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Letter

Pseudourea-mediated dehydration of tertiary and benzylic alcohols

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Tertiary and benzylic alcohols readily form pseudoureas, which eliminate in good yield either at room temperature or upon gentle warming. In contrast, the dehydration of primary and secondary alcohols *via* this procedure requires elevated temperatures and gave low yields.

The final step in our synthesis of faveline methyl ether (**2**) was the dehydration of alcohol **1** at 140 °C using $KHSO_4$.[1] However, the formation of byproducts under these acidic conditions led us to consider other methods for elimination.[2] While carbamates[3a] and acetates[3b] typically eliminate in good yield at 375–480 °C and 200–250 °C, respectively, the elimination of xanthates requires temperatures between 100 and 250 °C.[3c] We were curious whether the pseudourea,[4a,b] generated *in situ* by treating alcohol **1** with a carbodiimide (Scheme 1), would dehydrate through an E_i mechanism (*i.e.*, **i** → **ii** → **2**), typical of pyrolytic eliminations, or an E_1 mechanism (*i.e.*, **i** → **iii** → **iv** → **2**).[4c–e] We found that treatment of **1** with a catalytic quantity of CuCl and dicyclohexylcarbodiimide (DCC) in THF generated the pseudourea *in situ*; heating the crude pseudourea at 90 °C for 4 h gave **2** in 76% yield, along with 1,3-dicyclohexylurea (DCU).[5] This prompted us to investigate the generality of this dehydration procedure.[6]

Eight benzylic alcohols were studied (Chart 1). The dehydration of tertiary benzylic alcohols **4** and **7** occurred in a single operation and at lower temperatures than required for the dehydration of secondary alcohols **3** and **6**. While the formation of a styrenyl double bond is generally favored, in the cases of secondary alcohol **9** and tertiary alcohol **10** only ether formation occurred. These results are best accounted for by an E_1 process.

The pseudourea-mediated dehydration of tertiary alcohols **12** and **13** gave mixtures of the di- and trisubstituted olefins (Chart 2). Here the pseudourea moiety functions as an easily ionized leaving group, thereby favoring an E_1 mechanism. Carrying out the reaction in polar aprotic solvents, such as DMF, THF, acetonitrile or acetone, had little influence on the elimination yield.

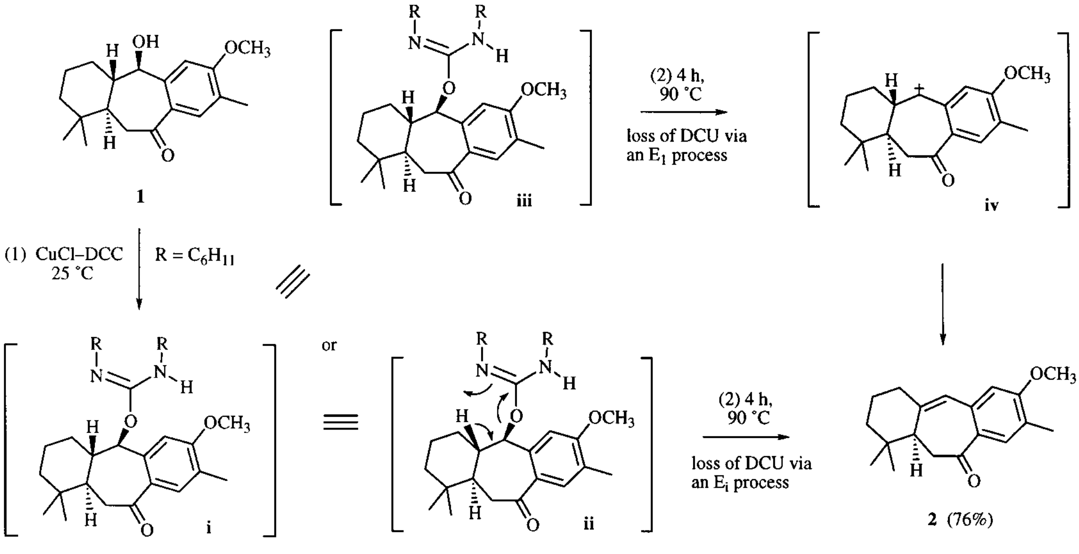
The elimination of the pseudourea derived from simple primary and secondary alcohols requires higher reaction temperatures than those needed for benzylic or tertiary alcohols. For example, hexanol was converted to 1-hexane in <5% yield when the crude pseudourea was heated at 260–290 °C for 6 h (Chart 3). Like hexanol, 2-methylheptan-3-ol (**15**) and cyclohexanol (**16**) readily formed the corresponding pseudoureas; however, the elimination of these intermediates proceeded in poor yield. In contrast, the formation of a conjugated double bond facilitates elimination (*cf.* entries **11** and **17**). This observation led us to examine the dehydration of allylic alcohols. Three allylic alcohols were dehydrated to generate conjugated dienes (Chart 4). While the elimination of diene **18** was straightforward, not all of these eliminations were regiospecific. For example, the dehydration of geraniol produced 3,7-dimethyl-1,3,6-octatriene as a 1 : 1 mixture of *E* and *Z* isomers. In contrast, alcohol **20** produced ureas **20a** and **20b**, as a result of a [3,3]-sigmatropic rearrangement.[7]

