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Working with Hazardous Chemicals

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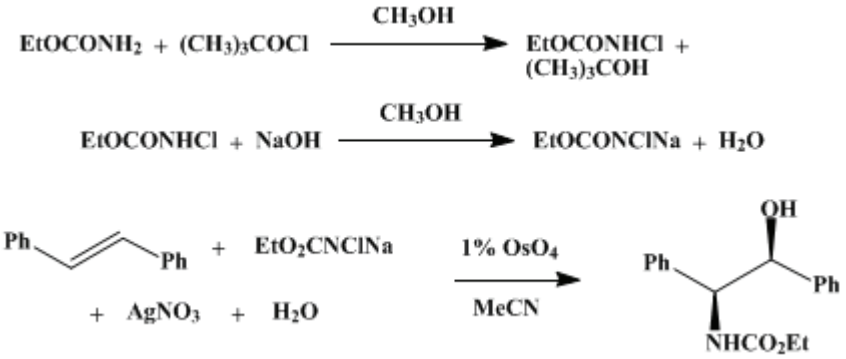
OSMIUM-CATALYZED VICINAL OXYAMINATION OF OLEFINS BY *N*-CHLORO-*N*-ARGENTOCARBAMATES: ETHYL *threo*-[1-(2-HYDROXY-1,2-DIPHENYLETHYL)]CARBAMATE

[Carbamic acid (2-hydroxy-1,2-diphenylethyl),-ethyl ester, (*R**,*R**)-]



Submitted by Eugenio Herranz and K. Barry Sharpless[1].
Checked by Steven D. Young and Clayton H. Heathcock.

1. Procedure

A 1-L, one-necked, round-bottomed flask is equipped with a magnetic stirring bar and a 100-mL addition funnel. The flask is placed in an ice bath and charged with 13.36 g (0.15 mol) of ethyl carbamate (Note 1) and 100 mL of reagent-grade methanol. Vigorous stirring is begun and to the ice-cold solution is carefully added 16.9 mL (16.2 g, 0.15 mol) of *tert*-butyl hypochlorite (Note 2). Fifteen minutes after the addition of the *tert*-butyl hypochlorite is complete, a methanolic solution (75 mL) of sodium hydroxide (6.43 g, 0.158 mol) is added dropwise over a period of several minutes (Note 3). After addition of the sodium hydroxide is complete, the ice bath is removed and stirring is continued for a further 10 min. The solvent is removed using a rotary evaporator (bath <60°C) to give the crude ethyl *N*-chloro-*N*-sodiocarbamate as a white solid (Note 4). Addition of 400 mL of reagent-grade acetonitrile and 26.33 g (0.1 mol) of silver nitrate (Note 5) results in the gradual appearance of a brown suspension. The solution is stirred for 5 min at room temperature; 18.23 g (0.1 mol) of (*E*)-stilbene (Note 6), 10 mL (~ 1.0 mmol) of a solution of OsO_4 in *tert*-butyl alcohol (Note 7), and 8.1 mL (0.45 mol) of water are then added. The milky brown suspension that results is stirred for 18 hr at room temperature. Filtration of the reaction mixture through a Celite mat on a sintered-glass funnel gives a yellow–brown solution (Note 8). The filtrate is refluxed for 3 hr with 200 mL of 5% aqueous sodium sulfite (Note 9). The resulting mixture is concentrated at aspirator pressure using a rotary evaporator until acetonitrile no longer distills. The residue, which is primarily aqueous, is extracted with two 60-mL portions of methylene chloride (Note 10). The organic phase is dried ($MgSO_4$) and concentrated to give 24.6 g of crude product as a pale-yellow solid. Crystallization from 50 mL of hot toluene affords 18.6–19.8 g (66–69%) of almost pure ethyl *threo*-1-(2-hydroxy-1,2-diphenylethyl)carbamate, mp 120–122°C (Note 11). Concentration of the mother liquors yields an additional 0.6–0.8 g of the hydroxy carbamate (Note 12).

2. Notes

1. Ethyl carbamate was obtained from the Aldrich Chemical Company, Inc.
2. *tert*-Butyl hypochlorite was obtained from Frinton Laboratories.
3. A 5% excess of sodium hydroxide was used to make sure that the *N*-chloro-*N*-sodiocarbamate was in a basic environment. The sodium hydroxide was obtained from J. T. Baker Chemical Company; it was 97.9% pure.
4. To remove the last traces of methanol the crude *N*-chloro-*N*-sodiocarbamate is placed under high

