pressure until the uptake of hydrogen ceased (720 mL of hydrogen at 20 °C for ca. 2 h). Then the resulting mixture was filtered and evaporated under reduced pressure. The residue was washed with cold water, dried in air, and recrystallized from ethanol to give 4.10 g (91%) of **2**.

General Preparation of Pyrazine *N*-Oxides. The peracetic acid oxidations were accomplished according to the procedure of the literature,[5,6,9,10,15] and the peroxysulfuric acid oxidation followed a procedure by Mixan and Pew.[7] The ratio of the 1- and 4-oxides of **1** in the reaction mixture was determined by GC (5% PEG succinate on Chromosorb WAW DMCS, 1 m glass column at 135 °C), and the separation was achieved by the procedure of Gumprecht and coworkers.[10] As the *N*-oxides of **4** and **5** were contaminated with a considerable amount of the starting pyrazines, the *N*-oxides were purified by column chromatography on silica gel (1 g/10 g). The first elution with benzene gave the starting pyrazine, and the second elution with benzene–chloroform or chloroform provided the *N*-oxide. The separation of the 1- and 4-oxides of **5** was carried out on a Merck PLC plate (silica gel 60 F_{254}) eluted with benzene.

2-Phenylpyrazine 1-Oxide. A solution of 2-chloro-3-phenylpyrazine (**4**) 4-oxide (1.652 g, 8.0 mmol) in 40 mL of ethyl acetate containing triethylamine (0.81 g, 8.0 mmol) was stirred with hydrogen (198 mL at 29 °C) in the presence of 5% palladium on carbon (0.5 g) under atmospheric pressure. The mixture was filtered and evaporated under reduced pressure. The residue was washed with cold water, dried in air, and dissolved in benzene, which was passed through a column of silica gel (30 g). The chromatogram was developed with benzene and successively benzene–chloroform (3:1), to afford **2**, **4**, and the starting *N*-oxide. Further elution with chloroform gave 0.605 g (44%) of 2-phenylpyrazine 1-oxide, which was recrystallized from ethanol to give colorless prisms.

2-Chloro-6-phenylpyrazine 1-Oxide (6). A solution of phenylmagnesium bromide in dry tetrahydrofuran (THF) (2.2 mol/L, 20.0 mL, 0.044 mol) was added dropwise to a stirred solution of 2-chloropyrazine 1-oxide (2.512 g, 0.019 mol) in 80 mL of THF and refluxed for 5 h. The mixture was washed with saturated aqueous ammonium chloride, dried over magnesium sulfate, and evaporated under reduced pressure. The residue (ca. 5 g) was dissolved in benzene and the solution was passed through a column of silica gel (80 g). The first elution with petroleum ether–benzene (1:1) gave biphenyl, and the second elution with benzene afforded 2.934 g of **6**. Further development with chloroform gave 0.080 g (2%) of the *N*-oxide, which was recrystallized from ethanol to give colorless crystals.

Acknowledgment. The authors wish to thank Drs. J. Adachi and T. Nakagawa for their helpful suggestions.

Registry No.—**1**, 109-08-0; **2**, 29460-97-7; **3**, 14508-49-7; **4**, 41270-65-9; **5**, 25844-73-9; **6**, 41270-62-6; peracetic acid, 79-21-0; peroxysulfuric acid, 7722-86-3; 5-phenylpyrazinedicarboxylic acid, 39784-64-0.

References and Notes

(1) N. Sato, *J. Heterocycl. Chem.*, **15**, 665 (1978).
(2) E. Ochiai, "Aromatic Amine Oxides", Elsevier, Amsterdam, 1967.
(3) A. R. Katritzky and J. M. Lagowski, "Chemistry of the Heterocyclic *N*-Oxides", Academic Press, New York, N.Y., 1971, Chapter 2.
(4) G. W. H. Cheeseman and E. S. G. Werstiuk, *Adv. Heterocycl. Chem.*, **14**, 99 (1972).
(5) B. Klein, N. E. Heltman, and M. E. O'Donnell, *J. Org. Chem.*, **28**, 1682 (1963).
(6) S. Okada, A. Kosasayama, T. Konno, and F. Uchimaru, *Chem. Pharm. Bull.*, **19**, 1344 (1971).
(7) C. E. Mixan and R. G. Pew, *J. Org. Chem.*, **42**, 1869 (1977).
(8) Similar observation has emerged in monoperphthalic acid oxidation of 2-methylquinoxaline: E. Hayashi, Ch. Iijima, and Y. Nagasawa, *Yakugaku Zasshi*, **84**, 163 (1964); see also ref 2, p 44.
(9) M. Asai, *Yakugaku Zasshi*, **79**, 1273 (1959); *Chem. Abstr.*, **54**, 4607 (1960).
(10) W. H. Gumprecht, T. E. Beukelman, and R. Paju, *J. Org. Chem.*, **29**, 2477 (1964).
(11) J. K. Landquist and G. T. Stacy, *J. Chem. Soc.*, 2822 (1953).
(12) E. Hayashi and Ch. Iijima, *Yakugaku Zasshi*, **82**, 1093 (1962); see also ref 2, p 45.
(13) IR (KBr) 1-oxide, 1332 and 4-oxide, 1340 cm^{-1}.
(14) H. Shindo, *Chem. Pharm. Bull.*, **8**, 33 (1960).
(15) G. Karmas and P. E. Spoerri, *J. Am. Chem. Soc.*, **78**, 4071 (1956).
(16) S. Sugiura, S. Inoue, Y. Kishi, and T. Goto, *Yakugaku Zasshi*, **89**, 1646 (1969); *Chem. Abstr.*, **72**, 90404 (1970).
(17) P. J. Lont and H. C. van der Plas, *Recl. Trav. Chim. Pays-Bas*, **92**, 449 (1973).
(18) R. P. Duke, R. A. Y. Jones, A. R. Katritzky, J. M. Lagowski, and Yu. Sheinker, *J. Chem. Soc., Perkin Trans. 2*, 668 (1972).
(19) This interference of resonance conjugation is distinctly established by comparision of UV spectra of **4** with that of **5** and **6** (Table IV). Namely, **4** absorbs in the considerable shorter wavelength region than **5** or **6**, while the absorbances of **4** are smaller than those of **5** or **6**.
(20) Similar phenomena have emerged in percarboxylic acid oxidation of 2-methoxy- and 2-isopropyl-3-phenylquinoxaline: E. Hayashi, Ch. Iijima, and Y. Nagasawa, *Yakugaku Zasshi*, **84**, 163 (1964); see also ref 2, pp 46 and 47.
(21) I. F. Halverstadt and W. D. Kumler, *J. Am. Chem. Soc.*, **64**, 2988 (1942).
(22) C. P. Smyth, "Dielectric Behavior and Structure", McGraw-Hill, New York, N.Y., 1955.
(23) S. Yurugi and M. Hieda, *Yakugaku Zasshi*, **92**, 1322 (1972); *Chem. Abstr.*, **78**, 58353 (1973).
(24) S. Yasuda, T. Niwa, and N. Asegawa, Japanese Patent 74 117 480; *Chem. Abstr.*, **82**, 171053 (1975).

