Effect of Solvent on the Oxy–Cope Rearrangement of the 4-Isopropenyl-3,7-dimethylocta-1,6-dien-3-ol Diastereomeric System

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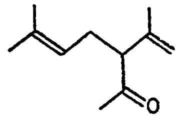
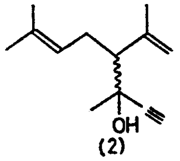
Summary The addition of *N*-methyl-2-pyrrolidone as solvent in the oxy–Cope rearrangement of (**3**) and (**4**) increases the yield, and affects the stereoselectivity of the products.

Synthetic use of the oxy-Cope rearrangement in the elongation of open chain carbon systems is considerably reduced owing to the β-hydroxyolefin cleavage side reaction, and various methods to eliminate this cleavage reaction have been developed.[1] However, little attention has been paid to the effect of solvent on this reaction in spite of extensive investigations on other [3,3]sigmatropic shifts.[2] Recently we reported a convenient solvent-assisted method to increase the selectivity of the [3,3] shift in some hexa-1,5-dienol systems.[3] Here we describe the effect of solvent on the yield and stereoselectivity in the diastereomeric dienol systems, 4-isopropenyl-3,7-dimethylocta-16-dien-3-ols (**3**) and (**4**), new key intermediates in the production of geranylacetone.


(1)



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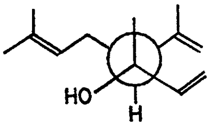

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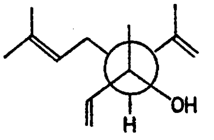

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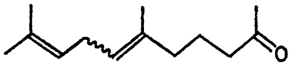

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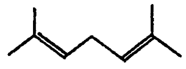
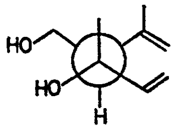

(6)

Treatment of the ketone (**1**) with vinylmagnesium bromide in tetrahydrofuran gave (**3**) (*ca.* 80%) as predicted by Cram's rule.[4] Pure dienol (**4**) (50 g) was obtained by fractional distillation of a mixture of (**3**) and (**4**) (55:45; 1500 g), derived from the thermodynamically controlled Favorskii ethynylation of (**2**) by partial hydrogenation with Lindlar catalyst.[5]

Thermolysis of (**3**) (neat) in the temperature range 160—190 °C gave (**5**) (*E*:*Z* = 59:41) in *ca.* 55% yield, along with cleavage products [(**6**), methyl vinyl ketone, and polymer]; thermolysis of (**4**), in comparison, gave a similar yield of (**5**), but more of the *E*-form was obtained (*E*:*Z* = 66:34).



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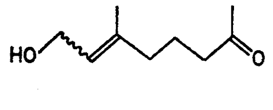

(8)

The use of *N*-methyl-2-pyrrolidone (NMP) as solvent in various amounts, as shown in the Figure, increased the yield of (**5**) to 80% with the amount of the *E*-isomer increasing from 59 to 71% in the case of (**3**), while with (**4**) it decreased from 66 to 58%. A small acceleration in rate was also observed: for (**4**) $k = 0{\cdot}407$, $0{\cdot}432$, $0{\cdot}470$, and $0{\cdot}564\ \mathrm{s}^{-1}$ at 170 °C with addition of NMP in the ratio of 0, 0·5, 1·0, and 2·0 by weight, respectively. Further addition of NMP, even as much as fifty-fold, did not cause a further increase in the yield, nor did it lead to a variation in the *E*:*Z* ratio, or an acceleration in rate. The decrease in the selectivity of the [3,3] shift during the reaction, which was observed in the neat system (initial stage 62%, end of reaction 53%) was not observed upon addition of NMP. This solvent effect was considerably reduced by the addition of primary alcohols (*e.g.* n-decyl alcohol or ethylene

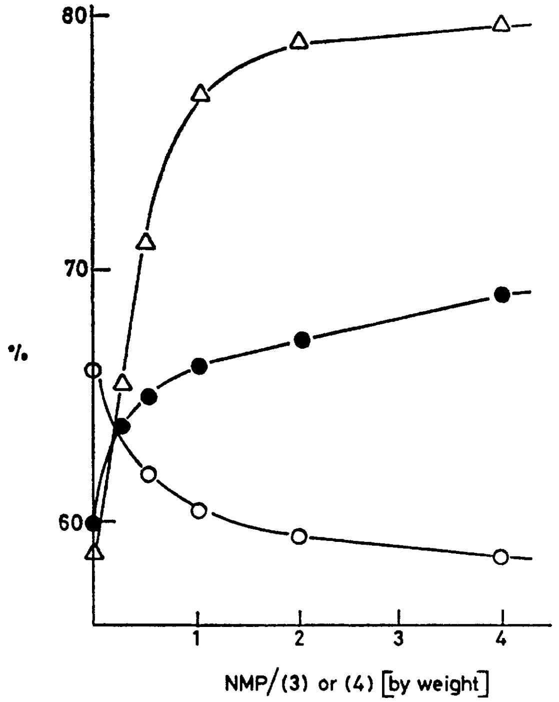

Figure. Effect of solvent on the oxy–Cope rearrangement of (**3**) and (**4**). △: Selectivity of [3,3]-shift; ●: *E*-isomer from (**3**); ○: *E*-isomer from (**4**). NMP = *N*-methyl-2-pyrrolidone.

glycol), even though there was no effect on the selectivity of the [3,3] shift in the neat system.[6] Thus the system (**7**)† bearing another hydroxy group was investigated: thermolysis of (**7**) (neat) gave (**8**) only in *ca.* 35% yield. The amount of NMP required to increase the selectivity of the [3,3] shift to 56 and 65% was two and four times by weight, respectively.

These results indicate the interaction of the solvent with a hydroxy proton. The synthetic utility of this modification was confirmed by the large scale production (semi-commercial) of geranylacetone using mesityl oxide to extend the chain.

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† Prepared by the treatment of 3-hydroxymethylpent-4-en-2-one (R. Lantsch and D. Arlt, *Annalen*, 1976, 1757) with 3 equiv. of vinylmagnesium bromide in tetrahydrofuran.

[1] A. Viola, E. J. Iorio, K. K. Chen, G. M. Glover, U. Nayak, and P. J. Kocienski, *J. Amer. Chem. Soc.*, 1967, **89**, 3462; D. A. Evans and A. M. Golob, *ibid.*, 1975, **97**, 4765; R. W. Thies, *Chem. Comm.*, 1971, 237.

[2] D. C. Wigfield and S. Feiner, *Canad. J. Chem.*, 1970, **48**, 855.

[3] Y. Fujita, T. Onishi, and T. Nishida, *Synthesis*, 1978, in the press.

[4] D. J. Cram and F. A. Abd. Elhafez, *J. Amer. Chem. Soc.*, 1952, **74**, 5828.

[5] Y. Fujita, F. Wada, T. Onishi, and T. Nishida, *Chem. Letters*, 1977, 943.

[6] Recently diglyme was used for the oxy-Cope rearrangement in the hexa-1,5-dienol system (P. Place, M. L. Roumestant, and J. Gore, *J. Org. Chem.*, 1978, **43**, 1001).