



A Publication
of Reliable Methods
for the Preparation
of Organic Compounds

Working with Hazardous Chemicals

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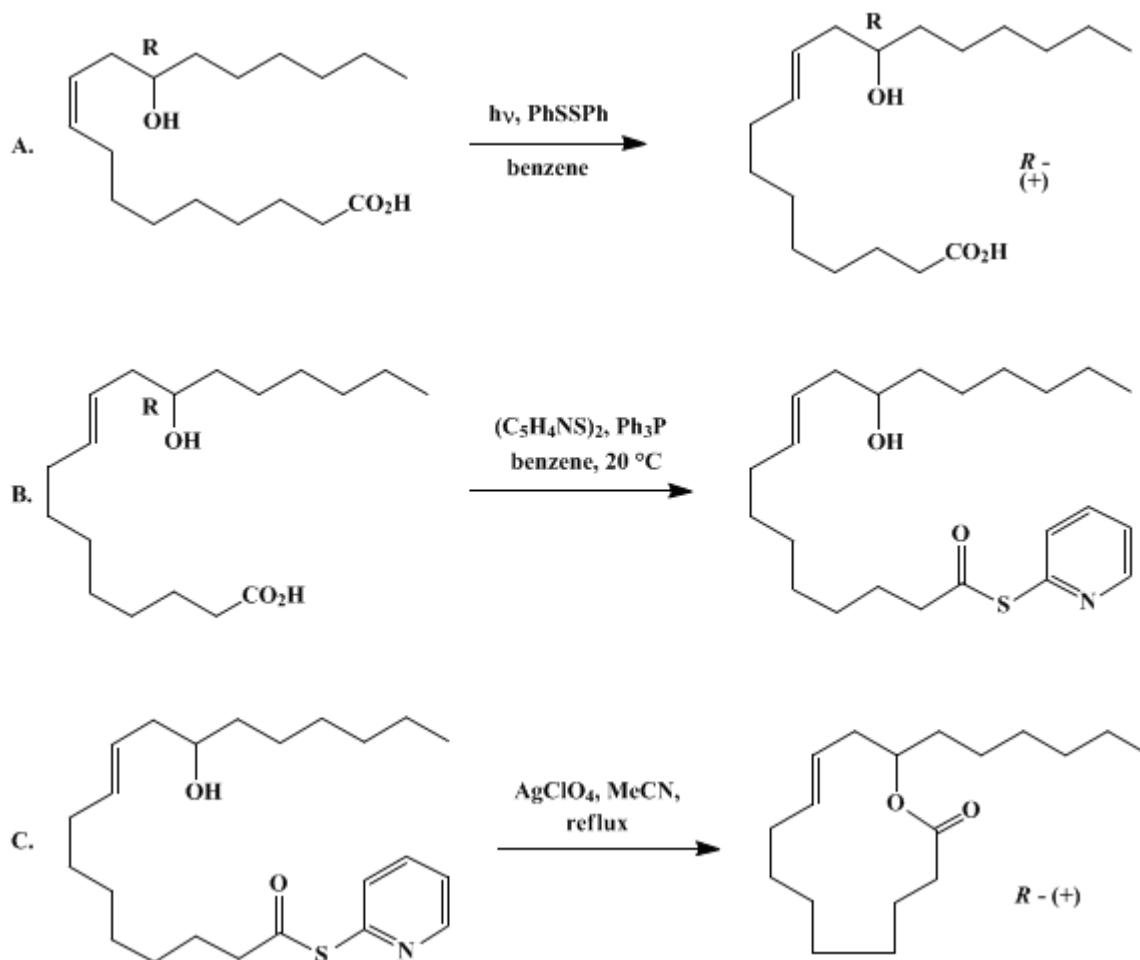
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These paragraphs were added in September 2014. The statements above do not supersede any specific hazard caution notes and safety instructions included in the procedure.

Organic Syntheses, Coll. Vol. 7, p.470 (1990); Vol. 63, p.192 (1985).

