Novel Synthesis of Dienones and Enones from Propargyl Alcohols and Allyl Alcohols with 2,2-Dimethoxypropane: Synthesis of Ionone and Irone

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A new synthetic procedure for dienone derivatives, *i.e.*, ionone and irone, is described. The key step is the pyrolytic rearrangement of allyl alcohols and 2,2-dimethoxypropane in the presence of an acid anhydride and phosphoric acid.

Syntheses of dienones,¹⁾ enones²⁾ and enesters³⁾ by rearrangement of an allyl vinyl ether (*i.e.*, Claisen-Cope type reaction) have already been achieved by many investigators. Developments in this field have been summarized in a detailed review.⁴⁾ In the perfumery field, an efficient method of synthesis of these enones is desired, because many odor components such as ionones, irone, damascone *etc.*, contain dienone or enone groups. We wish to describe a novel synthesis of enones and dienones, starting from allyl alcohols and acetylenic carbinols with 2,2-dimethoxypropane in the presence of acetic anhydride and phosphoric acid at 130~200°C for 15~24 hr.

In the synthesis of dienones by this method the reaction proceeded smoothly and dienones (II) were isolated as almost the sole product in moderate yields (55~65%).

In the case of enone synthesis, however,

the yields of enones were lower (25~35%), and considerable amounts of by-products, presumed to be diallyl ether (VI) and allyl acetate (V), were produced by allylic rearrangement of the starting materials. A representative example of the synthesis of dienones is as follows. A mixture of 1-methyl-3-butyne-2-ol (I, R₁=R₂=CH₃, 1 meq.), 2,2-dimethoxypropane (2.5 meq), a catalytic amount of 85% phosphoric acid (1 drop) and acetic anhydride (1.4 meq) was heated with stirring in an autoclave at 130°C under a nitrogen atmosphere for 24 hr. The reaction

mixture was neutralized with aqueous sodium bicarbonate solution and the resulting oil was washed with water and distilled under reduced pressure to afford 6-methyl-hepta-3,5-dien-2-one (IV, $\text{R}_1=\text{R}_2=\text{CH}_3$) in 60.2% yield. The merit of this method is that the reaction procedure can be carried out in a single operation and the product can be obtained by a simple process in fairly good yield.

Syntheses of ionone⁶⁾ and irone⁶⁾ were achieved by employing this procedure. As starting materials, substituted allyl alcohols ($\text{VII}_{\text{a,b}}$), were prepared by Grignard reaction of α,β -unsaturated esters and methyl magnesium halide.⁷⁾ In the preparation of VII_{b} , the yield was greatly improved by changing the solvent from ether to tetrahydrofuran and the halide

from methyl iodide or bromide to chloride. These results are summarized in Table I.

Pyrolysis of the alcohols and 2,2-dimethoxypropane by the previously described method afforded substituted heptenones ($\text{VIII}_{\text{a,b}}$) in 23.9 and 33.4% yield, respectively. These heptenones were identical with authentic samples, prepared by rearrangement of the acetoacetate esters of the alcohols ($\text{VII}_{\text{a,b}}$).⁸⁾ The enones ($\text{VIII}_{\text{a,b}}$) were ethynylated by the procedures of Kimel *et al.*⁹⁾ to give dehydro linalool (IX_{a}) and methyl dehydro linalool (IX_{b}) in good yield. Syntheses of pseudo-ionone (X_{a}) and pseudo-irone (X_{b}) from dehydro linalool and methyl dehydro linalool were achieved by the same procedure as described above in 62.5 and 58.2% yield, respectively.

TABLE I.

Alkyl halide	Solvent	Reaction conditions	Yield	Notes
CH_3I	Et_2O	reflux/2 hr	60%	Ref. 7)
CH_3Br	Et_2O	reflux/2 hr	62%	
	THF	30~40°C/1 hr	81%	
		reflux/1 hr		
CH_3Cl	THF	30~40°C/1 hr	95%	
		reflux/1 hr		

These products were obtained as 5-*cis* and *trans* mixtures. Cyclization of the pseudo-compounds by treatment with acetic acid-sulfuric acid (3:7)¹⁰ at 10~15°C for 30 min afforded β -ionone (XI_a) and β -irone (XI_b) almost exclusively, and these were isolated by steam distillation in good yields. The physical data for the prepared products were identical with the reported values.

