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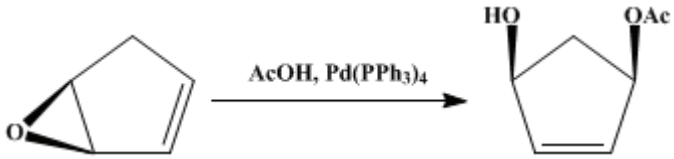
PALLADIUM(0)-CATALYZED *syn*-1,4-ADDITION OF CARBOXYLIC ACIDS TO CYCLOPENTADIENE MONOEPOXIDE: *cis*-3-ACETOXY-5-HYDROXYCYCLOPENT-1-ENE

[4-Cyclopentene-1,3-diol, monoacetate, *cis*-]



Submitted by Donald R. Deardorff and David C. Myles[1].
Checked by Helmut Grebe and Ekkehard Winterfeldt.

1. Procedure

An oven-dried, 300-mL, two-necked, round-bottomed flask is equipped with a Teflon-coated magnetic stirring bar, a pressure-equalizing dropping funnel, and a rubber septum with an 18-gauge needle connected to a dry-nitrogen source. The nitrogen-flushed apparatus is charged with 125 mL of dry tetrahydrofuran (Note 1) and 0.28 g (0.24 mmol, 0.2 mol%) of tetrakis(triphenylphosphine) palladium(0) (Note 2). The mixture is stirred at room temperature until all of the palladium catalyst dissolves (Note 3). The solution is cooled in an ice–water bath and 7.0 mL (7.3 g, 122 mmol) of acetic acid (Note 4) is added via syringe. At this point a slight darkening of the solution is observed. A room temperature solution containing 10.9 g of 92% cyclopentadiene monoepoxide (10.0 g, 122 mmol, (Note 5)) in 40 mL of tetrahydrofuran is added over 10 min with the aid of the addition funnel. The original pale-yellow color gives way to a deeper transparent orange. After 5 min (Note 6), the solution is concentrated at ambient temperature under reduced pressure and the resulting reddish-brown oil is passed through a plug of silica gel (50 g, (Note 7) with 450 mL of ethyl ether (Note 8). The slightly cloudy filtrate is washed through a plug of anhydrous magnesium sulfate (60 g, 5 × 7-cm coarse glass frit) with an additional 150 mL of ether (Note 9) The solvent is removed under reduced pressure to yield a pale-yellow oil. The material is distilled through a short-path apparatus at 73–75°C (0.15 mm) to afford 12.5–13.2 g (72–76%) of colorless oil that crystallizes upon refrigeration (mp 36–39°C) . The material is homogeneous by TLC and ^{1}H NMR (Note 10), but can be further purified by recrystallization from an ether–hexane mixture to give colorless crystals, mp 38.5–41°C (Note 11).

2. Notes

1. Tetrahydrofuran was predried over potassium hydroxide *Caution! See Org. Synth., Coll. Vol. V, **1973**, 976 for possible hazard.*), then dried by distillation from sodium/benzophenone ketyl under nitrogen.
2. Tetrakis(triphenylphosphine)palladium(0) was purchased from Aldrich Chemical Company, Inc., and used without further purification. No special precautions were taken in handling the catalyst.
3. Dissolution takes approximately 2–3 min.
4. Glacial acetic acid was purchased from J. T. Baker Chemical Company (Baker Analyzed Reagent) and distilled prior to use.
5. Cyclopentadiene monoepoxide was prepared from cyclopentadiene and peracetic acid according to the well-established procedure of Korach et al.[2] However, the submitters report that epoxidation of cyclopentadiene under conditions developed by Knapp et al.[3] for cyclohexadiene increased their isolated yields from 40% to 62%. The major impurity in distilled cyclopentadiene monoepoxide is 3-cyclopentenone. This by-product can be conveniently assayed by ^{1}H NMR integration of the four methylene protons that appear as a broad singlet at 2.80 δ. Epoxide purity can be determined by GLC analysis on a 25 M Carbowax capillary column operated at 50°C.
6. TLC analysis using Baker Si250F precoated glass plates with a hexane–ethyl acetate (1 : 1) solvent system indicates that all of the starting material is consumed.

7. Baker Analyzed Reagent silica gel 60–200 mesh was used in a 4.5 × 9.0-cm column. This step removes most palladium-containing compounds from the reaction mixture. In order to ensure that the palladium is efficiently separated, itis important that all tetrahydrofuran be removed from the crude oil prior to filtration.
8. Anhydrous ether (purified) was purchased from J. T. Baker Chemical Company and used without additional purification.
9. This step removes the final traces of palladium. It is imperative that all catalyst be removed prior to distillation since, on heating, this metal catalyzes the decomposition of *cis*-3-acetoxy-5-hydroxycyclopent-1-ene into isomeric cyclopentenones and acetic acid.
10. *cis*-3-Acetoxy-5-hydroxycyclopent-1-ene has the following spectral characteristics: ^{1}H NMR (200 MHz, $CDCl_3$) δ: 1.59 (dt, 1 H, J = 4.0 and 14.5, CH_2), 2.00 (s, 3 H, CH_3), 2.38 (br s, 1 H, OH), 2.76 (quintet, overlapping dt, 1 H, J = 7.4 and 14.5, CH_2), 4.67 (m, 1 H, CHOH), 5.45 (m, 1 H, CHOAc), 5.92 (m, 1 H, CH=CH), 6.05 (m, 1 H, CH=CH); IR (neat) cm^{-1}: 3410 (s), 1720 (s), 1250 (s).
11. 4-Acetoxy-2-cyclopentenone could be prepared in 85% yield by treatment of 1 equiv of this alcohol with 1.1 equiv of pyridinium chlorochromate in methylene chloride for 1 hr at room temperature, followed by washing with water, concentration, and distillation.