RICINELAIDIC ACID LACTONE

[9-Octadecenoic acid, 12-hydroxy-, [(+)-(R)-trans]-, lactone]



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1. Procedure

A. *Ricinelaidic acid*. Ricinoleic acid (Note 1) (39.75 g, 0.106 mol) and 586 mg (2 mol %) of diphenyl disulfide dissolved in 1000 mL of hexane are placed in a photochemical reactor (Note 2) and irradiated for 3 hr with a Philips HP(L) 250-W medium-pressure mercury lamp. After irradiation the solvent is removed under reduced pressure and the semisolid residue is recrystallized from 185 mL of hexane to yield 11.3 g of crude ricinelaidic acid, mp 39–43°C. The irradiation is repeated with the mother liquor under the same conditions to yield, after removal of the solvent and recrystallization of the residue from 135 mL of hexane, an additional 7.2 g, mp 38–42°C; total yield of crude ricinelaidic acid is 18.5 g (58%). The product after recrystallization from 220 mL of hexane weighs 15.6 g (49%), mp 43–45°C, and is suitable for the following step. Repeated recrystallization from hexane yields ricinelaidic acid with mp 51.0–51.5°C (Note 3) and (Note 4).

B. *Ricinelaidic acid S-(2-pyridyl)carbothioate*. In a dry, stoppered, 10-mL flask containing a magnetic stirring bar are placed 360 mg (1.2 mmol) of ricinelaidic acid (see above), 308 mg (1.4 mmol) of 2,2'-dipyridyl disulfide (Note 5), 1 mL of benzene, and 367 mg (1.4 mmol) of triphenylphosphine, and the mixture is stirred for 30 min. The resulting slurry is then dissolved in 55 mL of dry acetonitrile

(Note 6).

C. *Ricinelaiddic acid lactone*. Dry *acetonitrile* (100 mL), 3.5 mL of 1 M *silver perchlorate* in *toluene* (Note 7) and (Note 8), and a magnetic stirring bar are placed in a 500-mL flask equipped with a reflux condenser that carries a Hershberg dropping funnel. The solution is heated in an oil bath so that the boiling *acetonitrile* returns from the condenser at the rate of 5–10 drops per second (Note 9). Then the *acetonitrile* solution of the *ricinelaiddic acid S*-(2-pyridyl)carbothioate is added dropwise during 1 hr through the condenser to the magnetically stirred refluxing *silver perchlorate* solution (Note 9). The slightly turbid mixture is boiled for an additional 15 min and the solvent is removed under reduced pressure in a rotary evaporator. The residue is diluted with 30 mL of 0.5 M *potassium cyanide* solution and the mixture containing suspended solids is extracted with three 50-mL portions of *benzene*. The *benzene* extracts are washed with 30 mL of water, dried with anhydrous *magnesium sulfate*, and filtered, and the solvent is removed under reduced pressure. Crude product is obtained as an oil (710 mg). It can be purified by chromatography on 40 g of silica gel (Note 10) with *benzene* as eluant. Fractions of 10 mL are collected at 30-min intervals. Fractions 7–19 contain 283–296 mg (84–88%) of *ricinelaiddic acid lactone* (Note 11).

