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Annelation of Aromatic Oxo Compounds

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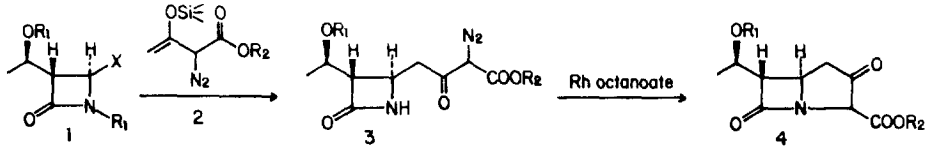
Abstract: The silyl enol ether of α-diazoacetoacetate is used for the annelation of aromatic oxo compounds. The method involves condensation with the oxo compound in the presence of $TiCl_4$ followed by rhodium octanoate-catalyzed ring closure to afford furan derivatives by direct carbene insertion and β-naphthol esters by a Wolff rearrangement pathway.

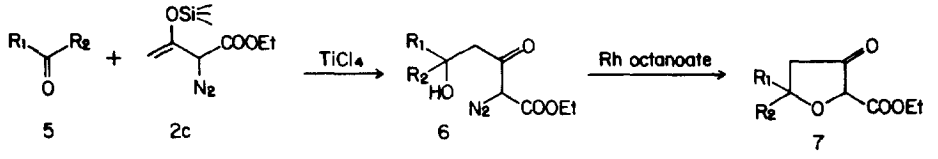
A new annelation method utilizing the bifunctional diazo silylenolether synthon **2** was developed by us [1a] for the construction of thienamycin precursor **4a** from the penicillin derived fragment **1a**. Subsequently, Reider and Grabowski[1b] of these laboratories, showed the generality of this type of annelation by the conversion of **1b** to **4b**. With the commercial avalilability of acetoxy azetidinone **1b**, this became the method of choice for the construction of the carbapenem skeleton[2].



a) R_1 = Si≡, X=Cl, R_2=ØCH$_2$; b) R_1=H, X=OAc, R_2=ØCH$_2$ or pNO_2-$C_6H_4CH_2$

In this paper we describe the use of synthon **2** for the annelation of aromatic oxo compounds to afford derivatives of furan , α- and β-naphthol.

The formation of furan derivatives is analogous to the original method (**1** to **4**) as it involves: a) condensation of the $TiCl_4$ activated oxo compound with enol silane **2** to afford **6** and b) ring closure by insertion of the rhodium octanoate-generated carbene into the OH bond.[3] This reaction appears to be general because the various oxo compounds listed reacted analogously.



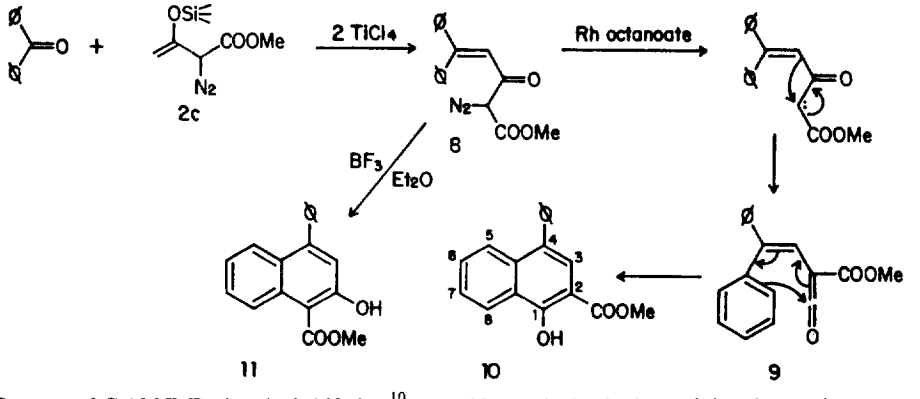
a) R_1=Ø, R_2=H; b) R_1=Ø, R_2=Me; c) R_1=2-Pyridyl, R_2=H; d) R_1=2-Furyl, R_2=H