In summary, we have found mild conditions suitable for the efficient dehydration of many tertiary and benzylic alcohols. This method also permits the dehydration of secondary and allylic alcohols.

Notes and references

1 G. Majetich, R. Hicks, Y. Zhang, X. Tian, T. L. Feltman, J. Fang and S. Duncan, Jr., *J. Org. Chem.*, 1996, **61**, 8169.

2 For other practical, non-pyrolytic-based dehydration procedures, see: (*a*) J. C. Martin and R. J. Arhart, *J. Am. Chem. Soc.*, 1971, **93**, 4327; (*b*) E. M. Burgess, H. R. Penton, Jr., and E. A. Taylor, *J. Am. Chem. Soc.*, 1970, **92**, 5224.



Scheme 1

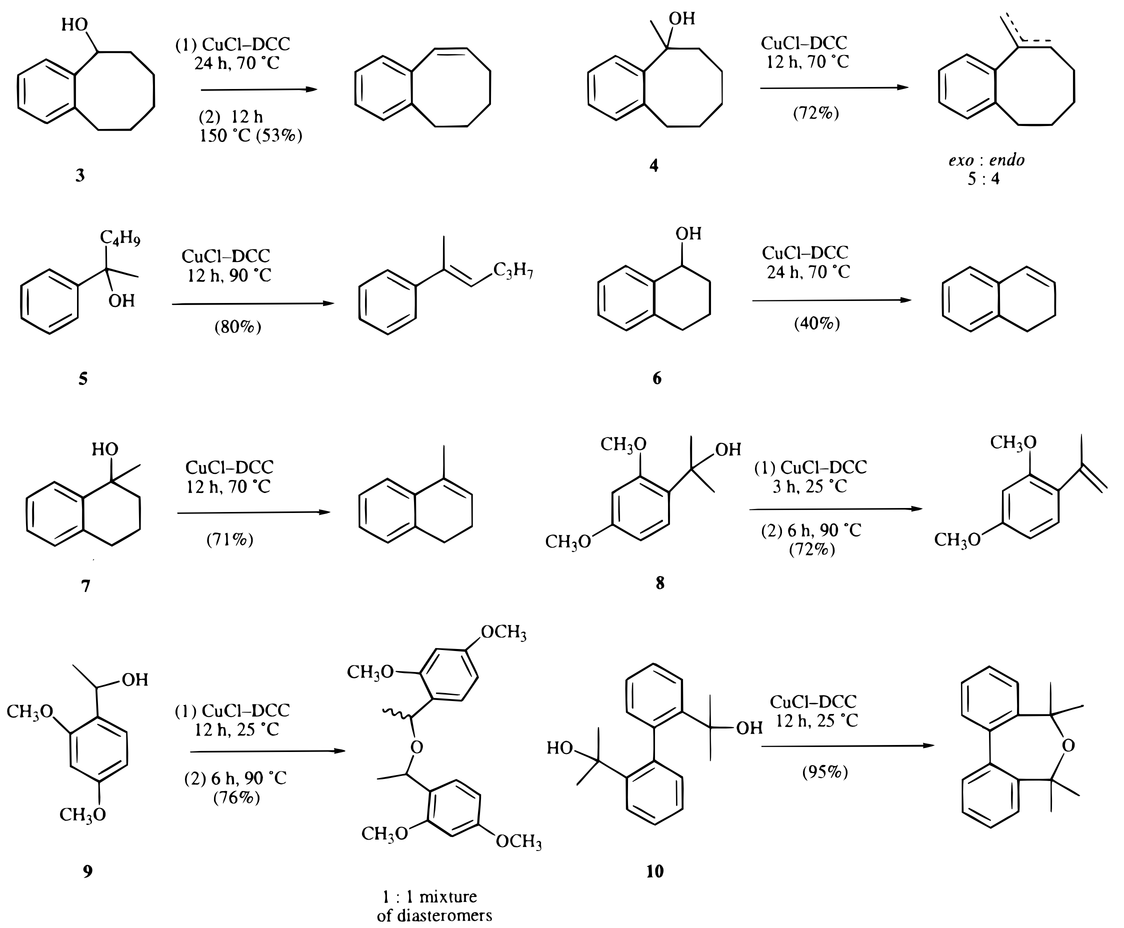


Chart 1

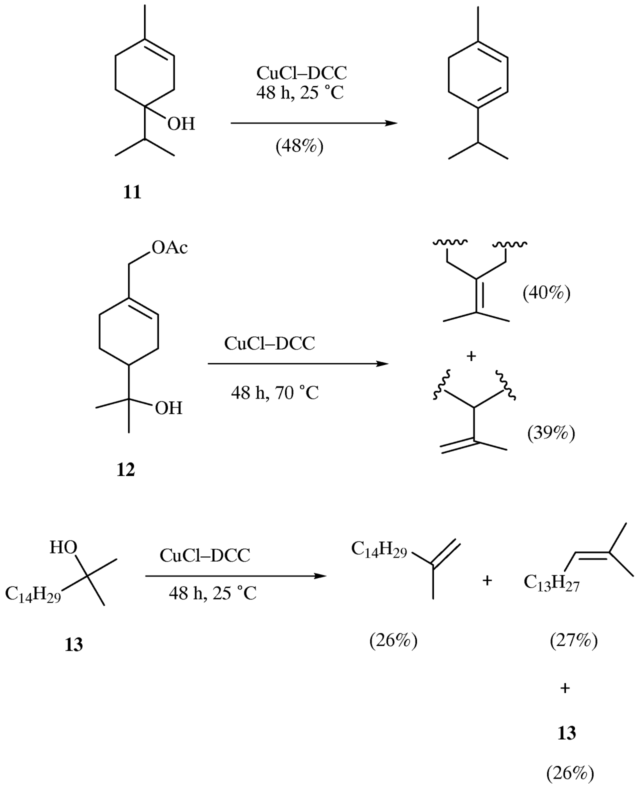


Chart 2

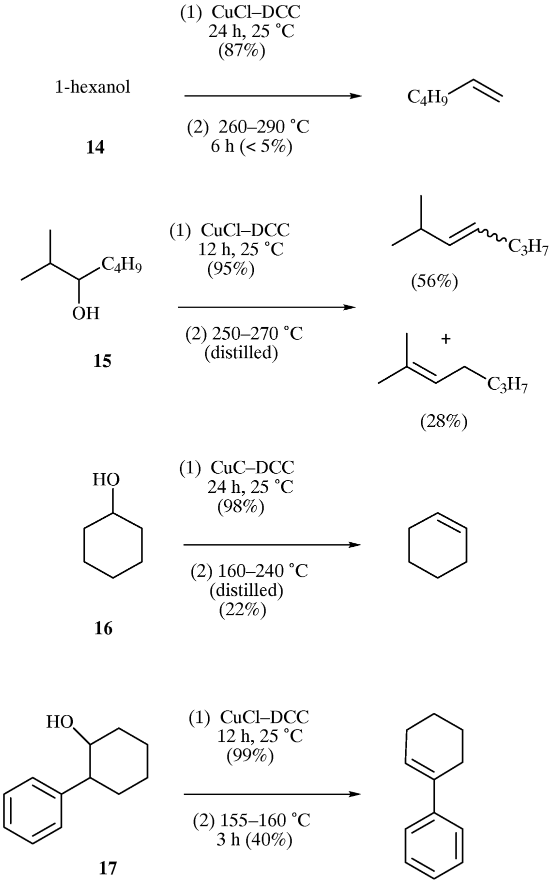


Chart 3

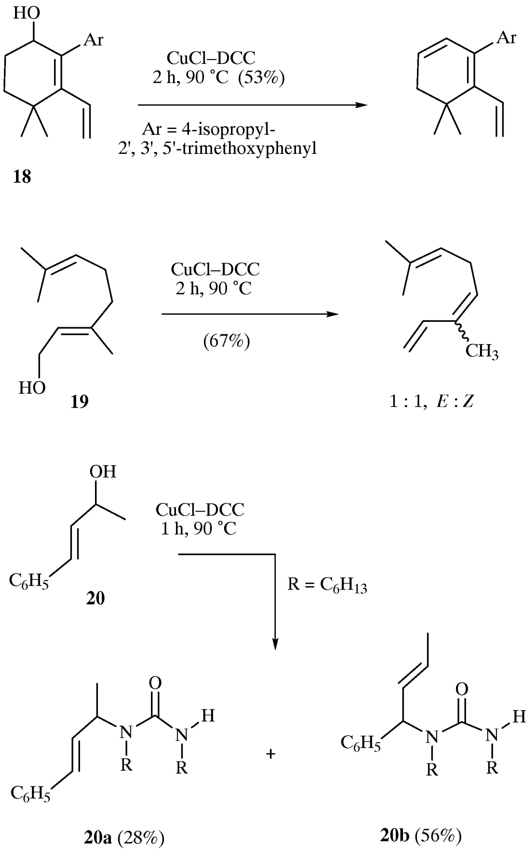


Chart 4

3 (*a*) R. F. Atkinson, T. W. Balko, T. R. Westman, G. C. Sypniewski, M. A. Carmody, C. T. Pauler, C. L. Schade, D. E. Coulter, H. T. Pham and F. Barea, *J. Org. Chem.*, 1981, **46**, 2804; (*b*) C. H. DePuy and R. W. King, *Chem. Rev.*, 1960, **60**, 431; (*c*) G. L. O'Connor and H. R. Nace, *J. Am. Chem. Soc.*, 1953, **75**, 2118.

