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Intramolecular O-H Insertion Reaction of Azido Substituted Diazoesters and its Relevance to the Mechanism of the Allylic Azide Rearrangement

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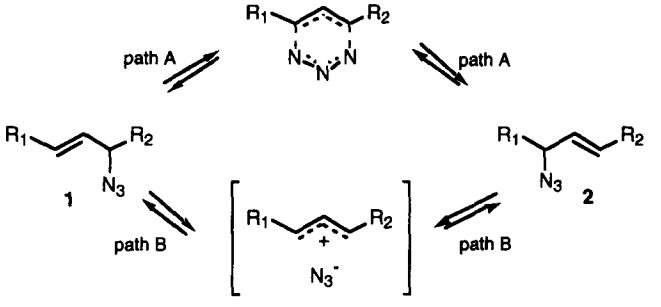
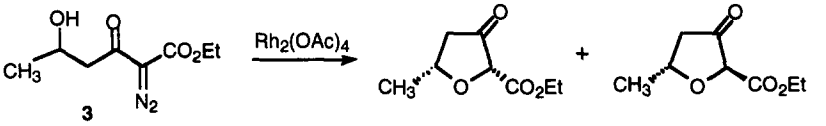
Abstract: The $Rh_2(OAc)_4$ catalyzed decomposition of γ-azido-δ-hydroxy diazoesters affords 3(2H)-furanones derived by a sequential O-H insertion followed by a concerted [3,3]-sigmatropic shift of the azido group. © 1997 Elsevier Science Ltd.

In 1960, Gagneux, Winstein, and Young reported that allylic azides exist as an equilibrating mixture of regioisomers.[1] They showed that α- and δ-methylallyl azide rapidly form an equilibrium mixture of the two isomers and the rate and equilibrium constants of this rearrangement were measured. Two mechanisms can be postulated to rationalize this equilibration: (1) a concerted [3,3]-sigmatropic rearrangement (path A) in which the stereochemical integrity of the molecule is preserved and (2) a dissociative process involving ion-pair formation (Path B) whereby the initial stereochemistry can be lost.



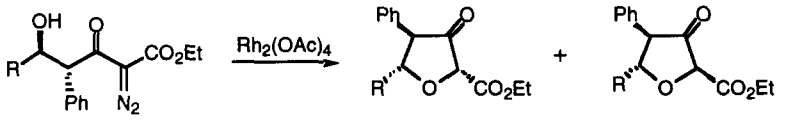
It was noted that the rearrangement was remarkably insensitive to changes in solvent as well as to alkyl substitution.[1-3] These observations are indicative of very little charge separation in the transition state, and it is generally assumed that the equilibration occurs *via* a cyclic transition state (*i.e.*, Path A). Recent examples of allylic azide isomerizations are available which support this notion.[4,5] No definitive proof has been presented to date, however, which unequivocally distinguishes between the above two mechanistic possibilities. Lacking a well-defined regio- and stereochemistry, the rearrangement has been underutilized and no general approach to effecting a controllable stereoselective isomerization has been reported. During the course of our studies dealing with the O-H insertion reaction of α-diazo-γ-azido-δ-hydroxy ketoesters, we encountered a novel reaction which bears significantly on the mechanism of the allylic azide rearrangement (*vide infra*). The results of these investigations are reported herein.

Transition metal mediated C-H insertion reactions have been extensively used in the synthesis of both theoretically interesting compounds and natural products.[6] In contrast, the use of diazo carbonyl precursors to prepare oxygen based heterocycles *via* O-H insertions is quite scarce.[7-9] We have been studying several aspects of the Rh(II)-catalyzed O-H insertion reaction in order to increase its synthetic utility toward the synthesis of 3(2H)-furanones.[10] While carrying out these studies, we observed that various δ-hydroxy diazo ketoesters[11] underwent smooth Rh(II)-catalyzed cyclization to afford 2-carboethoxy substituted 3(2H)-furanones.[12] For example, the $Rh_2(OAc)_4$ catalyzed reaction of diazoester **3** in CH_2Cl_2 at 25 °C afforded the expected O-H insertion products as a 2:1-mixture of diastereomers, the ratio of which could be determined from the ^{1}H-NMR spectrum of the crude mixture. Silica gel chromatography gave pure samples of both the *cis* and *trans* substituted furanones **4** and **5** in 90% yield. Although the Rh(II)-catalyzed reaction of **3** resulted in the formal insertion of the carbenoid into the O-H bond, it is perhaps better considered as proceeding *via* ylide formation or by the intermediacy of carbocations.[9] The stage at which the new metal-free sp^3 center is established remains unknown.

