Organic Preparations and Procedures International

ISSN: 0030-4948 (Print) 1945-5453 (Online) Journal homepage: http://www.tandfonline.com/loi/uopp20

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**To cite this article:** Edmund J. Eisenbraun , Kirk W. Payne & Jeremy S. Bymaster (2000) DEHYDRATION OF CEDROL TO α-CEDRENE USING COPPER(II) SULFATE AND OTHER ACIDIC SALTS, Organic Preparations and Procedures International, 32:6, 557-561, DOI: 10.1080/00304940009355950

**To link to this article:** http://dx.doi.org/10.1080/00304940009355950

Published online: 11 Feb 2009.

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ORGANIC PREPARATIONS AND PROCEDURES INT., 32 (6), 557-561 (2000)

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# DEHYDRATION OF CEDROL TO α-CEDRENE USING COPPER(II) SULFATE AND OTHER ACIDIC SALTS

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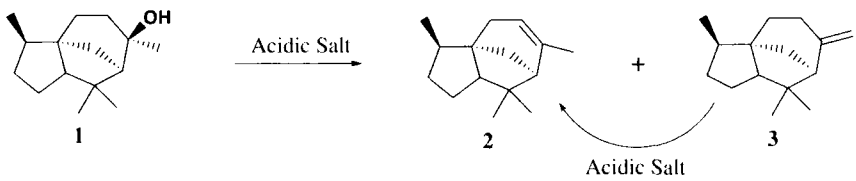
We sought pure α-cedrene (**2**) *via* the dehydration of cedrol (**1**). The acid-catalyzed dehydration of alcohols to alkenes is well documented through numerous procedures using a wide variety of dehydrating agents.[1] Heating cedrol and anhydrous $CuSO_4$ under reflux[2a] or in a Kugelrohr distillation apparatus proved unsatisfactory because some cedrol invariably survived the dehydration by subliming to the condenser or codistilling to the walls of the receiver. Complete dehydration and successful conversion to pure **2** was achieved by heating cedrol and anhydrous $CuSO_4$ in refluxing benzene using a modified Dean-Stark/molecular (mol) sieve apparatus containing AW-500 mol sieve to continuously dry the recycling solvent.[3] As shown later, the entire process serves to increase the reaction rate and complete the isomerization of β-cedrene (**3**) to α-cedrene.




This successful preparation of pure **2** suggested that the reaction could serve as a valuable and sensitive screen to evaluate other acidic reagents and to gain additional information about the role of water during dehydration. The aforementioned apparatus and procedure[3] were used to obtain the most effective molar ratio of cedrol to $CuSO_4$, required for studying the reaction, as shown by capillary GC. The final dehydration method resulted in 100% conversion to >99% pure α-cedrene and a 93-96% distilled yield. This method, with a molar ratio of alcohol to catalyst of 50:1 (50% unreacted alcohol at 1 h), is more effective than the Hoffman method[2] with a molar ratio 8.33:1 (84% unreacted at 1 h).

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GC studies (Figure 1) show **1** disappearing with simultaneous formation of **2** and **3**. Continuing the reaction leads to pure **2**. Since all previous $CuSO_4$-catalyzed dehydrations of alcohols[2] specify the use of the anhydrous salt, we sought evidence obviating the need for the anhydrous salt which requires a high temperature for preparation. To answer this question, comparison dehydration studies using the same molar concentration (50:1) of **1** to $CuSO_4$ (pentahydrate, monohydrate, and anhydrous) were carried out. The results are presented in Figure 2, which show the anhydrous salt to have a 17% faster reaction time. However, since all of these reactions resulted in the same purity of product and isolated yields, in our view the use of the anhydrous salt is not necessary This statement is qualified by the need to use an azeotroping solvent and mol sieves to remove water from the reaction. A separate dehydration experiment with complete retention of water by recycling the solvent and omitting the mol sieves was successful. However, the reaction time was substantially increased (ca. 50%) and **3** failed to be completely converted to **2**.

