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ON THE LEWIS ACID CATALYZED CYCLOCONDENSATION OF IMINES WITH A SILOXYDIENE

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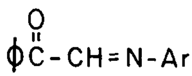
Summary: A hetero Diels-Alder route to 5,6-dihydro-γ-pyridones is described.

Recently, we described the Lewis Acid catalyzed cyclocondensation of aldehydes with siloxydienes to give 5,6-dihydro-γ-pyrones. It was of interest to attempt to extend this reaction to include the imino linkage. Certainly, there have been reports of intermolecular 2 + 4 cycloadditions to "C = N" dienophiles.[2] However, they have involved particularly activated glyoxyl imines (*cf.* 1),[3] acyl imines (*via* presumed precursor 2)[4] or doubly activated imines (*cf.* 3).[5] In addition, we note that Weinreb has elegantly exploited intramolecular Diels-Alder reactions of acyl imines[6] as a new strategem in alkaloid synthesis.



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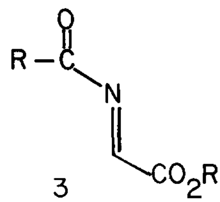
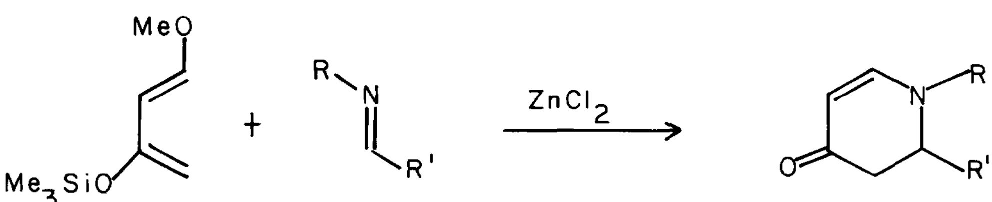
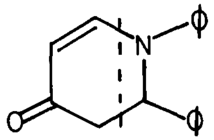


3

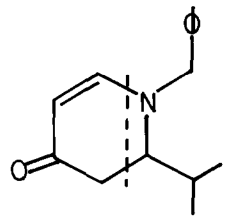
Below we describe the first general[7] condensation of imines with a diene. For this purpose we used siloxydiene 4 with zinc chloride catalysis. *Reaction occurs at room temperature and no special activating influences in the imine are necessary.* The Schiff bases (see dotted lines) which were used as substrates were obtained by standard means.[8] Yields refer to isolated homogeneous products. The relationship of the yields to the molar ratio of diene:imine is indicated. A typical experimental procedure is provided.



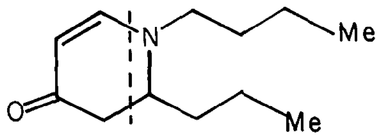
4 5



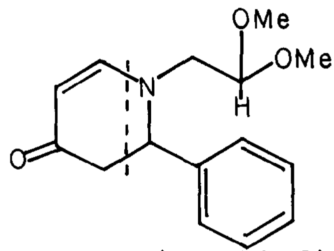
6 48% (1.1); 62%(4.3)



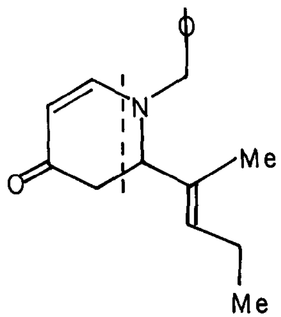
7 44%(1.1); 69%(3.8)



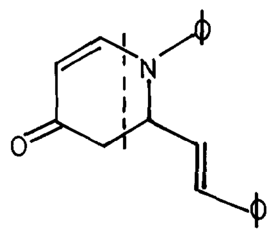
8 49%(1.1); 68%(3.1)



9 53%(1.1); 76%(4.2)



10 33 %(1.1); 47%(2.3)



11 41%(1.2); 72%(4.6)

General Procedure

To a flask, flame dried under inert atmosphere, was added the imine (1 eq) in dry tetrahydrofuran. To this solution was added neat 1-methoxy-3-trimethylsiloxydiene (3.0 - 4.6 eq) and anhydrous $ZnCl_2$ (1.0 eq) as a solution in THF, freshly prepared prior to use. The reaction mixture was diluted with anhydrous THF so as to make the concentration of imine *ca.* 0.1M. After stirrin at room temperature 36-48 hrs, water was added and the entire mixture was extracted with ethyl acetate. The extracts were combined, dried over magnesium sulfate, and filtered. Evaporation of the volatiles and flash chromatography[9] gave products which were homogeneous by t.l.c. and exhibited spectral properties which are indicated.[10]

As in the case of the cyclocondensation of aldehydes with compound **4** under similar conditions,[1] we defer any definitive statements regarding mechanism. The stereochemical implications of the reaction also remain to be determined. However, we note that systems **5** lend themselves to conversion to a variety of other products. Thus, the reaction reported here should prove of some consequence to the field of heterocyclic synthesis.