Novel Rearrangement of Ketazine Dianion: New Synthetic Route to Pyrrole, Tetrahydropyridazine, and Pyrazole

Yoshinao Tamaru, Toshiro Harada, and Zen-ichi Yoshida*

Department of Synthetic Chemistry, Kyoto University, Yoshida, Kyoto 606, Japan

Received March 6, 1978

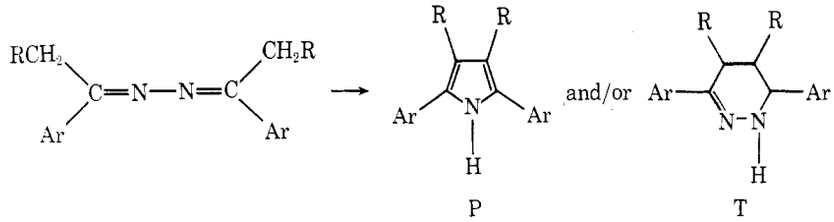
The dianions of alkyl aryl ketazines, generated by treating alkyl aryl ketazines with 2 equiv of lithium diisopropylamide, rearranged selectively to pyrrole, tetrahydropyridazine, or pyrazole depending on the nature of the ketazine. The main factor governing the course of the reaction is the electron density on the carbon termini. Ketazine dianions bearing electron-releasing groups (i.e., propiophenone, butyrophenone, and tetralone azines) on their carbon termini rearrange to pyrroles, while ketazine dianions without substituents (i.e., acetophenone and acetonaphthone azines) and with electron-withdrawing substituents rearrange to tetrahydropyridazines and pyrazoles, respectively.

Coupled with the development of versatile methods for preparing systems suitable for rearrangement, various modifications of the Cope and Claisen rearrangements have been exploited in recent years[1] and the high stereoselectivity has prompted several applications of these rearrangements in the syntheses of natural products.[2] One of the current topics in this field is the hetero-Claisen rearrangement[3] (especially thio-Claisen rearrangement[4]), which generally proceeds highly stereoselectively at relatively low temperatures. Further, interesting anion-assisted oxy-Cope and Claisen rearrangements have been reported; i.e., R. E. Ireland et al.[5] have reported that the rearrangement of the enolate anion of allyl esters proceeds easily at room temperature. The oxy-Cope rearrangement was also accelerated enormously by the metalation of the hydroxyl group.[6]

In this context, we have been interested in the possibility

0022-3263/78/1943-3370$01.00/0

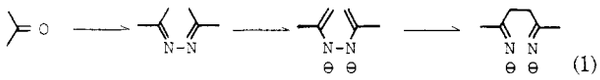
Table I. Reaction of Ketazine Dianion [a]



Entry	Ketazines Ar	Ketazines R	Registry no.	LDA, equiv	Solvent	Products[b] (isolated yield)	Registry no.
1	Ph	CH_3	17745-97-0	2.2	THF	P (52%)	17799-61-0
2	Ph	CH_3		2.2	Ether	P (25%)	
3	Ph	CH_3CH_2	17745-98-1	3.0	THF	P (34%)	66575-47-1
4			66575-46-0	3.0	THF	P (68%)	41403-73-0
5	*p*-Tolyl	H	21399-33-7	3.0	THF	P (24%)	21399-23-5
6	Ph	H	729-43-1	2.2	THF	T (34%)	16080-63-0
7	Ph	H		2.2	Ether	P (30%)	838-40-4
8	β-Naphthyl	H	55043-66-8	3.0	THF	T (17%)	62441-52-5
9	*p*-Anisyl	H	21399-23-5	3.0	THF	P (6%), T (7%)	21399-24-6, 66575-48-2
10	*p*-Anisyl	H		3.0	THF[c]	P (26%)	
11	*p*-Anisyl	H		4.4	THF-HMPA[c]	T (13%)[d]	

[a] Unless otherwise specified, the reaction was performed at room temperature and analyzed after 24 h. [b] The symbols P and T are meant to refer to pyrrole and tetrahydropyridazine, respectively. The other products were mainly constituted of tarry materials, which remained at the starting spot on a silica gel plate (8:1 PhH/EtOAc and/or 2:1 hexane/acetone). [c] Refluxed for 4 h. [d] In addition to tetrahydropyridazine, 1-(1-*p*-anisyl)ethyl-3-*p*-anisylpyrazole (registry no., 66531-47-3) was also isolated in 17% yield.[10]

of the rearrangement of the dianion of a ketazine, which might provide a new synthetic route to a 1,4-diketone or its equivalent from a simple ketone (eq 1).

