson, *ibid.*, **39**, 2031 (1974).
6) M. A. Battiste and T. J. Barton, *Tetrahedron Lett.*, **1967**, 1227.
7) M. Takahashi, S. Onizawa, and T. Satoh, This Bulletin, **47**, 2724 (1974).
8) D. J. Anderson and A. Hassner, *Chem. Commun.*, **1974**, 45.
9) G. C. Johnson and R. H. Levin, *Tetrahedron Lett.*, **1974**, 2303.
10) Presented in part at the 30th Spring Annual Meeting of the Chemical Society of Japan, Osaka, April 1, 1974.
11) L. A. Paquette and J. H. Barret, *J. Amer. Chem. Soc.*, **88**, 1718 (1966).
12) K. Nakahara and M. Ohta, *Nippon Kagaku Zasshi*, **77**, 388 (1956).
13) A. G. Hortmann, D. A. Robertson, and B. K. Gillard, *J. Org. Chem.*, **37**, 322 (1972).
14) W. A. Butte and F. H. Case, *ibid.*, **26**, 4690 (1961).
15) F. Dallacker, *Monatsh. Chem.*, **91**, 294 (1960).