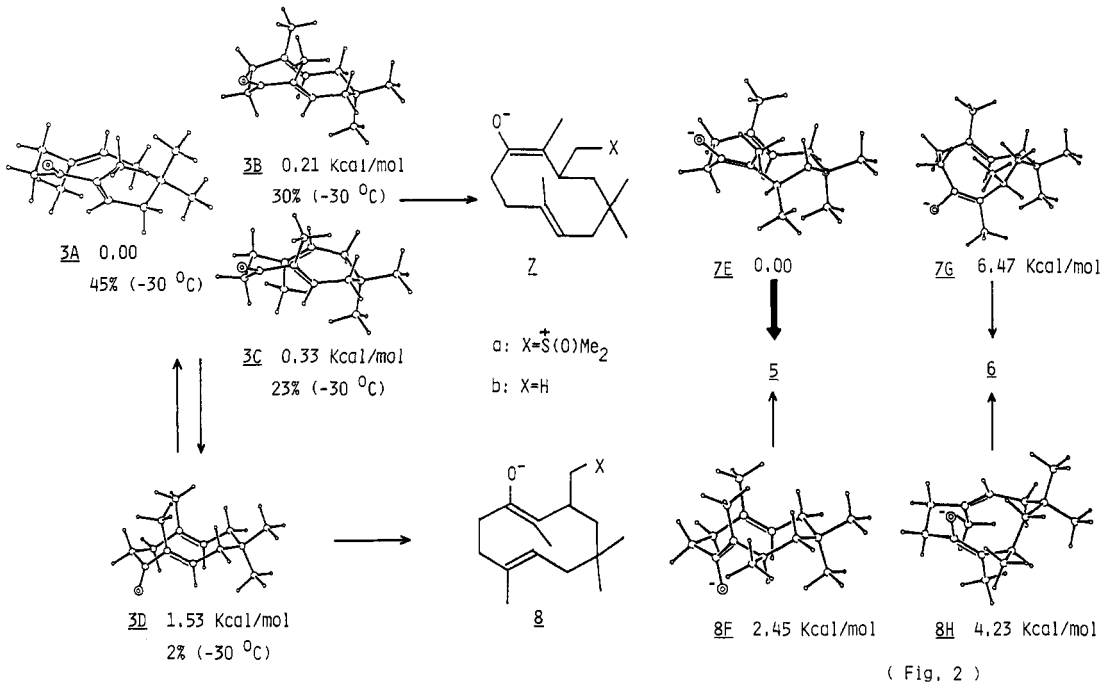

Figure 2.

and the β-elimination product of the tosylate, although this cyclization involved the alkylation of the homoallyl tosylate which was unstable to the strong basic condition.

The ^{1}H NMR spectrum of the enone **3** showed the broad olefinic peaks at 4.8–5.5 and 5.9–6.8 ppm in $CDCl_3$ at room temperature, while the each of the broad olefinic signals observed at room temperature separated into a pair of sharp peaks with an intensity ratio of about 56:44 in the same solvent at −30 °C. MM2 calculations and the Boltzmann distribution of conformers showed that the four conformers **3A**, **3B**, **3C**, and **3D** were equilibrated at −30 °C in a ratio 45:30:23:2. Assuming that two groups of conformers were constituted of **3B**, **3C**, and **3A**, conformational distribution ((**3B** + **3C**):**3A** = 53:45) based on calculations were consistent with those observed in NMR spectrum. Stereoselective cyclopropanation of **3** (Me_3S-(O)I–NaH/DMSO at 0 °C) gave the bicyclohumulenone (**5**)[18] in 90% yield; none of the cis stereoisomer **6** was detected in the crude product. Rationalization for this high trans stereoselectivity was available by MM2 calculations of the enone **3** and the model enolate **7E** as described above. They predict that the peripheral addition of oxysulfurane should proceed through the lower energy conformations **3B** (or **3A**, **3C**)[13] to lead the most likely enolate intermediate **4**, followed by ring closure gave the trans cyclopropane **5**. Thus conformational analyses of the enone (or enolates) are important to predict the stereoselectivity in macrocyclic reactions, and these considerations of stereochemical control based on MM2 calculations might have predictable value in organic syntheses.

Acknowledgment. We are grateful to Professor Y. Fukazawa (Hiroshima University) and Professor K. Yamamoto (Tokyo Institute of Technology) for helpful discussions on the MM2 calculations. We are indebted to Kuraray Co. for providing 5-acetoxy-3-methyl-(*E*)-2-pentenyl chloride.

Supplementary Material Available: Spectral data for new compounds, cyclization procedure, cyclopropanation procedure, and details of MM2 and NMR studies (8 pages). Ordering information is given on any current masthead page.

