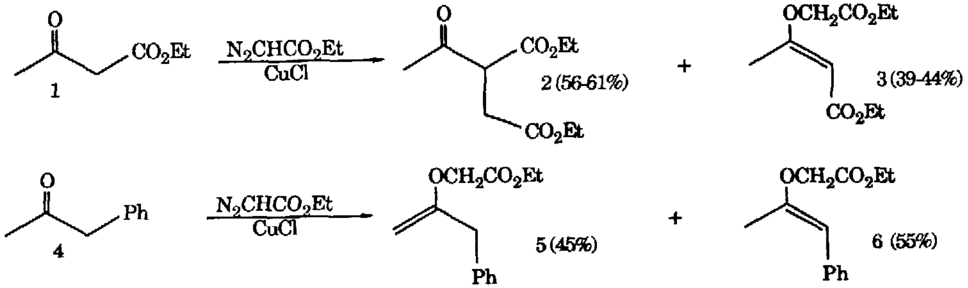
Tetrahedron Letters,Vol.30,No.31,pp 4093-4096,1989 0040-4039/89 $3.00 + .00
Printed in Great Britain Maxwell Pergamon Macmillan plc

CATALYST DEPENDENT MECHANISTIC PATHS IN THE REACTIONS OF ETHYL DIAZOACETATE WITH β-KETO ESTERS

Andrew C. Lottes, John A. Landgrebe*, and Kristin Larsen
Department of Chemistry, University of Kansas
Lawrence, Kansas 66045

Summary: The catalyzed decomposition of ethyl diazoacetate in the presence of β-keto esters produces regioisomeric enol ethers and the diester from formal carbenoid insertion into the α-C-H bond. The product distribution is very catalyst dependent.

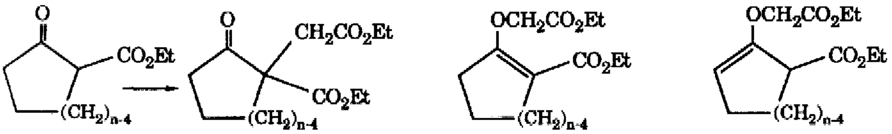
We have reported previously that the CuCl or $Rh_2(OAc)_4$ catalyzed decomposition of ethyl diazoacetate in the presence of various alkyl or phenyl substituted acyclic and cyclic ketones leads to enol ethers with understandable regiochemistry (and where applicable, stereochemistry) as the only 1:1 products, and that the product distribution was independent of catalyst.[1] We now report observations that for various β-keto esters, not only is the regiochemistry of enol ether formation catalyst dependent, but in the presence of CuCl, significant amounts of a new 1:1 product are observed. An example is shown below for ethyl acetoacetate (**1**) with a CuCl catalyst, and compared to the results previously reported under identical conditions for methyl benzyl ketone (**4**).[1]



In both cases, enol ethers **3** and **6** are formed with exclusive (E)-stereochemistry (confirmed by suitable NOE experiments) consistent with the mechanistic model developed previously.[1] Somewhat surprising is the observation that β-keto ester **1** produces none of the less-substituted enol ether, but instead forms diester **2**.

The results for various cyclic β-keto esters are summarized in Table I. What seems clear is that the use of $Rh_2(OAc)_4$ produces far less of the diester-type product than when CuCl is used. In addition, the regioselectivity of enol ether formation favors the less-substituted product when CuCl is used, and with the exception of the 7-membered ring, the more substituted product when $Rh_2(OAc)_4$ is employed. Although the more substituted enol ether is more thermodynamically stable, suitable control experiments on the less-substituted enol ether from 2-carbethoxycyclopentanone have clearly shown that no equilibration of the regioisomers occurs under the reaction conditions in the presence of either catalyst.[2] Isolated yields of the combined 1:1 adducts were in the range 40-55%.[3]

Table I. Product Distribution for cyclic β-Keto Esters[a]



n	CuCl	$Rh_2(OAc)_4$	CuCl	$Rh_2(OAc)_4$	CuCl	$Rh_2(OAc)_4$
5	12-13	2	36-38	57	49-51	41
6	42-43	4-5	18-19	83-85	38-39	11-13
7	64-65	10-11	5-6	13-15	31-33	74-76

---

[a] Expressed as a percent of all 1:1 adducts; results represent at least three runs; a 7-fold excess of ketone served as the solvent.

In contrast, note that for the catalyzed reaction of ethyl diazoacetate with 2-methyl and 2-phenylcycloalkanones summarized in Table II, no diester has ever been observed, the results are identical for both CuCl and $Rh_2(OAc)_4$, and the less-substituted enol ether always dominates.[1]

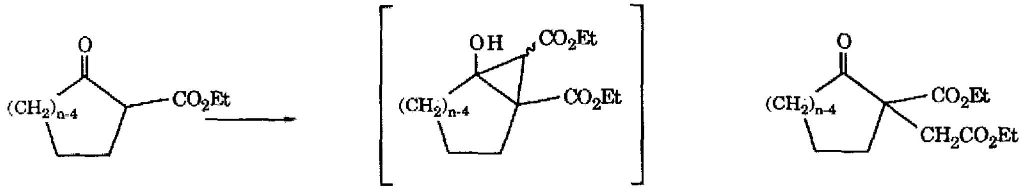
Table II. Enol Ether Distribution for 2-Methyl and 2-Phenylcycloalkanones[a]

Substituent	Ring Size	More-Substituted Prod.	Less-Substituted Prod.
Me	5	12.5-16.7	83.3-87.5
Me	6	7.7- 7.1	92.3-92.9
Ph	5	43.5	56.5
Ph	6	40	60