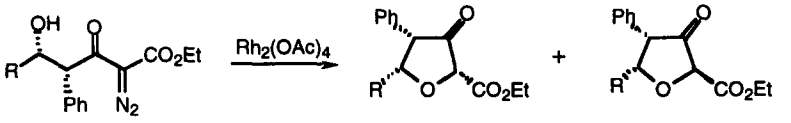


3 **4** (60%) **5** (30%)

Decomposition of the *anti* (**6**/**7**) and *syn* (**8**/**9**) δ-hydroxy diazoesters was carried out in a similar fashion, producing a 3:1-mixture of diastereomers which were separable by silica gel chromatography. In all four cases, the major product formed corresponded to the 2,5-substituted *cis*-isomer. The assignment of the relative stereochemistry was based on its characteristic ^{1}H and ^{13}C NMR spectra. It should be noted that the stereochemical relationship between the 4 and 5-substituents of the starting



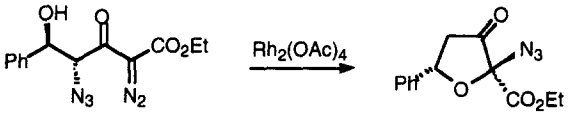
anti **6**; R=Me, **7**; R=Ph — **10**; R=Me (69%), **12**; R=Ph (65%) — **11**; R=Me (23%), **13**; R=Ph (21%)



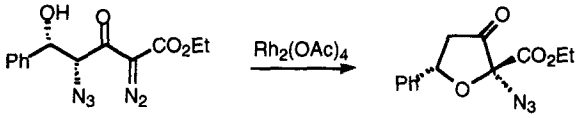
syn **8**; R=Me, **9**; R=Ph — **14**; R=Me (67%), **16**; R=Ph (66%) — **15**; R=Me (22%), **17**; R=Ph (20%)

materials is retained in the final products, as the O-H insertion reaction does not affect the relative disposition of these two stereocenters.

Extension of the carbenoid insertion methodology to the *anti* and *syn*-isomers of γ-azido-δ-hydroxy diazo ketoesters **18** and **19** was next investigated. Interestingly, the $Rh_2(OAc)_4$ catalyzed decomposition of these diazoesters gave rise to the unexpected 3(2H)-furanones **20** and **21** in *ca* 90% yield.[13] In both cases, only a single diastereomer was obtained. We believe that the mechanism for their formation

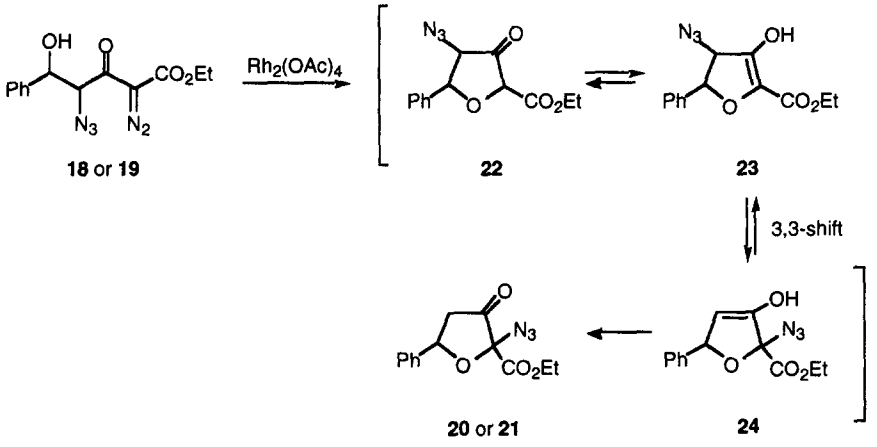


anti-**18** **20**



syn-**19** **21**

involves insertion of the rhodium carbenoid into the adjacent O-H bond to first produce the 4-azido substituted 3(2H)-furanone **22** as a transient which rapidly rearranges to afford the observed products. The results strongly suggest that the enol form of the initially generated furanone (*i.e.*, **22**→**23**) undergoes a subsequent [3,3]-sigmatropic shift with complete stereospecificity in a suprafacial manner.[14]



18 or **19** **22** **23**

20 or **21** **24**

In conclusion, the stereospecific transfer of the azido group to the migration terminus in the rearranged 3(2H)-furanone provides convincing support for a concerted [3,3]-shift as the mechanism for the interconversion of allylic azides.

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13. Ethyl *anti*-2-azido-3-oxo-5-phenyl-tetrahydrofuran-2-carboxylate (**20**); ^{1}H-NMR ($CDCl_3$, 300 MHz) δ 1.35 (t, 3H, J = 7.0 Hz), 2.75 (dd, 1H, J = 18.0 and 10.0 Hz), 3.04 (dd, 1H, J = 18.0 and 6.0 Hz), 4.37 (q, 2H, J = 7.0 Hz), 5.46 (dd, 1H, J = 10.0 and 6.0 Hz) and 7.30-7.50 (m, 5H); ^{13}C-NMR ($CDCl_3$, 75 MHz) δ 14.0, 43.2, 63.5, 78.5, 91.2, 126.3, 128.9, 129.1, 138.2, 164.7 and 202.5. Ethyl *syn*-2-azido-3-oxo-5-phenyl-tetrahydrofuran-2-carboxylate (**21**); ^{1}H-NMR ($CDCl_3$, 300 MHz) δ 1.37 (t, 3H, J = 7.0 Hz), 2.77 (dd, 1H, J = 18.0 and 8.5 Hz), 3.14 (dd, 1H, J = 18.0 and 7.0 Hz), 4.33 (q, 2H, J = 7.0 Hz), 5.59 (dd, 1H, J = 8.5 and 7.0 Hz) and 7.35-7.45 (m, 5H); ^{13}C-NMR ($CDCl_3$, 75 MHz) δ 14.1, 43.7, 63.1, 78.2, 90.6, 126.5, 128.8, 129.4, 139.0, 165.2 and 203.5.
14. A related set of results was encountered using the *anti* and *syn* diastereomers of ethyl 4-azido-2-diazo-5-hydroxy-3-oxo-hexanoate.[11]

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