EXPERIMENTAL

Gas-liquid chromatography was carried out with a Shimadzu GC-3A unit.

2,3'-Dimethyl-but-3-en-2-ol (VIIb)

Into a solution of MeMgCl, prepared by the passage of methyl chloride gas into Mg (12.0 g, 0.5 g atom) in anhydrous THF (400 ml) with stirring until the Mg was completely dissolved, methyl methacrylate (20 g, 0.2 M) in THF (100 ml) was added dropwise at 30~40°C during the course of 1 hr. After the addition was complete, the mixture was stirred under reflux for 1 hr. The reaction mixture was poured into an aqueous solution of NH₄Cl and HCl and extracted with ether. The extract was dried over Na₂SO₄. Fractional distillation gave a pure product (19.0 g, 95% yield). bp 115°C/760 mmHg, literature.⁷¹ Glpc: SE-30. 50°C 1 atm (He) retention time (*t*_R) 5.3 min. bp 115~116°C/760 mmHg.

6-Methyl-hept-5-en-2-one (VIIIa)

A mixture of 2-methyl-but-3-en-2-ol (30 g, 0.35 mole), 2,2-dimethoxypropane (DMP, 92 g, 1.0 mole), 85% phosphoric acid (H₃PO₄, 1 drop) and acetic anhydride (Ac₂O, 51 g, 0.5 mole) was heated to 130~140°C with stirring in an autoclave under a nitrogen atmosphere for 16 hr. The reaction mixture was neutralized with excess NaHCO₃ and the residual oil was dried over Na₂SO₄. Yields of products were determined by glpc analysis, and the data are as follows. Column, SE-30: temperature, 80°C; 1.1 atm (He) starting material: retention time (*t*_R) min, 19.8 g, 6-methyl-hept-5-en-2-one: *t*_R 10.5 min, 3.7 g, 23.9% and other by-products; *t*_R 6.7 min and 13.6 min. Authentic enone was prepared by rearrangement⁸¹ of the acetoacetate derivative of the allyl alcohol.

5,6-Dimethyl-hept-5-en-2-one⁺ (VIIIb)

The same procedure and scale as in the above experiment were employed. The yield of this enone was 33.4%, as determined by glpc analysis (*t*_R 10.5 min, column SE-30, 1 atm (He), temperature, 100°C).

Pseudo-ionone (Xa)

Dehydrolinalool (IXa) was prepared as described by Kimel *et al.*,⁹¹ and the physical properties were completely identical with those reported. A mixture of dehydrolinalool (5 g, 0.033 mole), DMP (8 g, 0.09 mole), H₃PO₄ (1 drop) and Ac₂O (5 g, 0.05 mole), was heated with stirring at 180°C for 1 hr and then at 140°C for 14 hr. The reaction mixture was treated with the same manner as described above. Yield was determined by glpc analysis; starting material (1.54 g), *t*_R 1.6 min, 5-*cis* and *trans*-pseudo-ionone (2.73 g, 62.5%), *t*_R 6.7 and 7.9 min, column OV-17, 60~180°C (10°C/min), 1 atm (N₂). Silica gel chromatography afforded the starting material (1.2 g) and pseudo-ionone (2.1 g, 49.3%). The formation of other by-products was almost negligible. Physical properties were identical with those of an authentic sample prepared by the procedure described by Saucy *et al.*¹¹

Pseudo-irone (Xb)

Methyl dehydro linalool (IXb) was prepared according to Reference.⁹¹ Exactly the same scale and procedure was employed as the case of pseudo-ionone synthesis. The yield of pseudo-irone was 58.2% and the recovered starting material amounted to 1.36 g, as determined by glpc analysis. Silica gel chromatography afforded pseudo-irone (2.0 g, 47.6%) and starting material (1.6 g). The physical properties were completely identical with those of an authentic sample.

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