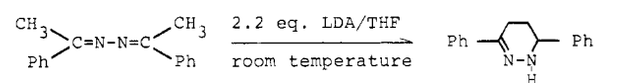


(1)

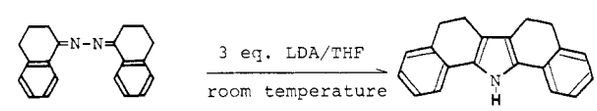
During the course of our study,[7] we have found that the dianions of alkyl aryl ketazines rearrange selectively to pyrroles, tetrahydropyridazines, or pyrazoles at temperatures ranging from room temperature to THF reflux depending on the nature of the ketazines and the reaction solvents. To our knowledge, this is the first reported example of the rearrangement in which a dianion participates. Herein we report the novel Cope-type rearrangement of ketazine dianions and some mechanistic aspects of this rearrangement.

Results and Discussion

Recently the rearrangement of monoanions of dialkyl ketazines to 1,3-disubstituted pyrazoles with one carbon homologation has been reported.[8] Compared with the relative difficulty even in monoanion generation of dialkyl ketazines, the dianions of alkyl aryl ketazines were easily generated by treatment with lithium diisopropylamide (LDA). Ketazine dianions were first generated by F. E. Henoch et al. in 1969,[9] who treated acetophenone azine with 2 equiv of *n*-butyllithium in ether and showed the generation of the dianion by alkylation of both methyl groups. This method was not satisfactory for the generation of dianions of ketazines other than acetophenone azine, owing to the nucleophilic attack of *n*-butyllithium on the C=N carbon of ketazines. The generation of dianion under the reaction conditions employed by us was confirmed by the introduction of one deuterium in each methyl group of acetophenone azine (**1**). Thus, **1** was treated with 2.2 equiv of lithium diisopropylamide (LDA) in THF at room temperature for 30 min and then quenched with degassed D_2O. The NMR spectrum of the recovered crude sample showed a decrease of area intensity of methyl groups by two protons and a change from a singlet to a triplet (J = 2.2 Hz). After allowing this deep reddish brown dianion solution to stir for 24 h at room temperature under argon, the reaction was quenched with degassed water. By thorough examination of the crude reaction mixture by means of column chromatography, 3,6-diphenyl-1,4,5,6-tetrahydropyridazine (**2**) was obtained in 34% yield as the only isolable product (eq 2). On the other hand, pyrrole derivative **4** was obtained by



1 2 (2)



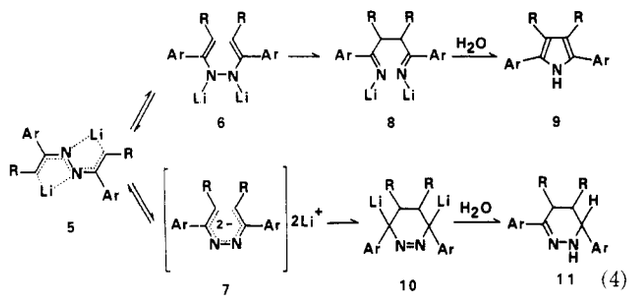
3 4 (3)

the similar treatment of α-tetralone azine (**3**) in 68% isolated yield (eq 3). Thus, **3** was treated with 3.0 equiv of LDA in THF at room temperature. Immediately after the addition of **3** to a THF solution of LDA, the yellow color of **3** turned to deep reddish brown and then to deep green within a few minutes. The completion of the rearrangement was observed within 1 h by TLC monitoring. In a similar fashion, seven alkyl aryl ketazines were examined and found to give pyrrole and/or tetrahydropyridazine depending on the nature of the ketazines and solvent systems. The results are summarized in Table I.

Generally, the reactions to give pyrroles proceeded faster than those to give tetrahydropyridazines. Propiophenone and butyrophenone azines (entires 1 and 3), like tetralone azine, rearranged completely to pyrroles within 1 or 2 h at room temperature, while the reactions of acetophenone and β-acetonaphthone azines (entries 6 and 8) were sluggish and even after 24 h a small amount of the starting azine remained.

Except for the case of *p*-methoxyacetophenone azine (entires 9 and 11[10]), the rearrangement was selective to give pyrrole or tetrahydropyridazine.

It seems worthwhile to consider some aspects of the reaction mechanism in order to understand the selectivity of this rearrangement. By analogy with the results of the x-ray analysis of hexatriene dianion[11] and taking into consideration the large coordination ability of a nitrogen atom to a metal cation, the structure of the most stable form of these dianions may be depicted as in **5** (eq 4), where lithium is coordinated by nitrogen to form a five-membered cyclic structure. On the bases of the selectivity and the large differences in reactivities between the two pathways to give pyrrole **9** and tetrahydropyridazine **11**, two different kinds of intermediates (**6** and **7**) which equilibrate with **5** seem to contribute to these rearrangements.