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7. For some structurally or mechanistically novel cases of imine cycloadditions see: (a) F. Bohlmann, D. Habeck, E. Poetsch and D. Schumann, Chem. Ber., 100, 2742, (1967); (b) T. Kametani, M. Kajiwara, T. Takahashi and K. Fukimoto, J. Chem. Soc., Perkin I, 737, (1975).
8. *cf.* S. Dayazi, Y. Degani, in the Chemistry of the Carbon-Nitrogen Double Bond, S. Patai ed. Interscience Publishers, New York, (1970). R. W. Layer, Chem. Rev., 63, 489, (1963).
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10. Spectral data for **6**: IR $\bar{\nu}$ 1640, 1580, 1500 cm^{-1}; ^1H NMR (90 MHz, $CDCl_3$) δ 7.62 (d, J = 7 Hz, 1 H), 6.9 - 7.4 (br m, 10 H), 5.22 (br d, J = 7 Hz, 2 H), 3.25 (dd, J = 7.5, 16 Hz, 1 H), 2.72 (dd, J = 3 Hz, 16 Hz, 1 H); ^{13}C NMR (22.5 MHz, $CDCl_3$) 190.2, 148.3, 144.8, 138.2,

129.7, 129.1, 128.0, 126.3, 124.5, 118.8, 103.1, 61.8, 43.6 ppm; m/e 249 (M^+), 172 (M^+-77), 145, 117. **7**: IR $\bar{\nu}$ 1640, 1585 cm^{-1}; 'H NMR (90 MHz, $CDCl_3$) δ 7.2 - 7.4 (brm, 5 H), 7.15 (d, J = 7.5 Hz, 1 H), 4.90 (d, J = 7.5 Hz, 1 H), 4.45 (brs, 2 H), 3.20 (br m, 1 H), 2.66 (dd, J = 7 Hz, 16 Hz, 1 H), 2.1 - 2.45 (m, 2 H), 0.95 (d, J = 7 Hz, 6 H); ^{13}C NMR (22.5 MHz, $CDCl_3$) 191.3, 153.8, 137.2, 129.3, 128.5, 127.6, 97.6, 61.6, 58.9, 36.7, 29.3, 20.0, 18.3 ppm; m/e 229 (M^+), 186 (M^+-43), 91. **8**: IR $\bar{\nu}$ 1640, 1585 cm^{-1}; 'H NMR (90 MHz, $CDCl_3$) δ 7.9 (d, J = 7.5 Hz, 1 H), 4.85 (d, J = 7.5 Hz, 1 H), 3.5 (br m, 1 H), 3.2 (t, J = 7 Hz, 2 H), 2.75 (dd, J = 6 Hz, 16 Hz, 1 H), 2.22 (dd, J = 3 Hz, 16 Hz, 1 H), 1.55 (br m, 8 H), 1.0 (br t, 6 H); ^{13}C NMR (22.5 MHz, $CDCl_3$) 190.9, 153.3, 96.8, 56.8, 54.5, 39.7, 32.3, 31.2, 20.2, 19.3, 14.4, 14.1 ppm; m/e 195 (M^+), 152 (M^+-43), 138 (M^+-57), 110. **9**: IR $\bar{\nu}$ 1640, 1590 cm^{-1}; 'H NMR (90 MHz, $CDCl_3$) δ 7.25 (br s, 5 H), 7.14 (d, J = 7.5 Hz, 1 H), 4.97 (d, J = 7.5 Hz, 1 H), 4.70 (t, J = 7 Hz, 1 H), 4.25 (t, J = 5 Hz, 1 H), 3.3 (s, 6 H), 3.11 (d, J = 5 Hz, 2 H), 2.85 (dd, J = 7 Hz, 16 Hz, 1 H), 2.58 (dd, J = 7 Hz, 16 Hz, 1 H); ^{13}C NMR (22.5 MHz, $CDCl_3$) 190.2, 154.9, 139.0, 129.1, 128.4, 127.1, 103.4, 98.7, 62.1, 55.1, 43.7 ppm; m/e 261 (M^+), 230 (M^+-31), 201, 200, 75. **10**: IR $\bar{\nu}$ 1640, 1585 cm^{-1}; 'H NMR (90 MHz, $CDCl_3$) δ 7.15 - 7.40 (br m, 5 H), 7.11 (d, J = 7.5 Hz, 1 H), 5.22 (br t, J = 6.5 Hz, 1 H), 4.9 (d, J = 7.5 Hz, 1 H), 4.35 (d, J = 15 Hz, 1 H), 4.10 (d, J = 15 Hz, 1 H), 3.85 (t, J = 8.0 Hz, 1 H), 2.55 (d, J = 8.0 Hz, 2 H), 2.04 (br m, 2 H), 1.63 (s, 3 H), 0.95 (t, J = 7.5 Hz, 3 H); ^{13}C NMR (22.5 MHz, $CDCl_3$) 191.6, 154.6, 136.9, 132.5, 130.9, 129.3, 128.4, 128.0, 98.2, 64.6, 57.0, 40.7, 21.3, 14.2, 12.5 ppm; m/e 255 (M^+), 226 (M^+-29), 198, 184, 160. **11**: IR $\bar{\nu}$ 1640, 1580, 1490 cm^{-1}; 'H NMR (90 MHz, $CDCl_3$) δ 7.48 (d, J = 7.5 Hz, 1 H), 7.10 - 7.40 (br m, 10 H), 6.56 (d, J = 16 Hz, 1 H), 6.30 (dd, J = 5 Hz, 16 Hz, 1 H), 5.27 (d, J = 7.5 Hz, 1 H), 4.85 (br m, 1 H), 3.15 (dd, J = 6.5 Hz, 16 Hz, 1 H), 2.55 (dd, J = 3 Hz, 16 Hz, 1 H); ^{13}C NMR (22.5 MHz, $CDCl_3$) 190.9, 147.6, 144.9, 136.2, 132.8, 130.0, 128.9, 128.4. 126.9, 125.1, 124.8, 119.1, 102.8, 60.6, 42.0 ppm; m/e 275 (M^+), 247, 172, 117; mp 137.5 - 138.5°C.

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