The general experimental procedure calls for consecutive addition of molar equivalents of $TiCl_4$ and synthon **2c** to the dry ice-acetone cooled methylene chloride solution of **5**. After one hour the product was isolated in 60-80% yield by the usual aqueous work-up, followed by filtration chromatography (silica gel, CH_2Cl_2-EtOAc). The aldol products **6** were identified by spectroscopic methods.[4] Ring closures were carried out by boiling the methylene chloride solution of **6** in the presence of a trace of rhodium octanoate. The catalyst and minor by-products were removed by filtration chromatography (silica gel, CH_2Cl_2-EtOAc). In this manner, excellent yields were obtained of compounds **7a,b,c,d,** as isomeric mixtures.

Condensation with benzophenone provided the unsaturated diazoketone **8** in 80% yield. It was reported that the Rhodium catalyzed ring closure of this and two ring substituted diazoketones yielded direct CH insertion products, analogous to **11**.[5] At the same time, the authors remarked the propensity of this system to Wolff rearrangement The authors and recent reviewers[6a,b] rationalized this unexpected result as the consequence of the aromatization of a norcaradiene-like cyclization intermediate. We report here that the Rhodium catalyzed decomposition of **8** did not yield **11**, but instead, the isomeric α-naphthol derivative **10** formed in near quantitative yield.[7a,8] This was clearly the result of a Wolff rearrangement followed by cyclization of the ketene intermediate **9**. Similar α-oxo ketenes, generated by photolysis of α-diazo β-diketones were detected by IR spectroscopy at 12K in argon matrix.[9] In our hands, ketene **9** could not be detected by FT-IR at room temperature, indicating that ring closure is faster then ketene formation.

The experimental procedure was the same as described above except that two equivalents of $TiCl_4$ were used for the condensation.

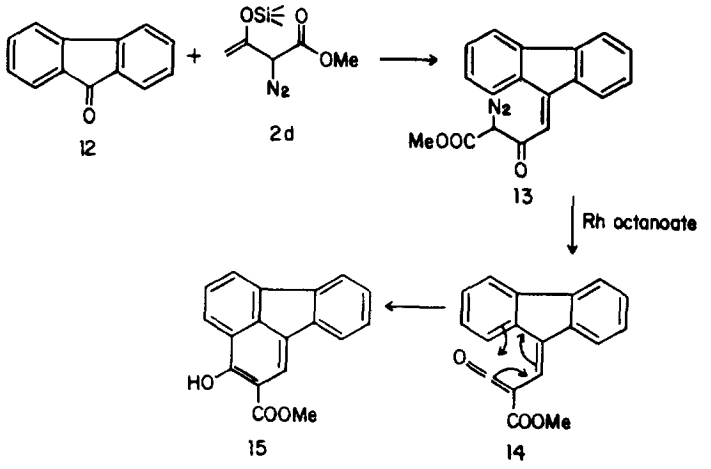
The direct cyclization product, β-naphthol **11,** was obtained by a Lewis acid promoted ring closure. Thus, diazoketone **8** was allowed to react in a CH_2Cl_2 solution with two equivalents of BF_3-etherate at room temperature for two days. Product **11**was isolated by flash chromatography in 45% yield.



Proton and C-13 NMR chemical shift data[10] proved inconclusive in determining the precise structures of the two cyclization products derived from **8**.[10] Coupled ^{13}C spectra, however, were diagnostic. The spectrum of **10** showed a pentet (J=5Hz) for the ester carbonyl which indicates the presence of an additional hydrogen (H_3) within three bonds of the carbonyl group. Further support came from ^1H NOE difference