4 For reviews of the chemistry of pseudoureas, see: (*a*) E. Schmidt and F. Moosmuller, *Liebigs Ann. Chem.*, 1955, **597**, 235; (*b*) L. J. Mathias, *Synthesis*, 1979, 561. Three examples of pseudourea-mediated dehydrations are known. However, each case involves the dehydration of a β-hydroxyl carbonyl compound, see: (*c*) E. J. Corey, N. H. Anderson, R. M. Carlson, J. Paust, E. Vedejs, I. Vlattas and R. E. K. Winter, *J. Am. Chem. Soc.*, 1968, **90**, 324; (*d*) M. J. Miller, *J. Org. Chem.*, 1980. **45**. 3131; (*e*) C. Alexandre and F. Rouessac, *Bull Soc. Chem. Fr.*, 1971, 1837.

5 (*a*) The spectroscopic data obtained for all compounds were consistent with the assigned structures. (*b*) Reaction conditions have not been optimized. (*c*) All yields are isolated yields. (*d*) Other carbodiimides, such as DIC (diisopropylcarbodiimide) or EDC (*N*-ethyl-*N*'-(3-dimethylaminopropyl)carbodiimide hydrochloride), were equally effective dehydrating agents.

6 *A general procedure:* The alcohol (0.50–2.00 mmol) was combined with 1.50 equiv. of the carbodiimide and 0.10 equiv. of finely powdered CuCl. Sufficient THF (approx. 10–15 mL) was added to dissolve the reactants and permit the uniform distribution of the insoluble catalyst. The reaction mixture was stirred at room temperature until TLC analysis confirmed that the starting alcohol had been consumed (<30 min). The reaction mixture was then concentrated *in vacuo* and the crude residue was placed under nitrogen. When dehydration was sluggish at room temperature, the reaction mixture was slowly heated until TLC analysis indicated that elimination was occurring; this temperature was maintained until the consumption of the pseudourea was complete. Low boiling olefins were collected as a distillate. Standard ethereal workup, followed by purification *via* silica gel chromatography, permitted the isolation of the olefin(s).

7 S. Tsuboi, P. Stromquist and L. E. Overman, *Tetrahedron Lett.*, 1976, **15**, 1145.

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