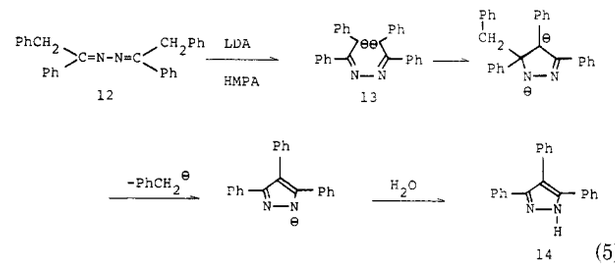


(4)

These intermediates **6** and **7** are two extremes, with the anionic charges localized on nitrogen atoms to which lithium ions are bound tightly in the former and the anionic charges delocalized over the system in the latter. In going from acetophenone azine to α-tetralone azine, the intermediate **6** might become more favorable than **7** due to the destabilization of the carbanion by introduction of an alkyl group (and to a lesser extent by the substitution of electron-releasing groups on the benzene ring; *p*-tolyl and *p*-anisyl). The intermediate **6** could be expected to rearrange to **8**, which is the direct precursor of pyrrole,[12] in a [3.3] sigmatropic fashion rapidly and exothermally owing to the large difference of the heat of formation[13] of these two intermediates and the separation of the vicinal anionic charges to 1,6 positions. The mechanism leading to tetrahydropyridazine is not clear. It may involve a stepwise cyclization mechanism or an 8π-electrocyclic reaction. This reaction could be expected to be slow owing to an electrostatic repulsion between the bond-forming carbon termini bearing anionic charges.

The reaction scheme proposed above is in good accord with the solvent effect observed for the reaction of acetophenone azine. That is, although propiophenone azine gave pyrrole selectively both in ether and THF (entries 1 and 2), acetophenone azine gave tetrahydropyridazine in THF, while it rearranged to pyrrole selectively in ether (entries 6 and 7). This intriguing contrast may be explained on the basis of the difference of solvation ability between these two solvents.[14a] In going to ether with its smaller solvation ability, the intermediate **6** with less ionic character becomes more favorable than **7** and results in pyrrole formation. Analogously, the solvent dependence of product distribution may be explained in the case of *p*-methoxyacetophenone azine (entries 10 and 11[10]). Furthermore, the temperature dependence on the product selectivity observed in entries 9 and 10 supports this rationale. That is, while at room temperature *p*-methoxyacetophenone azine rearranges to a 1:1 mixture of pyrrole **9** and tetrahydropyridazine **11**, at THF reflux temperature, owing to desolvation,[14] the equilibrium becomes favorable to an intermediate **6**, tightly bound by cations, and gives pyrrole **9** selectively.

As one extreme, where carbanions were stabilized by phenyl substituents, benzyl phenyl ketazine (**12**) was treated with 2 equiv of LDA in THF at room temperature for 24 h and in this case the complete recovery of **12** was observed. Under forcing conditions, **12** took a completely different course of reaction to provide 3,4,5-triphenylpyrazole (**14**; eq 5). That is, dianion



(5)

13 was heated at 65 °C for 1 h in THF–HMPA (3:1) to give **14** in 70% isolated yield (based on **12** consumed; 65% conversion).

For the formation of **14**, stepwise ionic cyclization, probably initiated first by the attack of benzylic carbanion on the C=N carbon followed by elimination of benzyl anion as shown in eq 5, seems to be most probable.

In conclusion, ketazine dianions rearrange selectively to one of three kinds of products, pyrrole, tetrahydropyridazine, and pyrazole, in a strikingly different reactivity. The main factor controlling this reactivity and selectivity seems to be the electron density on the carbon termini. Ketazine dianions bearing electron-releasing groups on carbon termini rearrange to pyrroles, whereas those without substituents (i.e., acetophenone and acetonaphthone azines) or with electron-withdrawing substituents rearrange sluggishly to tetrahydropyridazines or pyrazoles, respectively.

The pyrrole synthesis reported here is a contrast to the Piloty pyrrole synthesis,[15] the acid-catalyzed pyrrole synthesis from ketazine at high temperatures ($ZnCl_2$ or HCl at 180 to 220 °C), while it shows a similarity to the Fischer indole synthesis[16] in a mechanistic point of view.[17]

Experimental Section

Melting points were uncorrected. The elemental analyses were performed at the Microanalysis Center of Kyoto University. Infrared spectra were measured with a Hitachi Model EPI-G3 grating spectrophotometer, and ^1H NMR spectra were recorded with either a Varian HA 100 or a Jeol JNM-PMX 60 spectrometer. Mass spectra were measured with a Hitachi Model RMU 6C spectrometer.

Ketazines. Ketazines were prepared in quantitative yields from the corresponding ketones and hydrazine hydrate in refluxing ethanol in the presence of a catalytic amount of acetic acid. They were purified by repeated recrystallization.

Solvents. THF and diethyl ether were dried over sodium–benzophenone, and diisopropylamine and hexamethylphosphoric triamide were dried over calcium hydride and distilled under argon prior to use.

3,4-Dimethyl-2,5-diphenylpyrrole. Under argon, a solution of diisopropylamine (3.3 mmol) in dry THF (10 mL) was treated with *n*-butyllithium (15% hexane solution; 3.3 mmol) at 0 °C, and after 10 min propiophenone azine (1.5 mmol) dissolved in THF (5 mL) was added to the solution of lithium diisopropylamide in THF at room temperature. Immediately, the yellow color of the starting ketazine turned to deep reddish brown, and gradually to deep green within a few minutes. After stirring for 24 h at room temperature, the reaction mixture was quenched with degassed water and extracted with ether. After drying over sodium sulfate and evaporation of the solvent, 3,4-dimethyl-2,5-diphenylpyrrole was isolated in 52% yield by silica gel column chromatography using benzene as an eluent: mp 138–139 °C (lit.[18] mp 136 °C); MS *m/e* 247 (M^+, 100%), 246 (48); IR (KBr) ν_{max} 3410 (s), 1603 (s), 1495 (s), 765 (s), 702 (s), 694 (s) cm^{-1}; NMR ($CDCl_3$; Me_4Si) δ 2.13 (6 H, s), 7.43 (10 H, aromatic protons), 7.9 (1 H, br).

