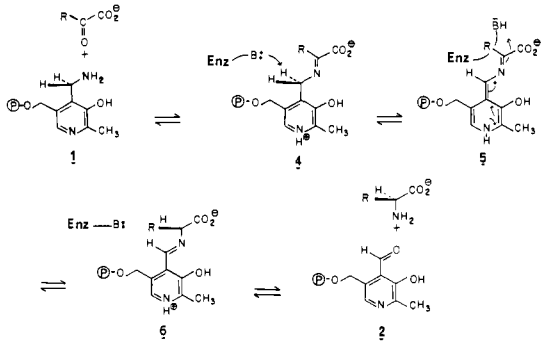
Scheme I



Scheme II

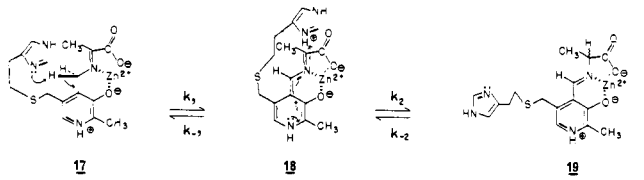


Table I. Rates of Conversion of Ketimines (e.g., 17) to Aldimines (e.g., 19) at pH 4.00[a] in Methanol (30.0 °C)

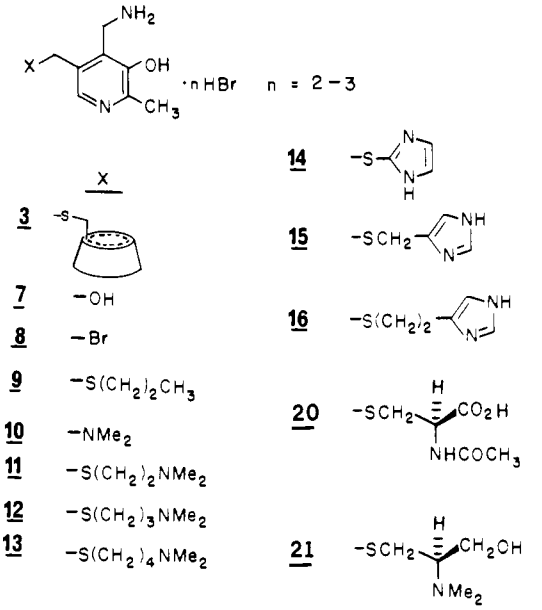
compd	side chain	k_{obsd}, s^{-1} [b]	rel rate
9	SPr	8.7×10^{-6}	1.0
7	OH	1.2×10^{-5}	1.4
10	NMe_2	1.3×10^{-4}	15.0
11	$S(CH_2)_2NMe_2$	2.3×10^{-4}	26.0
12	$S(CH_2)_3NMe_2$	3.3×10^{-4}	38.0
13	$S(CH_2)_4NMe_2$	1.1×10^{-4}	13.0
14	S(Im)	5.4×10^{-5}	6.0
15	SCH_2Im	1.1×10^{-4}	13.0
16	SCH_2CH_2Im	6.8×10^{-4}	78.0
20	*N*-acetylcysteine	9.6×10^{-5}	11.0
21	*N*,*N*-dimethylcysteinol	2.3×10^{-4}	26.0[c]

[a] "pH" as read with a glass electrode. The pHs were unchanged at the end of the reaction. [b] Standard deviation within each run less than 1%; duplicate runs usually within 1%, with a few within 10%. [c] With α-oxovaleric acid as substrate, which is ca. 20% slower than pyruvic acid.

As Table I shows, all the pyridoxamines with basic side chains (**10**–**16**) show significant accelerations relative to pyridoxamine itself (**7**) or **9**. However, the optimum catalysis occurs with side-chain groups long enough to reach the remote carbon of **18** to deliver a proton, forming **19** (Scheme II). Models show that the advantage of **12** over **11** is inexplicable if the basic group acts only in the step **17** → **18** but that the greater length of **12** is ideal for the protonation of **18** to form **19**. In **13** the entropy disadvantage of greater length is finally seen. The advantage of imidazole catalysts in **15** and **16** could reflect their rigidity or their lower basicity, and the consequent more favorable equilibrium of the principal protonated state with less favorable but required **17**.

We have also prepared the chiral derivatives **20** and **21**. With α-oxovaleric acid both catalyzed formation of the aldimine; hydrolysis formed norvaline, analyzed by dansylation[9] and chiral HPLC.[10] Compound **21** produced a 39% enantiomeric excess of D-norvaline after 2 h (65% conversion), but **20** showed negligible enantiomeric preference. The dimethylammonium group of **21** can reach the prochiral carbon of the intermediate related to **18**,

Chart I



but the carboxyl group of **20** in its normal conformation[11] cannot. This helps confirm[12] our conclusion that the best catalytic groups act as both bases and acids. With better chiral definition higher optical yields can be expected.

