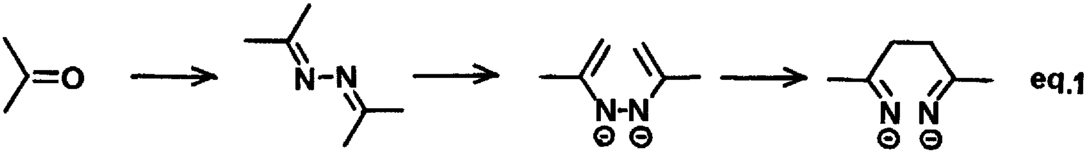
Tetrahedron Letters No. 42, pp 3823 - 3826, 1976. Pergamon Press. Printed in Great Britain.

# A NOVEL REARRANGEMENT OF KETAZINE DIANION: NEW SYNTHETIC ROUTE TO PYRROLES AND TETRAHYDROPYRIDAZINES

Zen-ichi Yoshida*, Toshiro Harada, and Yoshinao Tamaru
Department of Synthetic Chemistry, Kyoto University,
Yoshida, Kyoto 606, Japan

(Received in Japan 3 August 1976; received in UK for publication 6 September 1976)

Ketazine dianion has not been studied intensively since its first generation by F.E.Henoch in 1969.[1] We have been interested in its possibility of rearrangement (eq. 1) which might provide a new synthetic route to a 1,4-diketone equivalent from a simple ketone. It is also interesting because ketazine dianion has two anionic charges on its skeleton participating in rearrangement.



In the present communication, we wish to report a novel rearrangement of aromatic ketazine dianions leading to pyrroles and tetrahydropyridazines.

General reaction procedure is as follows. THF (tetrahydrofuran) solution of a ketazine[2] was added at room temperature into a THF solution of 2.2-3.0 eq. of LDA (lithium diisopropylamide), prepared from diisopropylamine and n-butyllithium (n-hexane solution). Soon the yellow color of a starting ketazine turned to dark reddish brown or dark green.[3] After stirring for 24 hr at room temperature, reaction mixture was quenched with aq. sodium bicarbonate and extracted with ether or dichloromethane.[4] After drying over sodium sulfate and subsequent evaporation of a solvent, products were isolated with recrystallization or columnchromatography.[5]

For example, acetophenone azine (1a) gave 3,6-diphenyl-1,4,5,6-tetrahydropyridazine (6a), mp 158-159.5° (lit.[6] 157-158°). β-Acetonaphthone azine (2a) also yielded 3,6-di-β-naphthyl-1,4,5,6-tetrahydropyridazine[7] (6b), mp 231-232°, ms 336 ($M^+$), $\nu_{KBr}$ 3210 $cm^{-1}$(m), 1604 (m), $\delta^{TMS}_{CDCl_3}$ 2.4 (2H, m), 2.8 (2H, m), 4.4 (1H, m), 6.0 (1H, br), 7.3-8.2 (14H, m). On the other hand, propiophenone azine (1c) gave 3,4-dimethyl-2,5-diphenylpyrrole (5c), mp 138-139° (lit.[8] 136°). p-Methylacetophenone azine (1d) gave 2,5-di-p-tolylpyrrole[7] (5d), mp 196.0-196.5° (lit.[10] 203-204°), ms 247 ($M^+$), $\nu_{KBr}$ 3475 $cm^{-1}$ (s), 1510 (m), 780 (s), $\delta^{TMS}_{CDCl_3}$ 2.36 (6H, s), 6.50 (2H, d, J=2.4 Hz), 7.30 (8H, AA'BB'), 8.50 (1H, br). Table summarizes the products and isolated yields.

The formation of pyrrole or tetrahydropyridazine from ketazine dianion clearly indicated the C-C bond formation to give an intermediate 3 (most likely via (3,3) sigmatropic rearrangement) or 4 selectively depending on the nature of substrates (see Table and eq. 2). Methyl substituted acetophenone azines (eg. 1c and 1d) seem to favor the intermediacy of 3 probably due to carbanion destabilizing effect of alkyl group for 4.