(18) The ^{1}H NMR, ^{13}C NMR, IR, and MS data of the synthetic (±)-bicyclohumulenone (mp 69–72 °C) were identical with those of natural product. We are indebted to Professor Asakawa for providing natural bicyclohumulenone.

Thermolysis of *N*-Benzyl-2,2-dichlorocyclopropanecarboxaldimines: A Novel Ring Enlargement to 2-Phenylpyridines

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Summary: Schiff bases of 2,2-dichlorocyclopropanecarbaldehydes with arylmethylamines were pyrolyzed to 2-arylpyridines. Tungsten(VI) oxide promoted the transformation. The reaction pathway is discussed.

Sir: The thermal rearrangement of vinylcyclopropanes has been the subject of many mechanistic and theoretical studies and recently has received attention as a synthetic tool.[1-10] In general, the thermolysis of vinylcyclopropane

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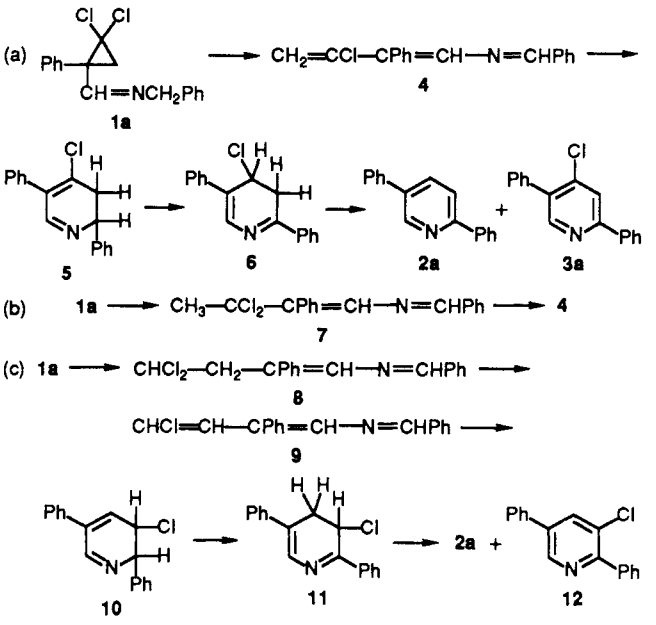
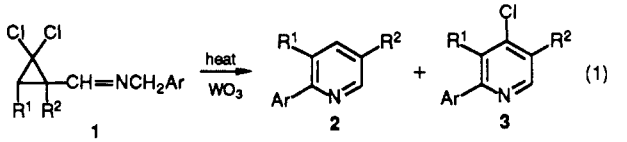
itself,[11] as well as alkyl-, alkenyl-, or phenyl-substituted derivatives,[12] affords principally cyclopentene(s) along with alkadienes as minor products.[13] Also, the thermal behavior of heterosubstituted vinylcyclopropanes has been studied. Thus, cyclopropyl imines rearrange to dihydropyrroles under rather forcing conditions.[15] Stevens et al. discovered that acid catalysts can facilitate the ring opening and have put the transformation to practical use, applying it to some alkaloid syntheses.[16]

Despite numerous reports on the vinylcyclopropane rearrangement, it has not thus far been reported that the atom or fragment joined at the vinyl terminus migrates or incorporates into the potential six-membered ring. In this paper, we add the first successful example of six-membered ring formation to the domain of the vinylcyclopropane thermal rearrangement. The pyrolysis of the Schiff bases of 2,2-dichlorocyclopropanecarbaldehydes[18] with benzylamines led to an unprecedented result involving formation of 2-phenylpyridines instead of dihydropyrroles or subsequent products. In this transformation, the phenyl–carbon part of the pyridine apparently stems from the benzyl portion of the imine in a six-electron process involving the rupture of the cyclopropane ring and dissociation of a benzyl hydrogen. Interestingly, some metal oxides enhance the transformation.

Scheme I



1-((Benzylimino)methyl)-2,2-dichloro-1-phenylcyclopropane (**1a**) was heated at 220 °C (in diphenyl ether, or in benzene in an autoclave) for 40 h to afford 2,5-diphenylpyridine (**2a**) and 4-chloro-2,5-diphenylpyridine (**3a**) in 41.3% and 1.4% yields, respectively (eq 1). The 1-



a: R^1 = H; R^2 = Ar = Ph
b: R^1 = H; R^2 = Me; Ar = Ph
c: R^1 = H; R^2 = *p*-tolyl; Ar = Ph
d: R^1 = H; R^2 = Ph; Ar = *p*-tolyl
e: R^1 = H; R^2 = Ph; Ar = *o*-ClC_6H_4
f: R^1 = Ar = Ph; R^2 = Me