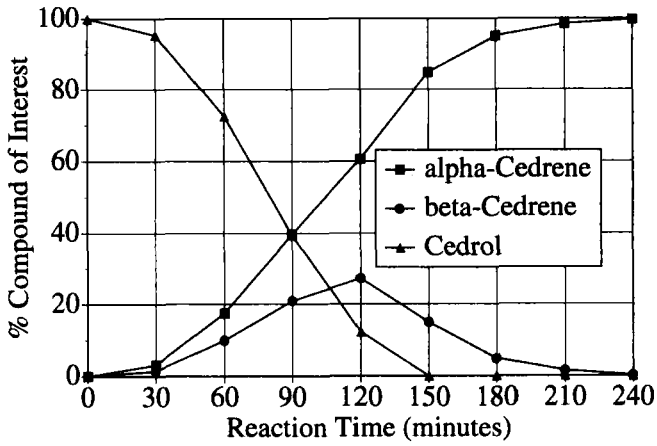


**Fig. 1.** Dehydration of **1** with $CuSO_4 \cdot 5H_2O$ (50:1)

The Bronsted acidity of inorganic sulfates is considered to result from polarized water molecules bonded to the metal cation with dissociation of the water related to the electronegativity of the cation.[4] Because the reaction produces water and a 50:1 ratio of cedrol to $CuSO_4$ is used, it is likely that the anhydrous salt is rapidly converted to a variety of hydrated salts with acidic sites which form and disappear during the *in situ* dehydration as the reaction proceeds.[5] Thus, the shape of the product curve representing β-cedrene (**3**) in Figure 1 is probably the result of a shift from Bronsted sites to sites exhibiting a higher order of acidity.[2c] This transition appears to be essential for the conversion of **3** to α-cedrene (**2**). It is of interest that once the reaction has passed an induction period, the slope of the pentahydrate curve (Figure 2) is indicative of a faster reaction rate than shown by the slope of the anhydrous curve, thus reinforcing the conclusion that preparation of the anhydrous salt is superfluous. To determine whether the behavior described in Figure 2 is also obtained with other inorganic sulfates, an analogous series of dehydration experiments at a 10:1 ratio were carried out using $FeSO_4$



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(heptahydrate, monohydrate, and anhydrous). These experiments indicate that the monohydrate salt is more reactive than the anhydrous salt; all forms produced pure **2**.

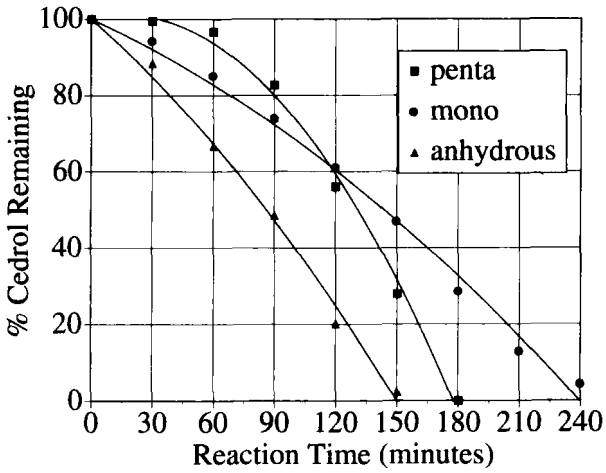


**Fig. 2.** Dehydration of **1** with $CuSO_4$ in Various Degrees of Hydration (50:1)

The study was extended to the hydrated inorganic sulfates listed alphabetically in Table 1. GC studies showed a similar pattern to the reaction curves of Figure 1. A ranking of their effectiveness, based on their reactivity and the resulting purity of α-cedrene, is similar to that found earlier for the free salts[2c] or salts supported on silica.[2g]