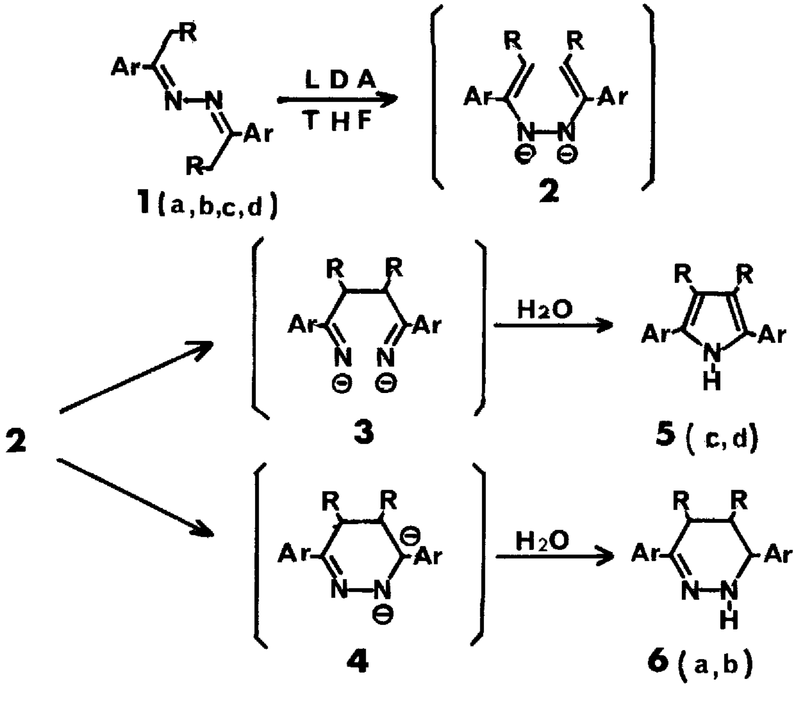
The generation of dianion under these reaction conditions was confirmed by the introduction of one deuterium in each methyl group of acetophenone azine. Thus, acetophenone azine was treated with 2.2 eq. of LDA at room temperature for 0.5 hr and quenched with $D_2O$. Nmr spectrum of the recovered crude sample showed decrease of area intensity of methyl group by two protons and a peak of triplet (J=2.2 Hz). No rearranged product was detected within this reaction time.

Finally it is worth-while to note that this new pyrrol synthesis makes a marked contrast to the Piloty pyrrole synthesis[11] from ketazines under acidic condition.

Extention of this interesting rearrangement to the aliphatic and other substituted aromatic ketazines and elucidation of mechanism of these reactions are now under way.

Table

| Ketazines | Products | Yields (%) | eq. of LDA |
|---|---|---|---|
| 1a (R=H, Ar=Phenyl) | 6a | 34 | 2.2 |
| 1b (R=H, Ar=β-Naphthyl) | 6b | 17 | 3.0 |
| 1c (R=Methyl, Ar=Phenyl) | 5c | 52 | 2.2 |
| 1d (R=H, Ar=p-Tolyl) | 5d | 24 | 3.0 |



a; R=H, Ar=Phenyl

b; R=H, Ar=β-Naphthyl

c; R=Methyl, Ar=Phenyl

d; R=H, Ar=p-Tolyl

## REFERENCES AND NOTES

1. F. E. Henoch, K. G. Hampton, and C. R. Hauser, *J. Amer. Chem. Soc.*, **91**, 676 (1969).
2. Ketazines **1** were prepared in high yield from hydrazine hydrate and ketone in refluxing ethanol in the presence of catalytic amount of acetic acid.
3. Dark reddish brown for **1a** and **1d** and dark green for **1b** and **1c**.
4. For **1b** and **1d** dichloromethane were used.
5. Recrystallization for **6a** and **5c**, columnchromatography for **6b** and **5d**.
6. K. Alder, and H. Niklas, *Liebigs Ann.*, **585**, 81 (1954).
7. These compounds had the correct composition established by microanalysis.
8. R. L. Jones, and C. W. Rees, *J. Chem. Soc.*, (C), 1969, 2249.
9. 2.5-Di-p-tolylpyrrole seems to have different melting point depending on crystal forms, namely 186-187° from ethanol (plates), 196.0-196.5° from benzene-hexane (needles), which gave a satisfactory result for elementary analysis, and 203-204°[10] (recrystallization solvent unknown) (prisms).
10. O. Tsuge, M. Tashiro, K. Hokama, and K. Yamada, *Kogyo Kagaku Zasshi*, **71**, 1667, (1968).
11. O. Piloty, *Chem. Ber.*, **43**, 489 (1910).