3. Discussion

Functionalized cyclopentenoids have been used extensively as key building blocks for the synthesis of many biologically active molecules.[4] This procedure details the facile preparation of one such versatile intermediate: *cis*-3-acetoxy-5-hydroxycyclopent-1-ene. Although important in its own right, this material also serves as a one-step precursor to the highly useful synthetic substrate 4-acetoxy-2-cyclopenten-1-one.[4] Only the acetic acid adduct with cyclopentadiene monoepoxide is described here. However, this palladium-catalyzed reaction appears to be general for other acidic substrates as well.[5,6] For example, the corresponding benzoate and phenyl ether adducts have been successfully prepared[5] from both benzoic acid and phenol in yields of 87 and 82%, respectively. Moreover, the reaction is not limited to just the monoprotected versions of *cis*-cyclopentene-3,5-diol. The corresponding diesters can be similarly prepared by replacement of the carboxylic acid component with an anhydride. This minor modification permits direct synthetic access to either the dibenzoate or diacetate in equally good yields (74 and 79%, respectively). Recently, silyl carboxylates and silyl phenoxides were also found to react analogously with cyclopentadiene monoepoxide in the presence of Pd(0) catalyst.[7] It should be stressed that in each case only the *cis*-1,4-adducts are observed, despite the fact that three other stereoisomers are possible. This remarkable stereo- and regiospecificity is undoubtedly a manifestation of an intermediate palladium π-allyl complex.[8]

Racemic *cis*-monoesters of cyclopentene-3,5-diol were previously prepared by the selective acylation[9] [10] [11] of the *meso*-diol and the copper-mediated[12] addition of carboxylic acid salts to cyclopentadiene monoepoxide. Optically active monoacetates can be accessed by enzymatic hydrolysis[13] [14] [15] [16] [17] of the corresponding diester. The present method offers four principal advantages over the earlier reports: (1) it is operationally simple; (2) it requires a much shorter reaction time; (3) it gives better yields; and (4) it has widespread applicability, since reactants other than carboxylic acids may be employed with equally good results.

A major disadvantage with the acylation method[9,10,11] is that the starting material, *cis*-cyclopentene-3,5-diol, is not readily available and must be prepared via photoxygenation procedures.[18] Furthermore, acylation occurs with the concomitant formation of diacylated product, which results in reduced yields and associated purification problems. The copper-mediated[12] and palladium-catalyzed procedures share some similarities in that both use cyclopentadiene monoepoxide as their starting material and deliver the desired product in good yield. But, unlike the palladium-catalyzed method, copper-mediated reactions require two full equivalents of carboxylate salt, much lower reaction temperatures (−78°C), and substantially longer reaction times. Finally, the enantioselective hydrolysis[13,14,15,16,17] of *cis*-3,5-diacetoxycyclopent-1-ene by hydrolase enzymes is an effective two-step method for generating optically enriched product.

This preparation is referenced from:

- Org. Syn. Coll. Vol. 9, 132
- Org. Syn. Coll. Vol. 9, 136
- Org. Syn. Coll. Vol. 9, 487

References and Notes

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

silica gel

sodium/benzophenone ketyl

Racemic cis-monoesters of cyclopentene-3,5-diol

acetic acid (64-19-7)

ethyl acetate (141-78-6)

ether,
ethyl ether (60-29-7)

phenol (108-95-2)

nitrogen (7727-37-9)

Benzoic acid (65-85-0)

potassium hydroxide (1310-58-3)

palladium (7440-05-3)

methylene chloride (75-09-2)

magnesium sulfate (7487-88-9)

Tetrahydrofuran (109-99-9)

peracetic acid (79-21-0)

hexane (110-54-3)

CYCLOPENTADIENE (542-92-7)

cyclohexadiene (592-57-4)

pyridinium chlorochromate (26299-14-9)

CYCLOPENTADIENE MONOEPOXIDE

3-cyclopentenone

4-Acetoxy-2-cyclopentenone,
4-Acetoxy-2-cyclopenten-1-one (768-48-9)

tetrakis(triphenylphosphine)palladium(0) (14221-01-3)

cis-3-Acetoxy-5-hydroxycyclopent-1-ene (60410-16-4)

cis-3,5-diacetoxycyclopent-1-ene (54664-61-8)

4-Cyclopentene-1,3-diol, monoacetate, cis- (60410-18-6)

cis-cyclopentene-3,5-diol