Organic Syntheses

A Publication
of Reliable Methods
for the Preparation
of Organic Compounds

Working with Hazardous Chemicals

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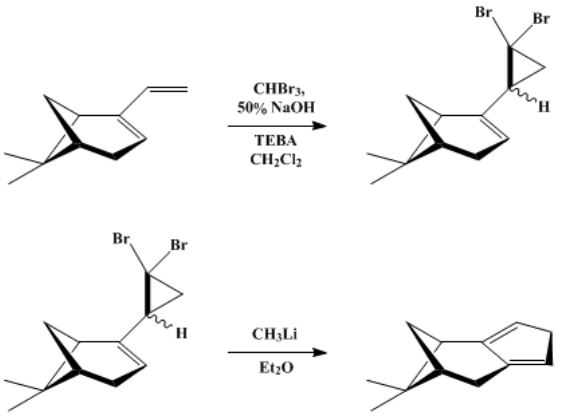
These paragraphs were added in September 2014. The statements above do not supersede any specific hazard caution notes and safety instructions included in the procedure.

Org. Synth. **1990**, *68*, 220
DOI: 10.15227/orgsyn.068.0220

CYCLOPENTADIENE ANNULATION VIA THE SKATTEBØL REARRANGEMENT: (1*R*)-9,9-DIMETHYLTRICYCLO-[6.1.1.$0^{2,6}$]DECA-2,5-DIENE



Submitted by Leo A. Paquette and Mark L. McLaughlin[1].
Checked by Nanine van Draanen and Clayton H. Heathcock.

1. Procedure

A. *Dibromocarbene addition to (1R)-nopadiene.* A 250-mL, three-necked flask is equipped with a mechanical stirrer, a nitrogen inlet, and a serum cap. The flask is charged with 26.2 mL (0.30 mol) of bromoform (Note 1), 29.6 g (0.20 mol) of (1*R*)-nopadiene (Note 2), 1.0 g (4.4 mmol) of benzyltriethylammonium chloride (TEBA), 0.8 mL of ethanol, and 20 mL of dichloromethane (Note 3). The suspension is stirred and cooled in an ice bath while 100 mL of 50% sodium hydroxide solution is added over 10 min from a dropping funnel. The reaction mixture is stirred at room temperature for 24 hr and poured into 250 mL of water. The lower layer is separated and the aqueous phase is extracted with three 25-mL portions of dichloromethane. The combined organic layers are washed with three 100-mL portions of water, dried over magnesium sulfate, and concentrated under reduced pressure to give a brown-black oil. The oil is dissolved in an equal volume of hexane and filtered through a 2-in. bed of silica with hexane (1.5 L) as eluant. The solvent is evaporated and the orange oil is distilled in an apparatus protected from light (Note 4) at 85–95°C and 0.08 mm. The yellow distillate is redistilled through a 4-in. Vigreux column to give 32.0–33.6 g (50–53%) of the diastereomeric dibromocyclopropanes (Note 5).

B. *(1R)-9,9-Dimethyltricyclo[6.1.1.$0^{2,6}$]deca-2,5-diene.* A flame-dried, 3-L flask is equipped with a large magnetic stirring bar and a serum cap and charged with 17.6 g (55.0 mmol) of the dibromide. A total of 2 L of anhydrous ether (Note 6) is transferred into the flask via cannula. The stirred solution is cooled in an ice bath and 147 mL of 1.5 *M* methyllithium in ether (220 mmol) is introduced via a second cannula (Note 7). The ice bath is removed and stirring is maintained for 10 hr before the solution is transferred by cannula into 1 L of ice-cold water. The ether layer is separated and the aqueous phase is extracted with two 200-mL portions of ether. The combined ethereal solutions are dried and concentrated (Note 8). The residual yellow oil is immediately diluted with an equal volume of hexane and passed through a short column of neutral alumina (Note 9). The solvent is carefully removed and the yellow oil is subjected to bulb-to-bulb distillation at 90°C and 5 mm (Note 10). The yield of colorless hydrocarbon is 6.9–7.1 g (78–80%) (Note 11) and (Note 12).

2. Notes

1. The submitters used a purified grade of bromoform purchased from the Fisher Chemical Company.

2. The (1*R*)-nopadiene is prepared from commercially available (Aldrich Chemical Company, Inc.) (1*R*)-(−)-nopol according to the following procedure.[2] A 1000-mL, three-necked flask is equipped with a mechanical stirrer, internal thermometer and nitrogen inlet. The flask is charged with 125 g (0.752 mol) of (1*R*)-(−)-nopol and 500 mL of pyridine. Stirring is begun and the solution is cooled to −10°C in an ice–salt bath under nitrogen. *p*-Toluenesulfonyl chloride (175 g, 0.918 mol) is added in one portion under an inert atmosphere via Gooch tubing (the checkers used a powder funnel for the addition). The temperature rises to 40°C for 15–20 min, but returns to 5°C, where it is maintained for 2 hr. Twenty 1-mL portions of water are next introduced at such a rate that the temperature does not exceed 5°C. The reaction mixture is poured into 1 L of ether and extracted with ice-cold 5 *M* sulfuric acid until the aqueous layer remains acidic, then with saturated $CuSO_4$ solution until the aqueous layer remains blue. The ethereal phase is washed with two 200-mL portions each of water and 5% sodium bicarbonate solution prior to drying over magnesium sulfate and solvent evaporation. A solid residue is obtained. If this material is dark, it may be dissolved in hexane and filtered through a pad of Celite to remove the black impurity. The tosylate is recrystallized by dissolving it in 500 mL of hot hexane and cooling to −78°C. Six such recrystallizations give material with mp 51.0–51.8°C and $[\alpha]_D^{25}$ −25.6° (C_2H_5OH, c 0.03). The yield is 62–72%. A 2000-mL, three-necked flask is equipped with a mechanical stirrer, an internal thermometer, and a nitrogen inlet. The flask is charged with 200 g (0.624 mol) of (1*R*)-nopyl tosylate and 1000 mL of dimethyl sulfoxide that has been freshly distilled from calcium hydride at 40 mm. The stirring solution is cooled briefly in a cold-water bath and 69.0 g (0.615 mol) of freshly sublimed potassium *tert*-butoxide is added rapidly while nitrogen is flowing above the solution (the checkers used potassium *tert*-butoxide from a freshly opened bottle). (The base must be the limiting reagent to offset isomerization of the product diene.) The temperature rises to approximately 45°C, and a brown color develops. As the reaction proceeds, the color dissipates to a light yellow. After the initial exotherm subsides, the mixture is heated at 75°C for 10 hr, cooled to room temperature, and diluted with 800 mL of hexane. The lower layer, mostly dimethyl sulfoxide, is diluted with 1 L of water and extracted with two 100-mL portions of hexane. The combined hexane layers are washed with water (5 × 200 mL), dried over magnesium sulfate, and rotary-evaporated at 40 mm and 25°C to leave a yellow oil. Distillation through a 5-in. Vigreux column gives 69.4–74.0 g (75–80%) of (1*R*)-nopadiene as a clear, colorless oil, bp 78–79°C/25 mm.