**Table 1.** Dehydration Effectiveness of Sulfate Salts[a]

| Reagent | Hydrate | Rating | Time to max yield (min.) | α-Cedrene purity |
|---|---|---|---|---|
| Aluminum potassium | tri[b] | 6 | 90 | 99.9 |
| Ammonium iron(III) | dodeca | 4 | 60 | 99.9+ |
| Chromium(III) | hydrate | 3 | 60 | 99.4 |
| Cobalt(II) | hepta | 10 | 240 | 99.7 |
| Copper(II) | penta | 2 | <60 | 99.9 |
| Iron(II) | hepta | 9 | 135 | 99.9+ |
| Iron(III) | penta | 1 | 15 | 99.9 |
| Manganese(II) | mono | 12[c] | 150 | 82.4 |
| Nickel(II) | hexa | 8 | 90 | 99.5 |
| Potassium hydrogen | | 11[d] | 210 | 99.3 |
| Sodium hydrogen | mono | 5 | 90 | 99.9 |
| Zinc(II) | hepta | 7 | 90 | 99.8 |

a) Alcohol to catalyst ratio of 10:1. b) Dodecahydrate exhibited stirring problems and incomplete conversion of **3** to **2**. c) Incomplete conversion of **3** to **2**. d) Alcohol to catalyst ratio of 5:1.



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Other acidic catalysts including $CuCl_2$, organic acids, and acidic resins were selected to expand the scope of this study. Phosphoric acid (85%) and *p*-toluenesulfonic acid monohydrate showed equivalent performance to the sulfates shown in Table 1. Benzenesulfonic acid proved unacceptable due to the presence of the anhydride, found by GC/MS, in the commercial reagent and in the product. Cupric chloride caused formation of side-products; therefore, inorganic chlorides were excluded. Organic acids (malonic, phthalic, succinic, sulfamic, and tartaric) were essentially unreactive as were the chloroacetic acids (mono-, di-, tri- with pKa's of 2.85, 1.48, and 0.7 respectively).[6] The ion-exchange resins either caused side products (Amberlyst-15) or were unreactive (Amberlite-IRC 50CP).

In addition to high yield and purity of product, the technique described provides a means of reaction-temperature control through selection of azeotroping solvent and minimizing the concentration of catalyst. The use of azeotroping solvent and mol sieves eliminates the need to prepare an anhydrous salt. The salts listed in Table 1 permit dehydration with reagents more environmentally acceptable than copper. Thus, the procedure should find broad application, particularly for alcohols yielding alkenes showing sensitivity to acid-catalyzed isomerization. While the dehydrations described were carried out at high alcohol to catalyst ratios for monitoring purposes, preparative reactions on a >0.05 mol scale were carried out by increasing the catalyst concentration resulting in rapid and controlled production of alkene.

## EXPERIMENTAL SECTION

Commercially available reagents and compounds were purchased from Acros Organics. Qualitative and quantitative analyses were preformed on a DB-5ms column (J&W Scientific) in a Varian 3700 GC coupled to a Shimadzu CR601 integrator. GC/MS was used to confirm the identity of cedrol, α-, and β-cedrene, were performed on a DB-5ms column (J&W Scientific) in a Hewlett Packard HP5890 coupled to a HP5989B quadrupole instrument.

**Cupric Sulfate Monohydrate**.- Prepared either by a two-hour, azeotropic dehydration of the pentahydrate using refluxing benzene and AW-500 mol sieve or by dehydrating the blue pentahydrate to constant weight in a stream of dry nitrogen using a modified Abderhalden apparatus[7] heated by refluxing toluene. These procedures give a pale blue amorphous-appearing solid previously described as the monohydrate.[5]

**Anhydrous Cupric Sulfate**.- Prepared by heating the pentahydrate at 285° (0.1 mmHg).[5]

**Anhydrous Ferrous Sulfate**.- Prepared from the heptahydrate, in the same manner as $CuSO_4$ monohydrate, using an Abderhalden apparatus followed by heating at 285° (0.1 mmHg).

**$AlK(SO_4)_2$ Trihydrate**.- Prepared from the dodecahydrate, in the same manner as $CuSO_4$ monohydrate, using an Abderhalden apparatus.

