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These paragraphs were added in September 2014. The statements above do not supersede any specific hazard caution notes and safety instructions included in the procedure.

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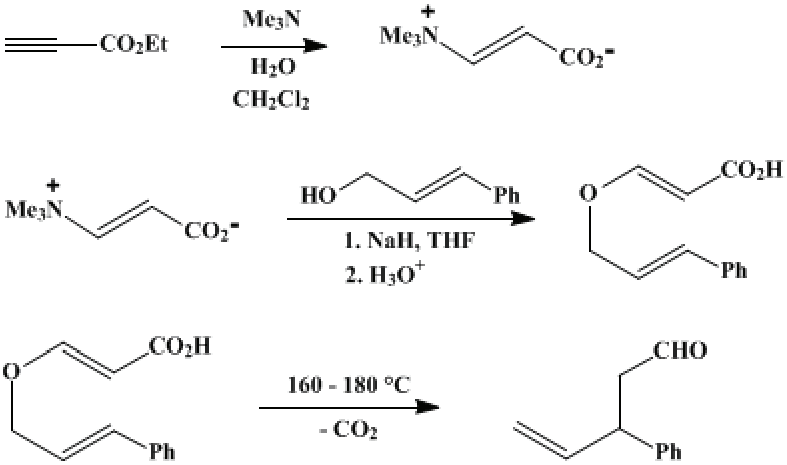
α-UNSUBSTITUTED γ,δ-UNSATURATED ALDEHYDES BY CLAISEN REARRANGEMENT: 3-PHENYL-4-PENTENAL

[Benzenepropanal, β-ethenyl-]



Submitted by Dennis E. Vogel and George H. Büchi[1].
Checked by Tadahito Nobori and Ryoji Noyori.

1. Procedure

A. *(E)-(Carboxyvinyl)trimethylammonium betaine*. A 1-L, three-necked, round-bottomed flask is equipped with a mechanical stirrer, a dropping funnel, and a thermometer. The flask is charged with 25.0 g (0.255 mol) of ethyl propiolate (Note 1), 14 mL of dichloromethane, and 440 mL of water. The mixture is cooled to 5°C (Note 2) and 90 mL (0.35 mol) of an aqueous 25% solution of trimethylamine (Note 3) is added under vigorous stirring over a 30-min period. The reaction temperature remains between 0 and 5°C during the addition and then is allowed to warm to 25°C for 3 hr. The dichloromethane layer is separated and the aqueous layer is washed 3 times with 100-mL portions of dichloromethane. The aqueous layer is placed in a 1-L, round-bottomed flask and concentrated at 15 mm pressure with a rotary evaporator equipped with a dry-ice condenser. The flask is heated to approximately 45°C. When the residue gives the appearance of a wet solid, it is treated with 150 mL of dioxane and concentrated as described above. Dioxane treatment followed by concentration is repeated 3 more times with 150-mL portions of dioxane (Note 4). The yellow solid residue is triturated with acetonitrile (Note 5) until a white solid is obtained. The solid is collected and dried at 0.1 mm, 25°C for 14 hr to give 25.0–26.9 g (76–82% yield) of (*E*)-(carboxyvinyl)trimethylammonium betaine, mp 176–177°C (dec) (Note 6).

B. *(E)-3-[(E)-3-Phenyl-2-propenoxy]acrylic acid.* An oven dried, 1-L, three-necked, round-bottomed flask equipped with a mechanical stirrer, a dropping funnel, and a reflux condenser is purged with argon and charged with 8.20 g (0.171 mol) of 50% sodium hydride in oil (Note 7) and 90 mL of anhydrous tetrahydrofuran (Note 8). To this mixture is added a solution of 19.0 g (0.143 mol) of cinnamyl alcohol (Note 9) in 180 mL of anhydrous tetrahydrofuran. The mixture is stirred for 30 min at which point 25.0 g (0.194 mol) of (*E*)-(carboxyvinyl)trimethylammonium betaine is added and the reaction mixture is heated at a gentle reflux for 15 hr. The cooled reaction mixture is slowly added to a mixture of 600 mL of water and 220 mL of a saturated aqueous solution of sodium chloride (Note 10). The residual material is removed with wet ether (Note 11) and added to the aqueous solution. The aqueous layer is washed 3 times with 450 mL of ether and acidified with approximately 21 mL of concentrated hydrochloric acid to pH 1. This mixture is extracted 3 times with 700 mL of ether and the ether layer is dried with 20 g of anhydrous magnesium sulfate for 30 min. The mixture is filtered and the filtrate is concentrated, first with a rotary evaporator and then at 0.1 mm for 24 hr at 25°C to give crude (*E*)-3-[(*E*)-3-phenyl-2-propenoxy]acrylic acid. This material can be used in Part C without further purification. However, purification by trituration with approximately 30 mL of anhydrous ether gives 24.7–25.0 g (85% yield) of white crystalline product, mp 140–141.5°C (dec) (Note 12).

