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REACTION OF ENAMINE WITH OXAZIRIDINE OR SCHIFF BASE FACILE PREPARATION OF SUBSTITUTED PYRIDINE

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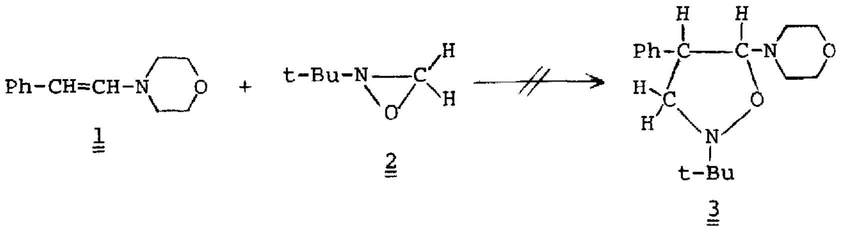
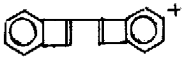
Oxaziridines are good precursors of various heterocyclic compounds and we have already reported cycloaddition reactions of oxaziridines with heterocumulenes which are classified as the compounds having an electrophilic double bond.[1,2] Nevertheless, few examples have been known for reactions with nucleophilic reagents.[3]

Now we wish to report the reaction of an oxaziridine with an enamine, a nucleophilic olefin, giving unexpectedly a pyridine derivative 4 instead of a 1:1 cycloadduct 3. As a logical off-shoot, we also studied the reaction of a Schiff base with the enamine forming the same pyridine. Although these reactions have not yet been optimized, we expect them to become one of the facile preparative methods for substituted pyridines.



To a solution of 3.8 g (20 mmole) of N-styrylmorpholine (1) in 25 ml of sodium-dried benzene, 2.0 g (20 mmole) of 2-tert-butyloxaziridine (2) was added dropwise during a 30-min period at 80°C with stirring which was continued for 27 hr after the addition. The reaction mixture was then distilled to give a mixture of N-tert-butylformamide (1.0 g, 50%), morpholine (1.1 g, 63%), and benzaldehyde (trace) which were identified and determined by glpc. The ir spectrum of the fraction riching in the formamide also showed good agreement with that of an authentic sample prepared from tert-butylamine and ethyl formate.[4] The residue was chromatographed (silica gel-benzene) to afford 0.23 g (10%) of 3,5-diphenylpyridine (4): colorless needles (from ether); mp 138-139°C (lit.[5] 136-137°C); ir (Nujol mull) 1595 and 1575 cm^{-1} (shoulder); nmr ($CDCl_3$) δ 7.3-7.6 (m, 10H, 2 Ph), 7.95 (t, 1 H, $J_{H^4-H^2} = J_{H^4-H^6} =$ 2.2 Hz, H^4), 8.76 (d, 2 H, J = 2.2 Hz, H^2 and

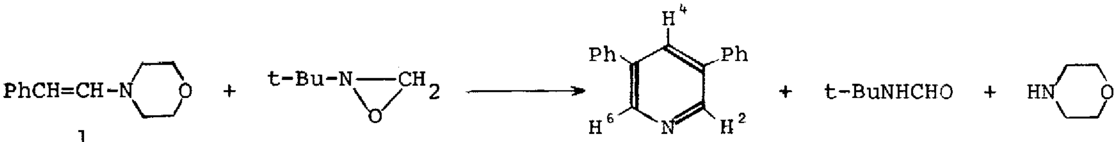
H^6); mass spectrum m/e (relative intensity, assignment) 231 (100, M^+), 202 (5.8,  or ), 154 (1.4, M^+ - Ph), 102 (4.8, $PhC{\equiv}CH^+$).

Anal. Calcd for $C_{17}H_{13}N$: C, 88.28; H, 5.67; N, 6.06. Found: C, 89.50; H, 5.45; N, 5.97.

We further confirmed the structure of 4 by treating it with n-butyl bromide in dioxane at 110°C. The resulting quaternary ammonium salts, 1-n-butyl-3,5-diphenylpyridinium bromide, was analyzed satisfactorily: colorless needles (from chloroform); ir (Nujol mull) 1590 and 1570 cm^{-1} (shoulder); nmr ($CDCl_3$) δ 0.91 (t, 3H, J = 8.0 Hz, CH_3), 1.5 (m, 2H, CH_2), 2.1 (m, 2H, CH_2), 5.32 (t, 2H, J = 7.1 Hz, NCH_2), 7.4-7.6 (m, 6H, aromatic protons), 7.8-8.0 (m, 4H, aromatic protons), 8.52 (t, 1H, $J_{H^4-H^2} = J_{H^4-H^6} = 1.6$ Hz, H^4), 9.78 (d, 2H, J = 1.6 Hz, H^2 and H^6).

Anal. Calcd for $C_{21}H_{22}NBr$: C, 68.48; H, 6.02; N, 3.80; Br, 21.70. Found: C, 68.27; H, 5.98; N, 3.82; Br, 21.57.