Acknowledgment. This work was supported by the National Institutes of Health.

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(8) The pH dependence is consistent with fastest rate at a maximum concentration of **17**. This is in equilibrium with a predominant isomer that has a protonated base group and unprotonated pyridine.
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(12) In an experiment with **12** and [2-^{13}C]pyruvic acid in CD_3OD, the product aldimine related to **19** had D, not H, on the C-2 carbon (by ^{13}C NMR) after 40 min. Exchange in the product should be slow, as judged by the chiral induction with **21**, so there is either fast exchange in the intermediate related to **18** (most likely) or a solvent-mediated general acid reaction.

Carbenes and the O-H Bond: 3-Cyclopentenylidene. A Novel Approach to Bis(homocyclopropenyl) Cations†

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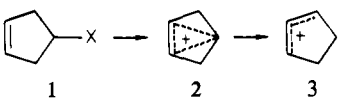
Retention of configuration in the formolysis of an appropriately labeled cyclopent-3-enyl tosylate (**1**-OTs) suggests intervention



of the bis(homocyclopropenyl) cation **2**.[1] All attempts to observe **2** under superacidic conditions were unsuccessful; ionization of **1**-OH or **1**-Cl even at −140 °C gave only the allylic ion **3**.[2] The 1,2-hydride shift leading to **3** was a minor process in the formolysis

† Dedicated to Professor William von Eggers Doering on the occasion of his 65th birthday.
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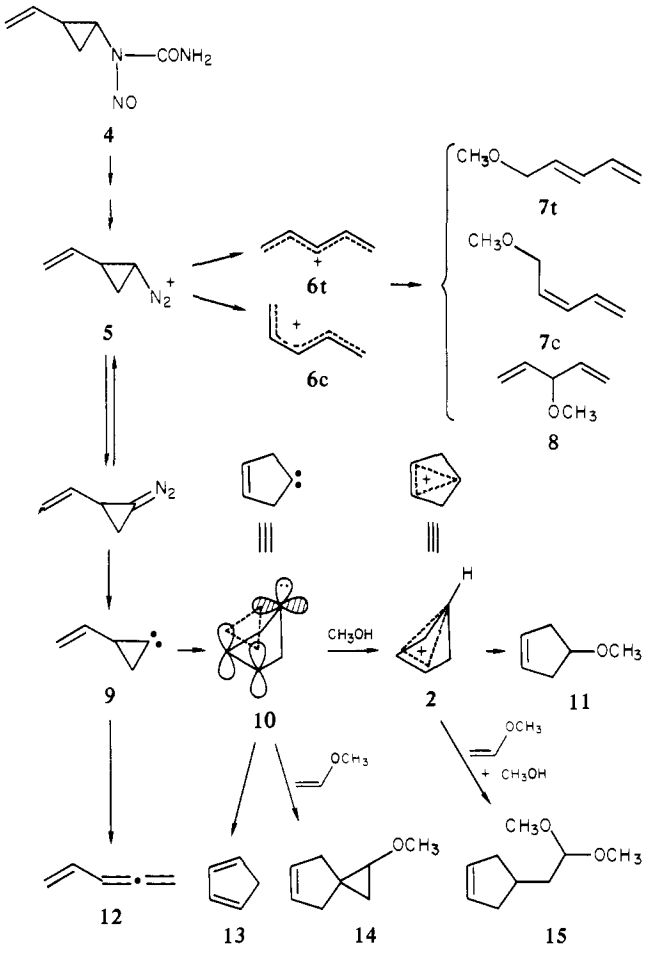
(2) Olah, G. A.; Prakash, G. K. S.; Rawdah, T. N.; Whittaker, D.; Rees, J. C. *J. Am. Chem. Soc.* **1979**, *101*, 3935.

0002-7863/83/1505-1695$01.50/0

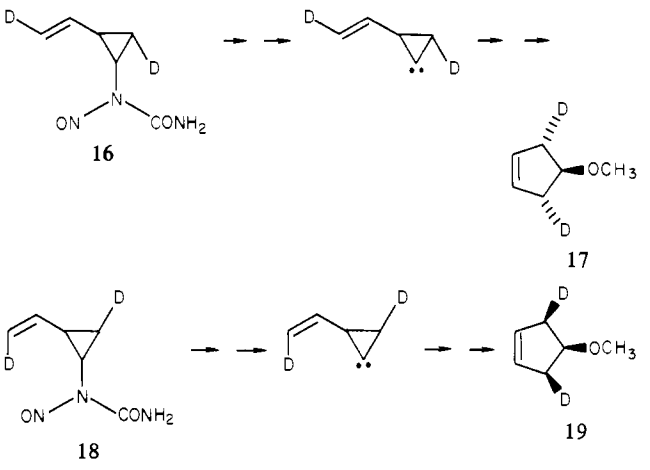
Scheme I



of **1**-OTs.[1] We report here on a different approach to **2**, the protonation of 3-cyclopentenylidene (**10**).