C. *3-Phenyl-4-pentenal.* In a 100-mL, round-bottomed flask equipped with a magnetic stirring bar is placed 20.1 g (0.098 mol) of (*E*)-3-[(*E*)-3-phenyl-2-propenoxy]acrylic acid from B (Note 13). The flask is fitted with a distillation head for vacuum distillation and heated at 0.1 mm pressure. The oil-bath temperature is maintained at 160–165°C while the mixture is stirred, until all the material melts. Once the initial reaction is under control, the oil bath is slowly heated to 180°C. The product is collected in a receiver flask cooled with a dry ice–acetone bath to give 13.3–14.3 g (84–91% yield) of 3-phenyl-4-pentenal, bp 114–115°C (15 mm) (Note 14).

2. Notes

1. Ethyl propiolate, purchased from Aldrich Chemical Company, Inc., is freshly distilled prior to use.
2. An ice–acetone bath is used to cool the reaction mixture.
3. An aqueous 25% solution of trimethylamine available from Aldrich Chemical Company, Inc. is used directly.
4. This procedure helps to concentrate further the product by forming an azeotrope with the water.
5. Continued trituration with small portions of acetonitrile (e.g., 8 times with 50-mL portions) eventually removes all traces of the yellow-colored impurity as well as any residual water.
6. The product exhibits the following spectral properties: IR (KBr) cm^{-1}: 1665, 1600, 1360; ^1H NMR (D_2O, DSS ref.) δ: 3.3 (br s, 9 H, $(CH_3)_3N$), 6.3 (br d, 1 H, *J* = 13, vinyl CH), 6.8 (br d, 1 H, *J* = 13, vinyl CH).
7. A suspension of 50% sodium hydride in mineral oil, purchased from Alfa Products, Johnson Mathey Co. or Nakarai Chemicals, Ltd., is used directly.
8. Anhydrous tetrahydrofuran is obtained by distillation from benzophenone ketyl prior to use.
9. Cinnamyl alcohol purchased from Aldrich Chemical Company, Inc. is freshly distilled before use. The checkers purchased it from Nakarai Chemicals, Ltd.
10. *Caution: Residual sodium hydride is present in the reaction mixture; however, it can be quenched safely by strict adherence to the procedure described.*
11. The use of wet ether has two purposes. Not only does the ether help wash residual product from the flask, but ether that has not been carefully dried contains traces of water, which allows for the safe quenching of the last traces of sodium hydride.
12. The product exhibits the following spectral properties: IR (KBr) cm^{-1}: 1680, 1615, 1600; ^1H NMR ($CDCl_3$ 60 MHz) δ: 4.5 (d, 2 H, *J* = 5.5, $OCH_2CH=$), 5.2 (d, 1 H, *J* = 12, $CH=CHCO_2H$), 6.5 (m, 2 H, PhCH=CH-), 7.2 (s, 5 H, Ph-), 7.5 (d, 1 H, *J* = 12, $O-CH=CHCO_2H$), 12.0 (s, 1 H, CO_2H).
13. The material obtained from trituration of the crude product in Part B can also be used at this point and gives similar results.
14. The product exhibits the following spectral properties: IR (neat) cm^{-1}: 2840, 2740, 1720, 1640, 1600; ^1H NMR ($CDCl_3$, 60 MHz) δ: 2.9 (d,d, 2 H, *J* = 2, 4, CH_2-CHO), 4.0 (q, 1 H, *J* = 7, Ph-CH), 5.0 (d, 1 H, *J* = 7, vinyl), 5.3 (s, 1 H, vinyl), 6.0 (m, 1 H, vinyl), 7.2 (s, 5 H, Ph), 9.5 (t, 1 H, *J* = 2, CHO).