2. Notes

1. Technical-grade (80%) *ricinoleic acid* was obtained from Fluka AG Buchs, Switzerland or from Tridom Chemicals, Inc. Saponification of *methyl ricinoleate*² also gives suitable material.
2. The photochemical reactor used is quite similar to the one described in *Org. Synth., Coll. Vol. V* **1973**, 298.
3. The purity of the products has been checked by capillary gas liquid chromatography of the corresponding methyl ester obtained with ethereal *diazomethane* solution (Carlo Erba Fractovap 20-m glass capillary coated with UCON HB at 160°C). *Ricinelaiddic acid*, mp 49–50°C, contains 4%, that with mp 51.0–51.5°C, less than 1% of *ricinoleic acid*. Submitters obtained higher yields (58%, mp 49–50°C), perhaps due to better quality starting material.
4. (+)-(*R*)-*Ricinelaiddic acid*, mp 51.0–51.5°C, has an optical rotation of $[\alpha]_D +6.6^\circ$ (C₂H₅OH, *c* 10).
5. 2,2'-Dipyridyl disulfide obtained from Fluka AG, Buchs, Switzerland, was recrystallized from *hexane* (30 mL/g) to yield a suitable product, mp 58–59°C.
6. Commercially available *acetonitrile* is distilled over *phosphorus pentoxide*.
7. *Silver perchlorate monohydrate* (9 g) (obtained from Fluka AG) is suspended in 110 mL of *toluene* together with a Teflon-coated magnetic stirring bar. The solution is magnetically stirred and heated in an oil bath until 70 mL of *toluene* has distilled.
8. The *silver perchlorate* solution may be substituted by 8.5 mL of 0.4 M *silver trifluoromethanesulfonate* (Fluka) in *toluene*.
9. This reflux rate is crucial for predilution of the carbothioate in the condenser. Lower reflux rates require an accordingly slower addition of the *S*-(2-pyridyl)carbothioate during 2–4 hr.
10. Silica gel 60 Merck in a 2.5-cm-diameter column was used.
11. The product distills at 110°C (0.01 mm) in a Kugelrohr distillation apparatus and has an optical rotation of $[\alpha]_D +42^\circ$ (CHCl₃, *c* 1).

3. Discussion

The silver ion-promoted lactonization of hydroxy-*S*-(2-pyridyl)carbothioates was introduced by the submitters³ as a mild method for the synthesis of naturally occurring macrolides as, for example, nonactin⁴ and ricifeiolide⁵ from the corresponding hydroxy acids. If the method of Mukaiyama et al.⁶ is used for the formation of the *S*-(2-pyridyl)carbothioate, no protection of the hydroxyl group is needed in this step. The cited examples show that silver ion-promoted lactonization can be used to effect ring closure of base-sensitive and unsaturated acid-sensitive hydroxy acids in good yield.

Similar methods to effect lactonization have been proposed by Corey et al.⁷ and Masamune et al.⁸ The first consists of prolonged heating of hydroxy-*S*-(2-pyridyl)carbothioates in boiling *xylene*; the second is the mercury trifluoroacetate-promoted cyclization of a *hydroxy-S-tert-butyl carbothioate*.

Ricinelaiddic acid was selected for the submitted procedure because it has a moderately complex

structure and can be prepared easily from commercially available technical grade [ricinoleic acid](#). This conversion represents an example of the facile *cis*–*trans* interconversion of olefins⁹ caused by photochemically generated phenylthiyl radicals leading to the thermodynamic equilibrium.

This preparation is referenced from:

- [Org. Syn. Coll. Vol. 7, 87](#)

References and Notes

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Appendix

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

silica gel

2,2'-dipyridyl disulfide

[Benzene](#) (71-43-2)

[acetonitrile](#) (75-05-8)

[potassium cyanide](#) (151-50-8)

[toluene](#) (108-88-3)

[xylene](#) (106-42-3)

[magnesium sulfate](#) (7487-88-9)

[ricinoleic acid](#)

[methyl ricinoleate](#) (141-24-2)

[Diazomethane](#) (334-88-3)

hexane (110-54-3)

triphenylphosphine (603-35-0)

diphenyl disulfide (882-33-7)

phosphorus pentoxide (1314-56-3)

Ricinelaidic acid lactone,
9-Octadecenoic acid, 12-hydroxy-, [(+)-(R)-trans]-, lactone (79894-06-7)

Ricinelaidic acid,
(+)-(R)-Ricinelaidic acid (540-12-5)

silver perchlorate (7783-93-9)

Silver perchlorate monohydrate (14242-05-8)

silver trifluoromethanesulfonate (2923-28-6)

Ricinelaidic acid S-(2-pyridyl)carbothioate (100819-69-0)

hydroxy-S-tert-butyl carbothioate