methyl analogue **1b** was pyrolyzed to the 5-methyl-2-phenylpyridine (**2b**) and the 4-chloro derivative **3b** in poorer isolated yields of 26.6% and 5.4%, respectively. Inferring from the equation stoichiometry, which involves the elimination of 2 mol of HCl for **2** or 1 mol each of HCl and H_2 for **3**, basic or oxidizing additives may act to lower the elimination barrier or select for one of the competing paths. Among the various organic and inorganic additives tried, tungsten(VI) oxide and molybdenum(VI) oxide promoted the rearrangement, guiding the reaction in favor of **2**. Thus, when 6 mol of WO_3 were added, the production of pyridines was complete in almost half the heating time and at lower temperature (170 °C in phenetole, 21 h). The yield of **2a** improved to as high as 62%, and the yield of **3a** increased to 5%. The same activation by tungsten trioxide was observed in the thermolysis of substituted variants of the imine **1c–f**.[21] Comparing the product yields, the formation of 4-chloropyridines was minor in the cases studied, even in the presence of powerful dehydro-

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(13) In some cases, specific substituents attached to the cyclopropane moiety in certain geometries may have a drastic effect upon the reaction path, as exemplified by the fact that *cis*-2-(methylvinyl)cyclopropane gave *cis*-1,4-hexadiene in quantitative yield.[14]
(14) (a) Ellis, R. J.; Frey, H. M. *Proc. Chem. Soc.* **1964**, 221. (b) Jorgenson, M. J.; Thacher, A. F. *Tetrahedron Lett.* **1969**, 4651. (c) Roth, W. R.; König, J. *Justus Liebigs Ann. Chem.* **1965**, *688*, 28. (d) Ellis, R. J.; Frey, H. M. *J. Chem. Soc.* **1964**, 5578.
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(18) The 2,2-dichlorocyclopropanecarbaldehydes were prepared by dichlorocarbene addition to the corresponding substituted acrolein diethyl acetals and subsequent hydrolysis. The acetals were prepared by the general method of Crossland[19] or Miginiac et al.[20]
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(21) The yields of **2c/3c**, **2d/3d**, and **2e/3e** were 50/22, 65/9, and 18.5/14.5 (%/%), respectively. In the thermolysis of **1f** we could not detect the corresponding chloro derivative. The yield of **2f** was 41%. The corresponding yields of the above compounds without the catalyst were 40/13, 60/5, 12/10, and 30 (%/%), respectively. The elemental analyses data and the spectral properties of the products are in accord with the structural assignments.

genating agents such as PbO_2, V_2O_5, PtO_2, or organic DDQ, suggesting that the oxidative aromatization occurs late on the reaction coordinate. It is noteworthy that the dichlorocyclopropane imines, as distinct from cyclopropane imines, were not affected by ammonium chloride, silver acetate, or HBr additives in ring opening. Additionally, polar solvents such as DMSO, sulfolane, or diglyme did not afford pyridines at all.

Several pathways (Scheme I) may be postulated for the 1-substituted 2,2-dichlorocyclopropane benzylamine rearrangement: (a) Dechlorination and 1,3-bond breaking of the cyclopropane ring accompanied by H abstraction from the benzyl site, yielding the triene **4**, which electrocyclizes to the dihydropyridine **5**. Then, **5** will rapidly isomerize to the energetically more stable, fully conjugated dihydropyridine **6** via a 1,5-H shift, followed by aromatization by dehydrochlorination to **2a** or dehydrogenation to **3a**. (b) Homo-1,5-sigmatropic hydrogen migration with 1,3-bond cleavage to diene **7**, followed by HCl-elimination to **4**.[22] (c) Homo-1,5-sigmatropic hydrogen shift with 1,2-bond cleavage to **8**, followed by HCl elimination to **9**, which will decay to pyridines.[23] Pathway c is excluded because the 1,2-bond cleavage must result in 3-chloro-2,5-diphenylpyridine (**12**).[24] Pathway b may be unrealistic because it involves an energetically unfavorable process of migration of the benzyl hydrogen to a cyclopropane ring.[29]

In order to determine the reaction path, we examined the products in WO_3-assisted pyrolysis of the Schiff base **1g** prepared from α,α-dideuteriobenzylamine. The isolated diphenylpyridine **2g** exhibited monodeuteration on the 4-position of the pyridine ring with a 96% D content. On the other hand, the 4-chloro-2,5-diphenylpyridine (**3g**) did not contain any detectable amount of deuterium.[31] Considering the high positional selectivity and absence of deuterium scrambling, both stereomutation and hydrogen-shift equilibria must be negligible in the overall process. Pathway a seems more plausible than the others, because in a, after the abstraction of the first deuterium, the remaining one must take a designated position without a choice. On the other hand, in the latter pathways, competitive eliminations and migrations between H and D should occur in several steps, resulting in monodeuterated chloropyridine and dideuterated diphenylpyridine, with a greater product partitioning due to the primary hydrogen isotope effect.[32]