3,4-Diethyl-2,5-diphenylpyrrole. *n*-Butyrophenone azine was reacted with 3.0 equiv of LDA in THF at room temperature for 24 h. After the usual workup and subsequent purification by column chromatography (silica gel, benzene elution), 3,4-diethyl-2,5-diphenylpyrrole was isolated in 34% yield: mp 81–85 °C; MS *m/e* 275

(M^+, 98%), 265 (100); IR (KBr) ν_{max} 3450 (m), 1607 (m), 770 (s), 702 (s) cm^{-1}; NMR ($CDCl_3$; Me_4Si) δ 1.22 (6 H, t, J = 7.0 Hz), 2.68 (4 H, q, J = 7.0 Hz), 7.1–7.6 (10 H, aromatic protons), 7.93 (1 H, br). Anal. Calcd for $C_{20}H_{21}N$: C, 87.23; H, 7.69. Found: C, 86.93; H, 7.63.

Dibenzo[*a,i*]-3,4,5,6-tetrahydrocarbazole (4). α-Tetralone azine was reacted in a similar way to propiophenone azine to give **4** in 68% isolated yield after purification by silica gel column chromatography with benzene elution: mp 162–163 °C; MS *m/e* 271 (M^+, 100%); IR (KBr) ν_{max} 3455 (m), 1613 (s), 760 (s) cm^{-1}; NMR ($CDCl_3$; Me_4Si) δ 2.7 (8 H, m), 7.2 (8 H, aromatic protons), 8.35 (1 H, br). Anal. Calcd for $C_{20}H_{17}N$: C, 88.53; H, 6.32; N, 5.16. Found: C, 88.69; H, 6.18; N, 5.13.

2,4-Di-*p*-tolypyrrole. *p*-Methylacetophenone azine was reacted and worked up in a similar way to propiophenone azine to give 2,4-di-*p*-tolylpyrrole in 24% isolated yield after purification by silica gel column chromatography with hexane–acetone gradient elution: mp 196.0–196.5 °C (lit.[19] mp 203–204 °C); MS *m/e* 247 (M^+); IR (KBr) ν_{max} 3475 (s), 1510 (m), 780 (s) cm^{-1}; NMR ($CDCl_3$; Me_4Si) δ 2.36 (6 H, s), 6.50 (2 H, d, J = 2.4 Hz), 7.30 (8 H, AA'BB'), 8.50 (1 H, br). Anal. Calcd for $C_{18}H_{17}N$: C, 87.40; H, 6.93; N, 5.66. Found: C, 87.63; H, 6.95; N, 5.42.

3,6-Diphenyl-1,4,5,6-tetrahydropyridazine (2). Acetophenone azine (1.5 mmol) was treated with LDA (3.3 mmol) in THF (15 mL) for 24 h at room temperature. In this case, the first formed deep reddish brown color of the reaction mixture did not change to deep green as in the case of propiophenone azine. After the usual workup, a 34% yield of 3,6-diphenyl-1,4,5,6-tetrahydropyridazine (**2**) was isolated by recrystallization from benzene–hexane: mp 158.0–159.5 °C (lit.[20] mp 157–158 °C); MS *m/e* 236 (M^+, 100%), 159 (32), 132 (57); IR (KBr) ν_{max} 3300 (m), 1596 (m), 1498 (s), 753 (s), 692 (s) cm^{-1}; NMR ($CDCl_3$; Me_4Si) δ 2.2 (2 H, m), 2.7 (2 H, m), 4.2 (1 H, m), 5.9 (1 H, br), 7.3–7.7 (10 H, aromatic protons).

3,6-Di-β-naphthyl-1,4,5,6-tetrahydropyridazine. β-Acetonaphthone azine was reacted in a similar way to acetophenone azine. Recrystallization of the reaction mixture from dichloromethane–benzene–hexane gave 3,6-di-β-naphthyl-1,4,5,6-tetrahydropyridazine in 17% yield: mp 231–232 °C; MS *m/e* 336 (M^+); IR (KBr) ν_{max} 3210 (m), 1604 (m) cm^{-1}; NMR($CDCl_3$; Me_4Si) δ 2.4 (2 H, m), 2.8 (2 H, m), 4.4 (1 H, m), 6.0 (1 H, br), 7.3–8.2 (14 H, aromatic protons). Anal. Calcd for $C_{24}H_{20}N_2$: C, 85.68; H, 5.99; N, 8.33. Found: C, 85.64; H, 5.78; N, 8.58.

Rearrangement of *p*-Methoxyacetophenone Azine in THF. To *p*-methoxyacetophenone azine (1.5 mmol) was added a solution of LDA (4.5 mmol) in THF (15 mL) at room temperature. Gradually the dark reddish brown homogeneous reaction mixture became heterogeneous, owing to the precipitation of solid. After stirring for 24 h at room temperature, the reaction mixture was quenched with degassed water and extracted with dichloromethane. The reaction mixture was subjected to column chromatography (silica gel, with benzene–ethyl acetate gradient elution) to give 6% of 2,5-di-*p*-anisylpyrrole and 7% of 3,6-di-*p*-anisyl-1,4,5,6-tetrahydropyridazine. 2,5-Di-*p*-anisylpyrrole: mp 228–229 °C (lit.[19] mp 232 °C); MS *m/e* 279 (M^+, 100%), 264 (94); IR (KBr) ν_{max} 3475 (m), 2850 (w), 1505 (s), 840 (s) cm^{-1}; NMR (acetone-d_6) δ 3.81 (6 H, s), 6.46 (2 H, d, J = 2.0 Hz), 7.32 (8 H, AA'BB').