3. These phase-transfer conditions are adapted from experimental procedures described earlier.[3,4]

4. The dibromocyclopropane is light-sensitive when hot. Exposure to light during distillation produces colored impurities that cause autocatalytic decomposition of the product when subsequently stored in the cold.

5. Both distillations must be performed with a pot temperature below 150°C in order to avoid thermal decomposition; ^1H NMR indicates the product to be a 4 : 1 mixture of diastereomers. All available evidence denotes that both are transformed efficiently into the cyclopentadiene.

6. The ether was freshly distilled from sodium benzophenone ketyl. The checkers used anhydrous ether from a freshly opened can.

7. The methyllithium was purchased from the Aldrich Chemical Company, Inc. and contains lithium bromide.

8. Solvent evaporation was accomplished at 40 mm and 25°C in order to counter product volatility.

9. The checkers used a 1 × 1-in. plug of alumina. The experience of the submitters has been that the use of silica gel at this point causes some decomposition.

10. The checkers found foaming to be a serious problem in this distillation. The problem is ameliorated by use of a ≥50-mL distillation flask.

11. Purified diene polymerizes within 24 hr if stored neat. Its lifetime can be indefinitely prolonged by storage as a 10% by weight solution in hexane under an argon atmosphere.

12. The product exhibits $[\alpha]_D^{24}$ −21.9° (C_2H_5OH, c 1.8) and the following ^1H NMR spectrum at 300 MHz in $CDCl_3$ solution δ: 0.72 (s, 3 H), 1.24 (m, 1 H), 1.33 (s, 3 H), 1.60 (s, 1 H), 2.11 (m, 1 H), 2.60 (m, 1 H), 2.70 (m, 2 H), 2.99 (s, 2 H), 5.77 (s, 1 H), 5.99 (s, 1 H).

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3. Discussion

Experience has shown[5,6] that cyclopentadiene annulation of 2,3-dimethylenebicyclo[2.2.2]octanes can be efficiently realized by means of the Skattebøl procedure.[7] However, the added strain in 2,3-dimethylenenorbornanes reroutes the rearrangement instead into vinylallene formation.[4] This phenomenon has been attributed to an inability on the part of the torsionally constrained empty carbene *p* orbital to interact with the flanking double bond.[8] This structural inhibition is entirely alleviated by positioning the cyclopropyl carbene completely external to the norbornene ring as in the present example. The heightened conformational maneuverability of the carbenoid center is conducive to exclusive cyclopentadiene ring formation.

(1*R*)-9,9-Dimethyltricyclo[6.1.1.$0^{2,6}$]deca-2,5-diene is a chiral, optically active homolog of isodicyclopentadiene, a molecule that has been extensively studied with regard to π-facial selectivity in cycloaddition reactions.[9] The response of the title compound to similar dienophiles has been described[10] and its complexation to various transition metals reported.[10,11] The steric contributions of the *gem*-dimethyl substituents relegate bonding to the opposite surface of the cyclopentadiene ring.

References and Notes

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

sodium benzophenone ketyl

Dibromocarbene addition to (1R)-nopadiene

(1R)-(−)-nopol

$CuSO_4$

(1R)-Nopadiene

2,3-dimethylenenorbornanes

ethanol (64-17-5)

sulfuric acid (7664-93-9)

ether (60-29-7)

sodium hydroxide (1310-73-2)

sodium bicarbonate (144-55-8)

nitrogen (7727-37-9)

pyridine (110-86-1)

bromoform (75-25-2)

dichloromethane (75-09-2)

magnesium sulfate (7487-88-9)

hexane (110-54-3)

Methyllithium (917-54-4)

dimethyl sulfoxide (67-68-5)

CYCLOPENTADIENE (542-92-7)

argon (7440-37-1)

calcium hydride (7789-78-8)

Dibromocyclopropane

p-Toluenesulfonyl chloride (98-59-9)

benzyltriethylammonium chloride (56-37-1)

lithium bromide (7550-35-8)

cyclopropyl carbene (19527-12-9)

vinylallene (10563-01-6)

potassium tert-butoxide (865-47-4)

(1R)-9,9-DIMETHYLTRICYCLO-[6.1.1.$0^{2,6}$]DECA-2,5-DIENE (108404-79-1)

(1R)-nopyl tosylate (81600-63-7)