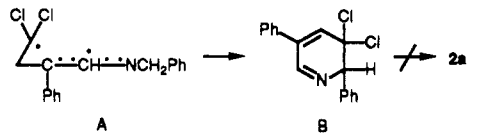
Compared with the vinylcyclopropane to cyclopentene rearrangement, the imino analogue tends to require more highly elevated temperatures, probably due to the stronger π-bond energy of the C=N over the C=C bond.[33] Stevens's discovery of reaction enhancement through the addition of ammonium chloride is attributed to the mobilization of the imino double bond by a cation from the catalyst and strong assistance by the anion in the cyclopropane ring opening. On the other hand, in the case of the dichlorocyclopropane imine, the leaving chloride ion is responsible for triggering the cyclopropane ring cleavage. The detailed function of tungsten oxide in the title reaction is not yet clear. Lewis acids without nucleophilic counterions may promote benzyl-hydrogen abstraction by complexing with the hetero π-bond.[35]

Further studies are under way to clarify the mechanism of this rearrangement, to define the scope and limitations of the process, and to develop unique methodology for the synthesis of substituted pyridines.

Acknowledgment. We are grateful to Professors T. Asao and N. Morita of Tohoku University and S. Inagaki of Gifu University for their helpful comments. We thank Dr. S. Kurogochi and K. Wada of Nihon Tokushu Noyaku Seizo Co. for their MS and NMR measurements and H. Horinouchi who carried out some of the experiments.

(22) Immediate aromatization from **5** to **2a**/**3a** or from **10** to **2a**/**12** may occur in some measure.

(23) Homolytic 1,2-bond cleavage to biradical A is excluded, because the subsequent sequence would not lead to the formation of 2,5-diphenylpyridine **2a**.



(24) The present result may be contrasted with the thermal behavior of 2,2-dichloro-1-vinylcyclopropane[25] and *N*-benzyl-1-phenylcyclopropanecarboxaldimine in the presence of acid catalysts,[26] in which the 1,2-bond cleavage takes place exclusively. However, it has been reported that *gem*-dichloro substituents on a cyclopropane ring give rise to a kinetic weakening of the specific C–C bond distal to the CCl_2 group, though this effect is not as strong as with the corresponding fluoride.[27] The thermal rearrangement of 2,2-difluoro-3-methyl-1-vinylcyclopropane to *cis*-3,3-difluoro-1,4-hexadiene with cleavage of the 1,3-bond has been well investigated.[28]

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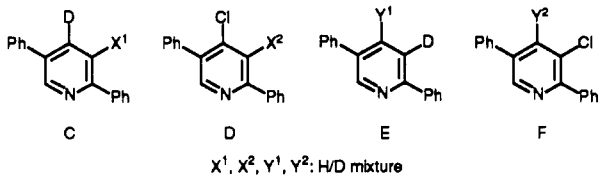
(29) Compared with the well-documented 1,5-homo-shift of alkyl hydrogen on the cyclopropane ring to the vinyl terminus in the *cis*-2-alkyl-1-vinylcyclopropane system, no example of the shift of alkyl hydrogen on the vinyl terminus to the cyclopropane ring has been observed to our knowledge. Even in an equilibrium mixture from the thermolysis of 4,5- and 5,6-diphenylbicyclo[3.1.0]hex-2-ene, the hydrogen shift on the allyl (simultaneously benzyl) site was not observed.[30] The high energy barrier for such a rearrangement is attributed partly to the weaker orbital interaction between the C–H bond of the alkyl residue in question and the cyclopropane C–C bond, rather than the C=C bond.

(30) Swenton, A. S.; Wexler, A. X. *J. Am. Chem. Soc.* **1971**, *93*, 3066.

(31) The deuterium contents of the products in the labeling experiment were determined by comparing their ion intensities with the corresponding cold standards. The position of deuterium was determined by NMR.

(32) According to pathways b and c, C/D and E/F should be formed.



(33) The π-bond strength for typical CH_2=CH_2 and CH_2=NH have been calculated to be 63.1 and 74.2 kcal/mol, respectively (*The Chemistry of the Carbon-Nitrogen Double Bond*; Sandorfy, G., Patai, S., Ed.; Wiley: New York, 1970; p 6). For recent theoretical analysis and experimental studies on the relative strengths of these bonds, see ref 34.

(34) (a) Schleyer, P. v. R.; Kost, D. *J. Am. Chem. Soc.* **1988**, *110*, 2105. (b) Wu, P.-L.; Fowler, F. W. *J. Org. Chem.* **1988**, *53*, 5998.

(35) Interestingly, addition of some basic metal oxides such as CaO provoked the reaction in quite a different fashion; 1-benzyl-3-phenylmaleimide was produced exclusively.