3,6-Di-*p*-anisyl-1,4,5,6-tetrahydropyridazine: mp 164–165 °C; MS *m/e* 296 (M^+); IR (KBr) ν_{max} 3390 (m), 1615 (m), 1510 (s), 828 (s) cm^{-1}; NMR ($CDCl_3$; Me_4Si) δ 2.2 (2 H, m), 2.66 (2 H, m), 3.80 (6 H, s), 4.1 (1 H, m), 5.68 (1 H, br), 6.9–7.6 (8 H, aromatic protons). Anal. Calcd for $C_{18}H_{20}N_2O_2$: C, 72.95; H, 6.80; O, 10.80; N, 9.45. Found: C, 72.66; H, 6.84; O, 11.07; N, 9.43.

To *p*-methoxyacetophenone azine (1.5 mmol) was added a solution of LDA (4.5 mmol) in THF (15 mL) at room temperature. Then the reaction mixture was refluxed for 3 h. After the usual workup, a 26% yield of 2,5-di-*p*-anisylpyrrole was isolated by silica gel column chromatography using benzene–ethyl acetate as an eluent. In this reaction the concomitant formation of tetrahydropyridazine was not observed by TLC examination of the reaction mixture.

Rearrangement of *p*-Methoxyacetophenone Azine in THF–HMPA. To a solution of LDA (4.4 mmol) in THF (10 mL)–HMPA (0.7 mL) was added a THF (5 mL) solution of *p*-methoxyacetophenone azine (1 mmol) at room temperature. Then the reaction mixture was refluxed for 4 h. After the usual workup, 13% of 3,6-di-*p*-anisyl-1,4,5,6-tetrahydropyridazine and 17% of 1-(1-*p*-anisyl)-ethyl-3-*p*-anisylpyrazole were isolated by means of column chromatography and subsequent recrystallization from ethanol. 1-(1-*p*-Anisyl)ethyl-3-*p*-anisylpyrazole (oil): MS *m/e* 281 ($M^+ - CH_3O$, <1%), 250 (22), 135 (100); IR (neat) ν_{max} 2440 (w), 1618 (s), 840 (s) cm^{-1}; NMR ($CDCl_3$; Me_4Si) δ 1.87 (3 H, d, J = 10.2 Hz), 3.75 (3 H, s), 5.50 (1 H, q, J = 10.2 Hz), 6.43 (1 H, d, J = 2.2 Hz), 7.27 (1 H, d, J = 2.2 Hz), 6.8–7.8 (8 H, m). Anal. Calcd for $C_{19}H_{20}N_2O_2$: C, 74.00; H, 6.54. Found: C, 74.00; H, 6.70.

Rearrangement of Acetophenone Azine in Ether. To acetophenone azine (1 mmol) was added an ether solution (15 mL) of LDA (2.2 mmol) at room temperature. The heterogeneous reaction mixture was stirred for 24 h at room temperature. After the usual workup and purification by silica gel column chromatography (using benzene as an eluent), 2,5-diphenylpyrrole was obtained in 30% of the isolated yield (based on the consumed ketazine; 65% conversion): mp 142–143 °C (lit.[19] mp 143 °C); MS *m/e* 219 (M^+); IR (KBr) ν_{max} 3460 (m), 1610 (s), 1490 (s), 755 (s), 695 (s) cm^{-1}; NMR (CCl_4; Me_4Si) δ 6.45 (2 H, d, J = 3.0 Hz), 7.0–7.7 (10 H, m), 7.85 (1 H, br s).

3,4,5-Triphenylpyrazole (14). Into a solution of LDA (9 mmol) in 20 mL of THF was added a solution of benzyl phenyl ketone azine (**12**) in 10 mL of THF and 10 mL of HMPA at room temperature, and then the reaction mixture was heated at 65 °C for 1 h. During the reaction, the color changed from deep blue to deep green. Degassed water was added, and the reaction mixture was extracted with benzene. Evaporation of solvent and subsequent recrystallization from acetone gave **14** as colorless crystals in 70% isolated yield (based on ketazine consumed; 65% conversion): mp 259–260 °C (lit.[21] mp 295–261 °C); IR (KBr) ν_{max} 3220 (vs), 1490 (m), 1440 (m), 1150 (m), 980 (s), 770 (s), 720 (s), 690 (s) cm^{-1}; NMR (Me_2SO-d_6) δ 7.7 (m, 15 H), 13.5 (br s, 1 H). Anal. Calcd for $C_{21}H_{16}N_2$: C, 85.11; H, 5.44; N, 9.45. Found: C, 85.39; H, 5.59; N, 9.51.

Deuterium Oxide Quenching of Acetophenone Azine Dianion. A 1.5-mmol amount of acetophenone azine dianion was treated with 3.3 mmol of LDA in THF at room temperature for 0.5 h. Then the reaction mixture was poured into ether–D_2O saturated with NaCl and degassed and cooled at 0 °C. The organic layer was separated and dryed over sodium sulfate. After subsequent evaporation of the solvent, starting acetophenone azine was recovered. The NMR spectrum of the recovered crude sample showed a decrease of area intensity of the methyl group by two protons and a triplet (J = 2.2 Hz). Rearranged product was not detected within this reaction time. The mass spectrum also supports the introduction of two deuteriums: MS *m/e* 239 (M + 1, 8.0%), 238 (M^+, 37), 237 (M − 1, 25), 236 (M − 2, 12), 77 (100). Cf. acetophenone azine: MS *m/e* 237 (M + 1, 9.4%), 236 (M^+, 53), 235 (M − 1, 12), 221 (100).

Acknowledgment. We are grateful to Professor M. Tashiro of Kyushu University for providing us with an authentic sample of 2,5-di-*p*-tolylpyrrole.

Registry No.—**12**, 30506-03-7; **14**, 18076-30-7.