Cleavage of the nitrosourea **4**[3] (Scheme I) by $NaHCO_3$/MeOH generated 2-vinylcyclopropanediazonium ions (**5**),[6] which underwent ring opening to yield the pentadienyl ethers **7t** (41%), **7c** (7%), and **8** (52%).[7] The stronger base NaOMe led to formation of 2-vinylcyclopropylidene (**9**) via deprotonation of **5**. The yield of the ethers **7t,c** (3%) and **8** (3%) was strongly diminished. The major products originating from **9** were 1,2,4-pentatriene (**12**, 46%), cyclopentadiene (**13**, 14%), and 4-methoxycyclopentene (**11**, 26%). 3-Methoxycyclopentene was not observed (<0.1%). When **9** was generated from organometallic precursors under aprotic conditions, **12** and **13** were obtained[8] in a temperature-dependent ratio (ca. 1:1 at 25 °C).[9] In competition with the cyclopropylidene–allene transformation **9** undergoes a 1,3-shift of the

Scheme II



divalent carbon (Skattebøl rearrangement)[8,10,11] to give **13** by way of 3-cyclopentenylidene (**10**). The present experiment in MeOH/NaOMe afforded 4-methoxycyclopentene (**11**) in addition to cyclopentadiene (**13**). The combined yields of **11** and **13** approximated that of **12**. Trapping of **10** by methanol, formally an O–H insertion, appears to compete efficiently with the intramolecular hydrogen shift leading to **13**.

MINDO/2 calculations on the Skattebøl rearrangement[12] indicate interaction of the empty p orbital of the divalent carbon with the π bond. According to these views the Skattebøl rearrangement generates 3-cyclopentenylidene as a "foiled carbene",[13] which might be accessible to protonation. Cleavage of **4** in a mixture of methanol and methyl vinyl ether produced 1-methoxyspiro[2.4]hept-5-ene (**14**,[14] 0.5%) and the acetal **15**[15] (7%). Obviously, the cation **2** is the major, if not exclusive, species that may be trapped by electrophilic addition to methyl vinyl ether. We infer that **2** is also the (major) precursor to **11**.

The bridged structure attributed to **2** implies stereospecific reaction with a nucleophile. The stereochemistry of the **9** → **11** transformation was explored with the aid of the deuterated precursors **16** and **18** (Scheme II), prepared from the appropriate butadienes-*1,4-d*$_2$.[16] Within the limits of NMR detection[17] (ca. 3%), the 4-methoxycyclopentene obtained from **16** was exclusively *trans*-3,5-d_2 (**17**), and that from **18** was exclusively *cis*-3,5-d_2 (**19**). Our stereochemical results exclude any planar intermediate on the reaction path **9** → **11**.

The protonation of "foiled" carbenes has precedent in the bicyclic series,[18,19] e.g., 7-norbornenylidene → 7-norbornenyl cation. The rigid structure of the bicyclic intermediates favors π–p interaction and prevents facile hydride shifts (analogous to **10** → **13** and **2** → **3**). The present study extends the scope of carbene protonation[20] to the more flexible 3-cyclopentenylidene (**10**), supporting experimentally the bridged formulations of **2** and **10**.

(3) The addition of ethoxycarbonylcarbene (from ethyl diazoacetate) to butadiene[4] is greatly improved by $Rh_2(OAc)_4$ as the catalyst.[5] Hydrolysis of the ester, Curtius degradation, addition of ammonia to the isocyanate, and nitrosation (N_2O_4, Et_2O) complete the synthesis of **4**.

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(7) Evidence for the intermediacy of pentadienyl cations (**6t,c**) has been obtained with the aid of deuterium labels; cf.: Henning, P. G. Dissertation, University of Bochum, 1978.

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(14) **14** was identified by comparison of its hydrogenation product with authentic 1-methoxyspiro[2.4]heptane, obtained from methylenecyclopentane and methoxycarbene(oid).

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(17) **11**: ^{1}H NMR δ 5.70 (s, 1,2-H), 4.10 (septet, J = 3.3 Hz, 4-H), 3.32 (s, OCH_3), 2.57 (dd, J = 15.3, 6.6 Hz, *trans*-3,5-H), 2.38 (dd, J = 15.3, 3.3 Hz, *cis*-3,5-H). **17** and **19** were analyzed by deuterium-decoupled ^{1}H NMR.

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