**Ferrous Sulfate Monohydrate**.- Prepared from the heptahydrate, in the same manner as $CuSO_4$ monohydrate, using an Abderhalden apparatus.

**Typical Procedure**.- Cupric sulfate pentahydrate (0.250 g, 0.001 mol) was added to a magnetically



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stirred solution of benzene (50 mL in the reaction flask and 46 mL wetting and filling the mol sieve chamber) and **1** (11.1 g, 0.05 mol, recrystallized from methanol and sublimed; shown to be pure and free of **2** and **3** by GC) in a 100-mL, 3-necked flask fitted with argon inlet and a Dean-Stark/mol sieve apparatus containing 47 g of AW-500 mol sieve in the water-jacketed chamber.[3] The reaction mixture was heated to reflux and samples were taken at specific intervals, filtered through anhydrous $MgSO_4$ layered over Dicalite, and analyzed by GC. The cooled reaction mixture was filtered through anhydrous $MgSO_4$, concentrated, and distilled at 105° (70 mmHg) in a Kugelrohr apparatus.

**Acknowledgment**.- We are grateful to International Flavors and Fragrances (IFF-US) for a generous gift of cedrol.

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## REFERENCES

1. a) J. March, "*Advanced Organic Chemistry*", 4th ed., pp 389-390 and 1011-1012, John Wiley & Sons, New York, NY, 1992; b) H. Knozinger, *The Dehydration of Alcohols*, in "*The Chemistry of the Hydroxyl Group*", part 2, pp 641-718, ed. by S. Patai, Interscience Publishers, John Wiley & Sons, New York, NY, 1971; c) "*Encyclopedia of Reagents for Organic Synthesis*" vol. 2, pp 1365-1367, vol. 4, pp 2890-2891, ed. by L. A. Paquette, John Wiley & Sons, New York, NY, 1995.

2. a) R. V. Hoffman, R. D. Bishop, P. M. Fitch and R. Hardenstein, *J. Org. Chem.*, **45**, 917 (1980); b) F. C. Whitmore and E. Rohrmann, *J. Am, Chem. Soc.*, **63**, 2033 (1941); c) G. W. Francis and J. F. Berg, *Acta Chem. Scand. B*, **31** 721 (1977); d) K. H. Shankaranarayana and K. S. Ayyar, *Current Science*, **48**, 683 (1979); e) T. Takeshita, R. Ohnishi, K. Tanabe, *Recent Survey of Catalysis by Solid Metal Sulfates*, in "*Catalysis Reviews*", Vol. 8, ed. by H. Heinemann, pp 29-63, Marcel Dekker, Inc, New York, NY, 1974; f) T. Nishiguchi, N. Machida and E. Yamamoto, *Tetrahedron Lett.*, **28**, 4565 (1987); g) T. Nishiguchi and C. Kamio, *J. Chem. Soc. Perkins Trans.*, 707 (1989).

3. E. J. Eisenbraun and K. W. Payne, *Ind. Eng. Chem. Res.*, **38**, 4521 (1999).

4. J. H. Clark, "*Catalysis of Organic Reactions by Supported Inorganic Reagents*", pp 36-37, VCH Publishers, Inc, New York, NY, 1994.

5. a) J. M. Sedlak and R. A. Beebe, *Thermochimica Acta*, **9**, 261 (1974); b) A. D. Harris and L. H. Kalbus, *J. Chem. Ed.*, **56**, 417 (1979); c) S. El-Houte and M. El-Sayed Ali, *Thermochimica Acta*, **138**, 107 (1989); d) T. A. Mills and C. S. G. Phillips, *J. Chrom.*, **557**, 495 (1991).

6. D. R Lide, Ed. "*Handbook of Chemistry and Physics*", CRC Press, Inc, New York, NY, 1996.

7. K. W. Payne, R. Wittwer, S. Anderson, and E. J. Eisenbraun, *Forest Prod. J.*, **48(7/8)**, 91 (1998).

***(Received September 25, 2000; in final form November 15, 2000)***