spectroscopy where irradiation of the methoxy group yielded NOE's to the aromatic proton singlet (H_3) and to the hydroxy at 12.0 ppm. These same experiments also confirmed the BF_3 mediated ring closure product as **11**. In the coupled ^{13}C spectrum the ester carbonyl was a quartet, spin-spin coupled only to the methyl group thus proving that no other protons are within three bonds. When irradiating the methyl ester group, NOE difference spectroscopy showed enhancement to the H_8 and the hydroxy at 12.2 ppm confirming the structure of **11**. Further structure proof was provided by the conversion of **10** to the known 1-hydroxy-4-phenyl-2-naphthoic acid,[7a,7b,11] followed by decarboxylation to 4-phenyl-1-naphthol.[7b,11] Similarly **11** was degraded to 4-phenyl-2-naphthol.[12]

These results represent an unequivocal structure proof for the cyclization products **10** and **11**. This efficient annelation method was further illustrated by the conversion of fluorenone **12** to **15**.[13] Again, the ring closure proceeded through Wolff rearrangement.



The structural assignment for similar cyclizations studies could have been influenced by the erroneous report of ref 5, and since detailed scrutiny is required to distinguish between the two isomeric structures, these results should be reexamined, considering our findings. Furthermore, the Wolff rearrangement pathway should be considered in all analogous ring closures.

Acknowledgments: We thank Dr. C.S. Rooney for enlightening discussions and for revising a structural assignment.

References and Notes:

1. (a) Karady, S.; Amato, J.S.; Reamer, R.A.; Weinstock, L.M. *J. Am. Chem. Soc.*, **1981**, *103*, 6765.
(b) Reider, P.J.; Grabowski, E.J.J. *Tetrahedron Lett.* **1982**, *23*, 2293.
2. (a) Kant, J.; Walker, D. G. in The Organic Chemstry of β-Lactams; Georg, G. I., Ed.; VCH Publishers, Inc. New York, 1992; p 179. (b) Encyclopedia of Reagents for Organic Synthesis; Paquette L. A., Ed.; J. Wiley& Sons, Ltd. Sussex , England, 1994; p 3733.