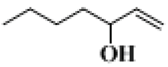
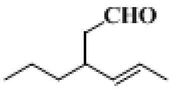
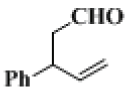
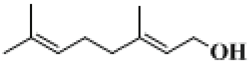
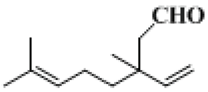
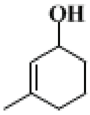
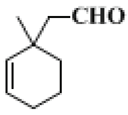
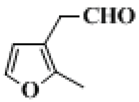
3. Discussion

The procedure described[2] illustrates a new general synthetic method for the preparation of (*E*)-3-allyloxyacrylic acids and their conversion to α-unsubstituted γ,δ-unsaturated aldehydes by subsequent Claisen rearrangement–decarboxylation. Such aldehydes are traditionally prepared by Claisen rearrangements of allyl vinyl ethers.[3] Allyl vinyl ethers are typically prepared by either mercury-catalyzed vinyl ether exchange with allylic alcohols or acid-catalyzed vinylation of allylic alcohols with acetals. The basic conditions required for alkoxide addition to the betaine to produce carboxyvinyl allyl ethers, as described in this report, nicely complements these two methods. In addition, this Claisen rearrangement is an experimentally very simple procedure, since sealed-tube and other high-pressure vessels are not required. The allyloxyacrylic acids are heated neat (in most cases a small amount of hydroquinone is added) and, by adjusting the pressure at which the reaction is performed, the aldehyde products distill from the reaction mixture in analytically pure form.

(*E*)-(Carboxyvinyl)trimethylammonium betaine is prepared by a modification of the procedure of McCulloch and McInnes.[4] They also reported the addition of simple alkoxides to this betaine, and that deuterium exchange is not observed when this reaction is performed with the deuterated betaine. We have also observed that replacement of the betaine with propiolic acid leads to the formation of 3-alkoxyacrylic acids in significantly lower yields.[2] These observations are best accounted for by an addition–elimination process.

This procedure provides a variety of allyloxyacrylic acids; however, it is sensitive to steric hindrance. Tertiary allylic alcohols do not add to the betaine and sterically hindered secondary alcohols add with decreasing facility. Table I indicates the scope of this reaction.

TABLE I
PREPARATION AND REARRANGEMENT OF 3-ALLYLOXYACRYLIC ACIDS

Starting Material	Yield of Adduct, %	Product	Yield, %
	89		68
	84		78
	92		quant.
	62		quant.
	96		quant.
	53,77		quant.
	82		79
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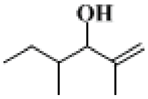
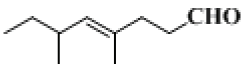
	55		82

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Appendix
Chemical Abstracts Nomenclature (Collective Index Number); (Registry Number)

benzophenone ketyl

(E)-(Carboxyvinyl)trimethylammonium betaine

hydrochloric acid (7647-01-0)

ether (60-29-7)

acetonitrile (75-05-8)

hydroquinone (123-31-9)

sodium chloride (7647-14-5)

dichloromethane (75-09-2)

Trimethylamine (75-50-3)

magnesium sulfate (7487-88-9)

dioxane (123-91-1)

Tetrahydrofuran (109-99-9)

cinnamyl alcohol (104-54-1)

sodium hydride (7646-69-7)

argon (7440-37-1)

ethyl propiolate (623-47-2)

deuterium (7782-39-0)

propiolic acid (471-25-0)

3-Phenyl-4-pentenal,
Benzenepropanal, β-ethenyl- (939-21-9)

(E)-3-[(E)-3-Phenyl-2-propenoxy]acrylic acid (88083-18-5)

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