---

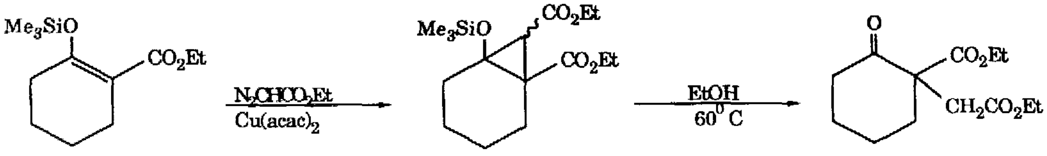
[a] Expressed as a percent of all 1:1 adducts; for liquid ketones, a 7-fold excess served as solvent; for solid ketones, a 6-fold excess was dissolved in CCl_4; results are for at least three runs per ketone and are identical for CuCl and $Rh_2(OAc)_4$.

While the reasons why substantial amounts of diester form from the α-ethoxycarbonyl ketones in Table I in the presence of CuCl but not $Rh_2(OAc)_4$ remain speculative, related differences in the chemical behavior of carbenoids derived from diazo esters have been noted.[4] It is of special interest that because our observations are contrary to the known effectiveness of rhodium(II) carboxylates in promoting C-H insertion,[4-7] the latter process is probably not involved. In fact, we suspect that diester **9** arises from cyclopropanol **8** produced from the addition of the copper carbenoid to the enol of **7**.



7 8 9

Such a path is made plausible by our observation that silyl cyclopropyl ether **11** prepared from **10** by the method of Reissig and Hirsch,[8] was converted to diester **12** in an isolated yield of 71% after heating for 24 h at 60 °C in ethanol.[9] Regioselective opening of the intermediate cyclopropanol under electrophilic conditions has some precedent.[10-14]



10 11 12

Although we have no unified explanation for the interesting differences in regioselectivity of enol ether formation as a function of catalyst for the various α-ethoxycarbonyl ketones in Table I, it seems inescapable that the catalyst must be present during the 1,4-sigmatropic shift of hydrogen. These interesting mechanistic questions remain under active investigation.

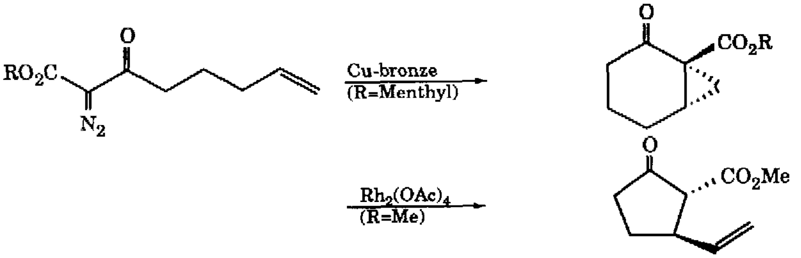
Acknowledgement: Supported by the University of Kansas General Research Fund; a Phillips Petroleum Company Fellowship for A.C.L.; an NSF REU Fellowship for K.L.

References and Notes

1. Lottes, A. C.; Landgrebe, J. A.; Larsen, K. Previous communication, this issue.
2. Equilibration does occur in benzene with $AlCl_3$ and leads to approximately 80-85% of the

more-substituted enol ether at 78 °C.

3. Structures of newly prepared compounds were identified by a combination of ^{1}H and ^{13}C NMR, IR, and MS (including an exact mass).
4. (a) Taber, D. F.; Saleh, S. A.; Korsmeyer, R. W. *J. Org. Chem.* **1980**, *45*, 4699; (b) Taber, D. F.; Petty, E. H. *J. Org. Chem.* **1982**, *47*, 4808; These articles note a preference for addition by copper carbenoids versus insertion by rhodium carbenoids derived from the nearly identical diazo esters shown below.



5. Doyle, M. P. *Chem. Rev.* **1986**, *86*, 919.
6. Wenkert, E.; Davis, L. L.; Mylari, B. L.; Solomon, M. F.; da Silva, R. R.; Shulman, S.; Warnet, R. J.; Ceccherelli, P.; Curini, M.; Pellicciari, R. *J. Org. Chem.* **1982**, *47*, 3242.
7. (a) Taber, D. F.; Raman, K. *J. Am. Chem. Soc.* **1983**, *105*, 5935; (b) Taber, D. F.; Ruckle, R. E., Jr. *Tetrahedron Lett.*, **1985**, *26*, 3059.
8. Reissig, H.-U.; Hirsch, E. *Angew. Chem., Inter. Ed. Engl.* **1980**, *19*, 813.
9. A trace of 2,3-diethoxycarbonylcycloheptanone was also noted. Treatment of **11** with 1 *M* tetraethylammonium fluoride in THF resulted in a 1.1:1 mixture of diester **12** and 2,3-diethoxycarbonylcycloheptanone.
10. (a) DePuy, C. H.; Breitbeil, F. W.; DeBruin, K. R. *J. Am. Chem. Soc.* **1966**, *88*, 3347; (b) DePuy, C. H.; Breitbeil, F. W. *J. Am. Chem. Soc.* **1963**, *85*, 2176.
11. Wharton, P. S.; Bair, T. I. *J. Org. Chem.* **1966**, *31*, 2480.
12. Davis, Br. R.; Woodgate, P. D. *J. Chem. Soc., Chem. Commun.* **1966**, 65.
13. Wenkert, E.; Kariv, E. *J. Chem. Soc., Chem. Commun.* **1965**, 570.
14. Girard, C; Conia, J. M. *Tetrahedron Lett.* **1974**, 3333.

(Received in USA 25 April 1989)