3. The $Rh(OAc)_2$ ring closure of the type **3** to **4** was first described by Ratcliffe, R.W.; Salzmann,T.N.; Christensen, B.G. *Tetrahedron Lett.* **1980**, *21*, 31. The use of the more soluble Rh octanoate was introduced by F.E. Roberts and W.K. Russ of these laboratories. We thank them for samples and procedures.
4. Since most of the products were not crystalline, the chromatographically purified intermediates were identified by spectral methods. Satisfactory IR and NMR spectra were obtained on all intermediates. Diagnostic data are summarized as follows: Apart from the usual signals associated with aromatic and ethoxy groups, the ^1H NMR spectrum of compounds **6a,c,d** showed a characteristic ABX pattern. **6a** ($CDCl_3$) d 3.3 (m, 2H, CH_2CO), 5.2 (m, 1H, CHOH). **6b** ($CDCl_3$) d 1.55 (s, 3H, CH_3), 3.0 and 3.8 (AB, 2H J=16 Hz, CH_2CO). Furan derivatives **7a,b,c,d** were isomeric mixtures as indicated by the doubling of most NMR signals associated with the alicylic ring. **7a**, ^1H NMR ($CDCl_3$) d 2.7 (ABX, 2H, CH_2CO), 4.5 and 4.7 (s, 1H, CHCOOEt), 5.2 and 5.7 (ABX, 1H, OCHO-). ^{13}C NMR ($CDCl_3$) dc 43.9 and 44.5 ($\underline{C}H_2CO$), 78.25 and 79.04 (Ø$\underline{C}$HO-), 80.2 and 80.9 (-$\underline{C}$-COOEt), 206.8 and 207.2 ($CH_2\underline{C}O$). **7b**, ^{1}HNMR ($CDCl_3$) d 1.5 and 1.7 (s, 3H, CH_3), 2.8 (AB, 2H, $\underline{C}H_2CO$), 4.4 and 4.6 (s, 1 H, H$\underline{C}$-COOEt).^{13}C NMR ($CDCl_3$) dc 27.4 and 30.7 (CH_3), 48.9 and 49.6 ($\underline{C}H_2CO$) 79.0 and 79.4 (H$\underline{C}$-COOEt), 82.2 and 83.1 (Ø$\underline{C}$O). The ^1H and ^{13}C NMR spectra of **7c** and **7d** were completely analogous to **7a**.
5. Taylor, E.C.; Davies, H.M.L. *Tetrahedron Lett.* **1983**, *24*, 5453, reported the preparation of the ethyl ester and ring substituted analogs of **8** by another route and that rhodium acetate catalyzed cyclization afforded the ethyl ester analog of **11**.
6. For recent reviews see: (a) Tao,Y.; McKervey, A. *Chem. Rev.* **1994**, *94*, 1091 (b). Adams, J.; Spero, D.M. *Tetrahedron Lett.* **1991**, *47*, 1765 .(c). Smith, A.B.; Dieter, R.K. *Tetrahedron Lett.* **1981**, *37*, 2407.
7. (a) The ethyl ester and free acid of **10** were described by Taylor, G.A. *J. Chem. Soc.* Perkins I, **1981**, 3132.(b) Tetenbaum, M.T.; Hauser, C.R. *J. Org. Chem.***1958**, *23*, 229.
8. The rhodium catalyzed decomposition of **8**, utilizing our conditions and the exact procedure described in ref 5, yielded 10 and only 1-2 LC area % of a peak corresponding to **11**.
9. Leung-Toung, R.; Wentrup, C. *J. Org. Chem.* **1992**, *57*, 4850.
10. **8** ^{13}C NMR ($CDCl_3$) dc 78.3 (C-N_2), 121.9 (C=$\underline{C}$-CO), 156.2 (Ø $_2\underline{C}$=C), 163.0 (COO$\underline{Me}$), 181.9 (CO). **10**, mp: 140-142 °C, ^1H NMR ($CDCl_3$) d 3.9 (s, OMe), 7.7 (s, H_3), 7.8 (m, H_5), 8.5 (m, H_8), 12.0 (s, OH). ^{13}C NMR ($CDCl_3$) dc 105.1 (C_2), 124.8 (C_3), 124.9 (C_{8a}), 131.2 (C_4), 135.4 (C_{4a}), 160.3 (C_1), 171.4 ($\underline{C}$OOMe). **11**, ^1H NMR ($CDCl_3$) d 4.1 (s, OMe), 7.1 (s, H_3), 7.8 (d, J = 8.8 Hz, H_5), 8.8 (d, J = 8.2 Hz, H_8) 12.2 (s, OH). ^{13}C NMR ($CDCl_3$) d_c 104.2 (C_1), 120.1 (C_3), 148.8 (C_4), 163.3 (C_2), 172.4 ($\underline{C}$OOMe).
11. The carboxylic acid was obtained by saponification of **10** with MeOH and 2n NaOH (2:1, 3 hr reflux) mp: 229-231 °C (lit.[7b] 227-228 °C). Thermal decarboxylation (200-230 °C, neat, 10 min) followed by vacuum sublimation, afforded 4-phenyl-1-naphthol, mp:136-138 °C (lit.[7b] 139-142 °C).
12. The carboxylic acid had mp: 158-161°C. 4-Phenyl-2-naphthol remained a resin and was identified by: ^1H NMR ($CDCl_3$)d 7.05 (d, J = 2.5 Hz, H_1), 7.15 (d, J = 2,5 Hz, H_3).
13. Identification of this compound is based on the coupled ^{13}C spectrum, where the ester carbonyl gave a pentet indicating coupling to the ester methyl and to an additional hydrogen. NOE difference spectroscopy was also diagnostic: irradiation of $COOCH_3$ gave NOE enhancement to the -OH and the isolated C-H. These spectral characteristics are analogous to those of **10**.

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