References and Notes

(1) S. J. Rhoads and N. R.Raulins, *Org. React.* **22,** Chapter 1 (1975), and references cited therein.
(2) (a) W. S. Johnson, T. J. Brocksom, P. Loew, D. H. Reich, L. Werthemann, R. A. Arnold, T.-T. Li, and D. J. Faulkner, *J. Am. Chem. Soc.*, **92,** 4463 (1970); (b) W. S. Johnson, L. Werthemann, W. R. Bartlett, T. J. Brocksom, T.-T. Li, D. J. Faulkner, and M. R. Petersen, *ibid.*, **92,** 741 (1970); (c) W. L. Scott and D. A. Evans, *ibid.*, **94,** 4779 (1972); (d) R. E. Ireland, R. H. Mueller, and A. K. Willard, *J. Org. Chem.*, **41,** 986 (1976); (e) G. Stork and S. Raucher, *J. Am. Chem. Soc.*, **98,** 1583 (1976); (f) F. E. Ziegler, *Acc. Chem. Res.*, **10,** 227 (1977).
(3) G. B. Bennett, *Synthesis*, 589 (1977).
(4) (a) H. Takahashi, K. Oshima, H. Yamamoto, and H. Nozaki, *J. Am. Chem. Soc.*, **95,** 5803 (1973); (b) T. Nakai, H. Shiono, and M. Okawara, *Tetrahedron Lett.*, 3625 (1974); (c) R. Gompper and W-R. Ulrick, *Angew, Chem.*, **88,** 300 (1976); (d) S. Takano, M. Hirama, T. Araki, and K. Ogasawara, *J. Am. Chem. Soc.*, **98,** 7084 (1976).
(5) R. E. Ireland and R. H. Mueller, *J. Am. Chem. Soc.*, **94,** 5897 (1972).
(6) D. A. Evans and A. M. Golob, *J. Am. Chem. Soc.*, **97,** 4765 (1975).
(7) For a preliminary communication, see Z. Yoshida, T. Harada, and Y. Tamaru, *Tetrahedron Lett.*, 3823 (1976).
(8) Y. Tamaru, T. Harada, and Z. Yoshida, *Tetrahedron Lett.*, 4323 (1977); *Chem. Lett.*, 263 (1978).
(9) F. E. Henoch, K. G. Hampton, and C. R. Hauser, *J. Am. Chem. Soc.*, **91,** 676 (1969).
(10) Under the same conditions, except for the equivalency of LDA, i.e., with 2.2 equiv of LDA, only 1-(1-*p*-anisyl)ethyl-3-*p*-anisylpyrazole was obtained as the only isolable product in 40% isolated yield; see ref 8.
(11) S. K. Arora, R. B. Bates, W. A. Beavers, and R. S. Cutler, *J. Am. Chem. Soc.*, **97,** 6271 (1975).
(12) A. Gossuaer, "Die Chemie der Pyrrole", Springer-Verlag, Berlin, Heidelberg, and New York, 1974.
(13) By neglecting the effect of anion charges, the heat of formation of the framework participating in the rearrangement was calculated taking the values from W. G. Palmer, "Valency", 2nd ed, Cambridge University Press, New York, N.Y., 1959, p 125, as follows: H_f^0 (25 °C) of **6** = −468 kcal/mol and H_f^0 (25 °C) of **8** = −533 kcal/mol.
(14) (a) D. H. O'Brien, C. R. Russell, and A. J. Hart, *J. Am. Chem. Soc.*, **98,** 7427 (1976), and references cited therein; (b) G. Levin, B. Lungren, M. Mohammad, and M. Szwarc, *ibid.*, **98,** 1461 (1976).

(15) O. Piloty, *Chem. Ber.*, **43**, 489 (1910).
(16) (a) E. Fischer and O. Hess, *Chem. Ber.*, **17**, 559 (1884); (b) M. Nakazaki and K. Yamamoto, *J. Org. Chem.*, **41**, 1877 (1976).
(17) (a) R. Robinson and G. M. Robinson, *J. Chem. Soc.*, 113, 639 (1918); (b) R. B.Carlin and E. E. Fischer, *J. Am. Chem. Soc.*, **70**, 3421 (1948); (c) R. B. Carlin, *ibid.*, **74**, 1077 (1952).
(18) R. L. Jones and C. W. Rees, *J. Chem. Soc. C*, 2249 (1969).
(19) O. Tsuge, M. Tashiro, K. Hokama, and K. Yamada, *Kogyo Kagaku Zasshi*, **71**, 1667 (1968).
(20) K. Alder and H. Niklas, *Justus Liebigs Ann. Chem.*, **585**, 81 (1954).
(21) L. A. Carpino, L. V. McAdams, III, R. H. Ryndbrandt, and J. W. Spiewak, *J. Am. Chem. Soc.*, **93**, 476 (1971).

3*H*-1,2-Benzodithiole Oxides: Studies Directed toward the Generation of *o*-Thiobenzoquinone Methide and Benzo[*b*]thiete