The results of the reaction of the enamine 1 with the oxaziridine 2 are summarized in Table 1.



1 2 4

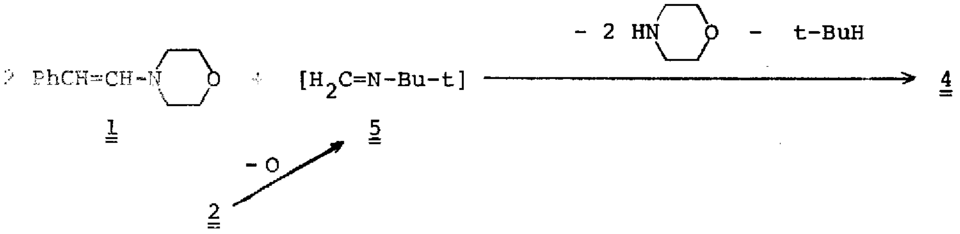
Table 1. Reaction of Enamine with Oxaziridine

mole ratio 2/1	solvent	reaction temp. (°C)	reaction time (hr)	yield of 4 (%)[a]
1.0	benzene	80	27	10
1.0	benzene	80	18	24
0.5	toluene	110	13	14

a: based on 1.

Under the same conditions as above, 2-tert-butyl-3-phenyloxaziridine reacted with the enamine 1 very slowly and gave no significant product such as a pyridine derivative or a 1:1 cycloadduct.

Formation of large amount of N-tert-butylformamide is ascribable to thermal rearrangement of the oxaziridine 2,[3] and benzaldehyde implies oxidative decomposition of the enamine 1. Thus formation of the unexpected product 4 suggested the participation of the Schiff base 5 which was formed from the oxaziridine 2 in the course of the reaction because the equation for the reaction can be formally described as follows.



Hence, we examined the reaction of enamine 1 with the Schiff base 5 which exists as its trimer at room temperature. The formation of the same pyridine 4 better yields revealed the intermediacy of the Schiff base in the above tion with the oxaziridine 2. The results are listed in Table 2.

Table 2. Reaction of Enamine with Schiff Base

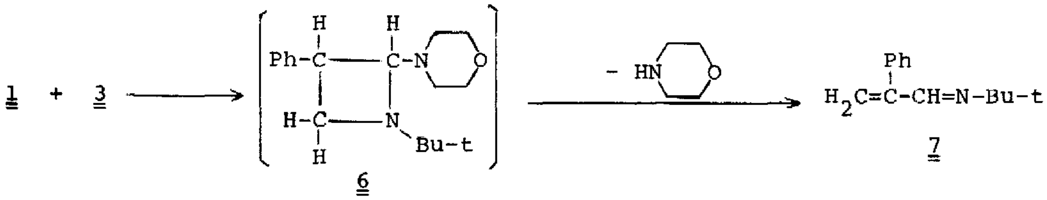
mole ratio $5^a/1$	solvent	reaction temp. (°C)	reaction time (hr)	yield of 4 (%)^b
1.0	benzene	80	50	0^d
1.0	toluene	110	18	18
1.0	benzene^c	160	9	12
1.0	benzene^c	200	9	36
1.0	benzene^c	200	18	23
1.0	benzene^c	250	9	34
0.5	benzene^c	200	9	33
0.5	benzene^c	200	18	34

a: 1,3,5-tri-tert-butylhexahydro-1,3,5-triazine was employed as its precursor.
b: based on 1.
c: in a sealed tube.
d: the starting materials were recovered.

In contrast to the oxaziridine 2, the trimer of the Schiff base did not react with the enamine 1 at 80°C. The formation of the pyridine 4 at 110°C showed that the rate of dissociation of the trimer to the monomer 5 is rather slow and the oxaziridine 2 is a better source of 5 at lower temperatures. The yield of the pyridine 4 increased up to 36% at 200°C and, hence, the Schiff base seems to be a better starting material for the synthesis of the pyridine.

Though the rate of dissociation of the trimer becomes greater as the temperature goes higher, no improvement in the yield of the pyridine was observed at 250°C as compared with the result at 200°C. The other fact which is worthy to be noted here is that a decrease in the mole ratio of Schiff base/enamine did cause no increase in the yield of **4**. A longer reaction time had no significant effect on the yield either.

It is interesting to know how the oxaziridine loses its oxygen or how the tert-butyl group eliminates. The enamine is probably oxidized[6] with the oxaziridine and isobutane or isobutene generates in the course of the reaction. At the moment, mechanism of the reaction is not clear enough since other products have not yet been identified. However, one of the possible intermediates of this reaction may be the azabutadiene **7** which in turn reacts with another molecule of the enamine.



Such a formation of an azabutadiene from an enamine and a Schiff base via a 1:1 cycloadduct as **6** has already been reported.[7]

Limitation of this reaction as well as its mechanism are now under investigation.

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