vacuum (0.1 mm) for 15 min. Slightly higher yields of final product are obtained if the crude *N*-chloro-*N*-sodiocarbamate is purified by trituration with ether.
5. Silver nitrate was obtained from Apache Chemicals Inc.
6. (*E*)-Stilbene was used as obtained from Aldrich Chemical Company. The olefin should be added in small portions to avoid overheating of the reaction mixture.
7. Osmium tetroxide was supplied by Matthey-Bishop, Inc. in 1-g amounts in sealed glass ampuls. The procedure that we describe below should be followed to prepare the osmium tetroxide catalyst solution. Work in a well-ventilated hood. One ampul is scored in the middle, broken open, and the two halves are dropped into a clean, brown bottle containing 39.8 mL of reagent grade *tert*-butyl alcohol and 0.20 mL of 70 or 90% *tert*-butyl hydroperoxide (Aldrich). The bottle is capped (use caps with Teflon liners) and then swirled to ensure dissolution of the OsO_4. These solutions are stored in the hood at room temperature and seem to be very stable.
8. In this way the silver salts (AgCl) are removed from the reaction mixture. The precipitate is washed twice with 20-mL portions of acetonitrile.
9. The purpose of this sulfite treatment is to reduce and thereby remove the small amount of osmium that is bound to the organic products.
10. If an emulsion forms, addition of Celite and subsequent filtration through a sintered-glass funnel gives a clear separation of the two phases. The checkers found that extraction with three 100-mL portions of methylene chloride avoids emulsion formation.
11. Crystallization occurs at room temperature over a period of ca. 12 hr. The crystals are washed once with 15 mL of toluene or 50 mL of petroleum ether (bp 40–60°C). The product is quite pure. A product of higher purity, however, mp 122–123.5°C, can be obtained by a second crystallization from toluene.
12. After 24 hr at high vacuum (0.1 mm), some crystals appear. Addition of 15 mL of ether, filtration, and washing with 10 mL of ether gives more product, mp 110–121°C. The checkers found that a higher overall yield was obtained if the mother liquors from the first recrystallization were dissolved in 50 mL of boiling diethyl ether. The solution is then brought to cloudiness by addition of petroleum ether (bp 40–60°C). When this mixture is stored at 0°C overnight, brown crystals are deposited. Recrystallization of this material from 10 mL of hot toluene provides an additional 2.25–3.51 g of hydroxy carbamate, mp 114–117°C.

3. Discussion

This new procedure[2] for vicinal, cis addition of an oxygen and a nitrogen to an olefinic bond constitutes a major improvement over earlier methods, [3], [4] since the nitrogen is introduced bearing an easily removed protecting group. Although the procedure described here employs ethyl carbamate, both *tert*-butyl carbamate and benzyl carbamate can also be used. In fact, in most cases, higher yields are realized in oxyaminations using the latter carbamates.

N-Chloro-*N*-argentocarbamates are generated *in situ* by reaction of the corresponding *N*-chlorosodiocarbamates with silver nitrate in acetonitrile. The *N*-chlorosodiocarbamates are prepared from the carbamates according to the method of Campbell and Johnson.[5] There are conflicting statements in the literature about the stability of these *N*-chlorosodiocarbamates.[6] On one occasion, when EtOCONNaCl was prepared by the submitters on a 250-mmol scale, it decomposed rapidly (but not explosively), turning dark and releasing heat and gases. However, this same chloramine salt has been prepared on a 100-mmol scale without incident. The submitters have found that acidic conditions (which lead to contamination by the *N*-chlorocarbamate) are responsible for the spontaneous decomposition of these salts at room temperature. A simple modification of Campbell's procedure for preparing *N*-chloro-*N*-sodiocarbamates avoids this problem. By adding 5% more sodium hydroxide than the calculated amount, it is assured that all the *N*-chlorocarbamate in the reaction mixture is neutralized. No spontaneous decomposition has occurred in the batches of *N*-chloro-*N*-sodiocarbamates prepared in this way.

The regioselectivity of this new procedure toward terminal olefins is considerably better than that realized with the earlier catalytic oxyamination procedures based on chloramine-T[3]. However, the catalytic procedure cannot compete with the regiospecificity exhibited by the stoichiometric *tert*-alkyl imido osmium reagents.[3]

This new catalytic procedure shows a different range of reactivity when compared with the chloramine-T based procedures, being very effective for mono- and 1,2-disubstituted olefins, especially electron-deficient olefins such as dimethyl fumaratex and (*E*)-stilbene. However, when the steric hindrance of the olefin increases (trisubstituted olefins), the oxyamination reaction proceeds slowly and affords mixtures of products. Very recently we have been able to oxyaminate trisubstituted olefins (2-methyl-2-heptene, 1-methylcyclohexene, 1-phenylcyclohexene, 3-methyl-2-cyclohexenone) using other *N*-chloro-*N*-metallocarbamates in conjunction with the addition of tetraethylammonium acetate (Et_4NOAc).[7]

References and Notes

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

petroleum ether

Ethyl threo-[1-(2-hydroxy-1,2-diphenylethyl)]carbamate

Carbamic acid (2-hydroxy-1,2-diphenylethyl),-ethyl ester, (R^*R^*)-

OsO_4

ethyl threo-1-(2-hydroxy-1,2-diphenylethyl)carbamate

methanol (67-56-1)

ether,
diethyl ether (60-29-7)

acetonitrile (75-05-8)

sodium sulfite (7757-83-7)

sodium hydroxide (1310-73-2)

silver nitrate (7761-88-8)

oxygen (7782-44-7)

nitrogen (7727-37-9)

toluene (108-88-3)

methylene chloride (75-09-2)

$MgSO_4$ (7487-88-9)

1-phenylcyclohexene (771-98-2)

ethyl carbamate (51-79-6)

Benzyl carbamate (621-84-1)

osmium tetroxide (20816-12-0)

1-methylcyclohexene

tert-butyl alcohol (75-65-0)

Dimethyl fumarate (624-49-7)

3-methyl-2-cyclohexenone

osmium

tert-butyl hydroperoxide (75-91-2)

2-methyl-2-heptene (627-97-4)

tetraethylammonium acetate (67533-12-4)

tert-Butyl carbamate (4248-19-5)

(E)-stilbene (103-30-0)

tert-Butyl hypochlorite (507-40-4)

ethyl N-chloro-N-sodiocarbamate

N-chloro-N-sodiocarbamate

N-chlorocarbamate

chloramine-T