Rapid Communication

Enantiospecific synthesis of (+)-3-valeranone and (+)-valerane†

A Srikrishna* & C Dinesh
Department of Organic Chemistry, Indian Institute of Science, Bangalore 560 012

Received 24 March 2000; accepted 20 April 2000

An enantiospecific synthesis of (+)-valerane via 3-valeranone, starting from (R)-carvone employing a stereo- and regiospecific intramolecular diazo ketone cyclopropanation as key reaction for the generation of two vicinal stereogenic quaternary carbons, is described.

Valeranone 1, isolated from an European valerian, Valeriana officinalis L. and other valerians, was the first member of a small group of irregular sesquiterpenes valeranes containing a rearranged eudesmane carbon framework with two methyl groups at the ring junctions of a cis-decalin framework, valeran 2. In addition to valeranone, subsequently few other members of the valerane group of sesquiterpenes, depicted in the Chart 1, were isolated from Japanese valerians. Stereospecific introduction of two methyl groups at the ring junction carbon atoms of decalin cis to each other and trans with respect to isopropyl group makes valeranes interesting synthetic targets.

In continuation of our interest in the synthesis of sesquiterpenes containing contiguous quaternary carbon atoms, herein we describe a new route to valerane 2 via 3-valeranone 3 starting from (R)-carvone employing a stereo- and regiospecific intramolecular diazo ketone cyclopropanation as the key reaction.

It was anticipated that intramolecular cyclopropanation of the diazo ketone derived from the acid 4 generates the tricyclic ketone 5, which could be transformed into valerane 2 via reductive cyclopropane ring cleavage, catalytic hydrogenation followed by reductive deoxygenation of the resulting 3-valeranone (Scheme 1). The acid 4 could be generated by homologation of the γδ-unsaturated aldehyde 6, which could be obtained stereospecifically by Claisen rearrangement of the allyl alcohol 7, an intermediate obtained from R-carvone and used in our earlier syntheses of valeranes. The synthetic sequence starting from R-carvone is depicted in (Scheme II). To begin with R-carvone was converted into the allyl alcohol 7 in three steps. A one pot Claisen rearrangement of the allyl alcohol 7 with ethyl vinyl ether in the presence of a catalytic amount of mercuric acetate in a sealed tube at 175°C furnished the aldehyde 6 in a stereospecific manner. A Wittig reaction based homologation was adopted for the conversion of the aldehyde 6 into the acid 4. Thus, reaction of the aldehyde 6 with methoxymethylene-triphenylphosphorane followed by treatment of the resulting Wittig

The two stereogenic quaternary centers were created and enantiospecific synthesis of (+)-valerane 2 starting from R-carvone, via (+)-3-valeranone 3 wherein the two stereogenic quaternary centers were created employing a stereospecific Claisen rearrangement, a regio- and stereospecific intramolecular cyclopropaneolation of a diazo ketone and regiospecific cyclopropane cleavage as key reactions.

For the ketone 5: [α]D 23 +28 (c 1.8, CHCl3). IR (neat): νmax/cm−1 1690, 1635, 885. 1H NMR (300 MHz, CDCl3+CCL4): δ 4.67 (1 H, s) and 4.61 (1 H, s) [C=CH2], 2.35-1.80 (4 H, series of m), 1.67 (3 H, s, olefinic CH3), 1.60-0.90 (7 H, series of m), 1.24 (3 H, s) and 1.11 (3 H, s) [2×tert. CH3]. 13C NMR (75 MHz, CDCl3+CCL4): δ 210.7 (C, C=O), 148.7 (C) and 109.4 (CH3) [C=CH2], 39.9 (CH2), 39.7 (CH), 38.4 (CH2), 37.3 (CH3), 33.4 (CH), 31.1 (C), 29.9 (CH), 29.6 (CH2), 26.3 (CH2), 24.6 (C), 24.2 (CH2), 21.0 (CH2).

For the ketone 10: [α]D 23 +47.5 (c 1.6, CHCl3). IR (neat): νmax/cm−1 1705, 1635, 885. 1H NMR (300 MHz, CDCl3+CCL4): δ 4.71 (2 H, s, C=CH2), 2.87 (1 H, d, J=14.1 Hz), 2.49 (1 H, d of t, J=14.6 and 6.9 Hz), 2.35-2.10 (2 H, m), 2.05-1.85 (2 H, m), 1.75-1.10 (7 H, m), 1.75 (3 H, s, olefinic CH3), 1.02 (3 H, s) and 0.86 (3 H, s) [2×tert. CH3]. 13C NMR (75 MHz, CDCl3+CCL4): δ 212.1 (C, C=O), 149.7 (C) and 108.9 (CH3) [C=CH2], 49.1 (CH2), 40.7 (C), 40.1 (CH), 38.4 (CH2), 37.9 (CH3), 37.7 (CH2), 36.2 (CH2), 35.7 (C), 27.0 (CH2), 24.0 (CH2), 23.5 (CH2), 21.3 (CH). For 3-valeranone 3: [α]D 23 +28.1 (c 1.6, CHCl3). IR (neat): νmax/cm−1 1700. 1H NMR (300 MHz, CDCl3+CCL4): δ 2.83 (1 H, d, J=4 Hz), 2.46 (1 H, d of t, J=14.3 and 6.9 Hz), 2.18 (1 H, m of d, J=14.7 Hz), 1.92 (1 H, d of t, J=14 and 5.1 Hz), 1.72 (1 H, t, J=12.4 Hz), 1.64 (1 H, dd, J=14 and 2.5 Hz), 1.70-1.30 (8 H, m), 0.97 (3 H, s) and 0.84 (3 H, s) [2×tert. CH3]. 0.90 (6 H, d, 3H, s)
RAPID COMMUNICATIONS

1=6.2 Hz, 2×sec. CH3). 13C NMR (75 MHz, CDCl3+CCI4): δ 212.5 (C, C=O), 49.1 (CH2), 40.7 (C), 39.1 (CH), 38.0 (CH2), 37.9 (CH2), 36.9 (CH2), 36.3 (CH2), 35.5 (C), 33.2 (CH), 25.4 (CH2), 24.0 (CH2), 23.6 (CH3), 20.2 (CH2), 19.9 (CH3).

Acknowledgement
We thank the Council of Scientific and Industrial Research, New Delhi for financial support and for the award of a research fellowship to CD.

References