Alfred G. Hortmann,* Alan J. Aron, and Ajit K. Bhattacharya

Department of Chemistry, Washington University, St. Louis, Missouri 63130

Received January 30, 1978

o-Thiobenzoquinone methide (**1**) has been generated by photodesulfonylation of 3*H*-1,2-benzodithiole 2,2-dioxide (**3**) in benzene and was trapped with added *N*-phenylmaleimide as the [4 + 2] (or [8 + 2]) adduct (**4**). The 2,2-dioxide **3** was prepared in ~10% yield by either oxidation of 3*H*-1,2-benzodithiole (**5**) or oxidative cyclization of 2-mercaptomethylthiophenol (**7**) with *m*-chloroperoxybenzoic acid (MCPBA). Peroxyacetic acid oxidation of **7** also afforded **3** in low yield, along with the monoxides **3a** and **6a**; under somewhat more vigorous conditions **7** gave 3*H*-1,2-benzodithiol-3-one 1-oxide (**8**) in 29% yield. The 1-oxide **8** was also isolated (15% yield) along with a 65% yield of the corresponding 1,1-dioxide **9** from a direct oxidation of 3*H*-1,2-benzodithiol-3-one with MCPBA. Mild periodate oxidation of **5** at 24 °C cleanly afforded the monoxides **3a** and **6a** in a 1:1 ratio; brief treatment of this difficultly separable mixture with aqueous Na_2CO_3 led to complete disproportionation of **3a** to **3** and **5** under conditions which left **6a** unaffected and allowed its isolation and further oxidation with periodate (65 °C) to yield pure 3*H*-1,2-benzodithiole 1,1-dioxide (**6**). Alternatively, a 1:1 mixture of **3** and **6** could be obtained directly from **5** by vigorous periodate oxidation run at 70 °C and catalyzed by I_2. Irradiation of pure **6** under conditions used for the photolysis of **3**, as well as in the presence of benzophenone as a sensitizer, did not yield any of the desired benzo[*b*]thiete (**2**), nor was the formation of any adduct (**4**) of **1** (assuming that a conversion of **2** to **1** might occur) with added *N*-phenylmaleimide observed.

The original objectives of the research described in this report were the generation of *o*-thiobenzoquinone methide (**1**)[2] and a determination of whether or not **1** exists in equilibrium with its valence tautomer, benzothiete (**2**).[3] In pursuing these goals we reasoned that photochemically or thermally induced extrusion of SO_2 from 3*H*-1,2-benzodithiole 2,2-dioxide (**3**) might yield **1** and/or **2** directly[4] and that **1** would be sufficiently reactive toward dienophiles to undergo [4 + 2] (or [8 + 2]) cycloaddition reactions to yield stable adducts (e.g., **4** via condensation with *N*-phenylmaleimide[2]), thereby demonstrating its potential use in synthesis[5] as well as providing proof of its generation in solution. The 2,2-dioxide **3** might, in turn, be readily accessible by regioselective peroxyacid oxidation of the 2-sulfur atom (i.e., the presumably more electron-rich alkyl-substituted sulfur) of 3*H*-1,2-benzodithiole (**5**), an assumption that we initially felt was warranted by the results of a model study of the *m*-chloroperoxybenzoic acid oxidation of benzyl and ethyl phenyl disulfides.[6] In the event that nonregioselectivity proved to be the case in the oxidation of **5**,[7,8] obtention of **6** (and/or **6a**) would allow us, in addition, to test a direct and previously unexplored route to the parent benzothiete system (**2**) via extrusion of SO_2 from **6**.[9]

Results and Discussion

3*H*-1,2-Benzodithiole (**5**) was first prepared by slow addition of a 2% solution of 2-mercaptomethylthiophenol (**7**) to a 7.5% solution of ferric chloride in acetic acid–methanol at 10 °C as described by Lüttringhaus and Hägele.[10] Attempts to improve on their reported 40% yield of **5** led us to develop a modified procedure (see Experimental Section) whereby **5** was eventually obtainable in 81% yield (ca. 85% pure by ^1H NMR assay) by slow addition of a 1% alcoholic solution of **7** to a vigorously stirred 2% solution of cupric chloride dihydrate in either ethanol or methanol at 24 °C in the presence of air.[11] As had been observed previously,[10] **5** was found to deteriorate rapidly in the absence of solvent, and efforts to purify crude **5** by distillation in vacuo or by column chromatography (SiO_2; Al_2O_3) led to intractable decomposition products. Consequently, it was necessary to use **5** directly as obtained (after extraction) from the $CuCl_2$-catalyzed oxidation of **7** or to store **5** at −10 °C as a 2–3% solution in methylene chloride or diethyl ether until needed.

Preliminary studies on the oxidation of **5** with 2 mol equiv of *m*-chloroperoxybenzoic acid (MCPBA) in CH_2Cl_2 at 25 °C afforded small amounts (<10% yield) of a crystalline solid which analyzed correctly for $C_7H_6O_2S_2$. The product exhibited strong infrared bands at 1150 and 1335 cm^{-1} (–S–SO_2–) and ^1H NMR signals at δ 4.70 (s, 2) and 7.37 (broad s, 4). The data led to a tentative assignment of either **3** or **6** as possible structures for the new compound. A distinction in favor of structure **3** for the product was allowed by the observation that the ^{13}C NMR signal due to the $^{13}CH_2$ group in the new thiolsulfonate appears at 64.8 ppm downfield from Me_4Si, a typical value for ^{13}C in the $-SSO_2CH_2Ph$ moiety.[12]

Closer examination of the ^1H NMR spectrum of the crude product mixture derived from the oxidation of **5** with MCPBA indicated that two other products (which later proved to be **3a** and **6a**) were also formed in low yield. However, no improvement beyond the original optimum yield (ca. 10%) of isolable **3** could be effected despite considerable efforts in varying the reaction conditions.

A literature report[13] describing the peroxyacetic acid oxidation of the mercaptans RSH, where R = cyclopentyl and cyclohexyl, to yield the corresponding thiolsulfonates RSO_2SR in 34 and 61% yields led us to attempt a direct peroxyacid-mediated oxidative cyclization of 2-mercaptomethylthiophenol (**7**) to **3** and/or **6**. Indeed, upon treatment of **7** with 3 mol equiv of MCPBA in CH_2Cl_2 at 0 °C, an 11% yield of **3** was obtained. Similarly, treatment of **7** with excess commercial 40% peroxyacetic acid in $CHCl_3$ at 0–5 °C for 1 h afforded what later proved to be (by ^1H NMR assay) a 3:6:7 mixture of

0022-3263/78/1943-3374$01.00/0