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REACTIONS WITH ORGANOPHOSPHORUS COMPOUNDS, 50 [1].

TRIMETHYLSILYLETHOXYMETHYLENE TRIPHENYLPHOSPHORANE, A NOVEL REAGENT FOR THE HOMOLOGATION OF CARBONYL COMPOUNDS.

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Summary: Homologation of aldehydes and ketones is achieved by means of trimethylsilylethoxymethylene triphenylphosphorane.

Recently trimethylsilylethoxymethyl chloride 1 has been proposed as a new reagent for protecting hydroxy groups [2]. In this case the removal of the protecting group is not caused by the usual solvolytic process but by the fluoride ion affording a fragmentation pattern, which produces $(CH_3)_3SiF$, $CH_2=CH_2$, $CH_2=O$ and the corresponding alcohol. But trimethylsilylethoxymethyl chloride 1 can also be used for the preparation of the phosphonium salt 2 on reaction with triphenylphosphane in benzene (45°C, 48 h, 75%). Mp. 140-142°C, ($CH_2Cl_2/CH_3COOC_2H_5$), PMR ($CDCl_3$)(δ): 7.70 (m)(15H), 5.77 (d)(2H), J_{P-H} = 4 Hz, 3.83 (t)(2H), J = 8 Hz, 0.8 (t)(2H), J = 8 Hz, -0.2 (s)(9H).

$$(C_6H_5)_3P + ClCH_2OCH_2CH_2Si(CH_3)_3 \longrightarrow (C_6H_5)_3P^+CH_2OCH_2CH_2Si(CH_3)_3Cl^-$$

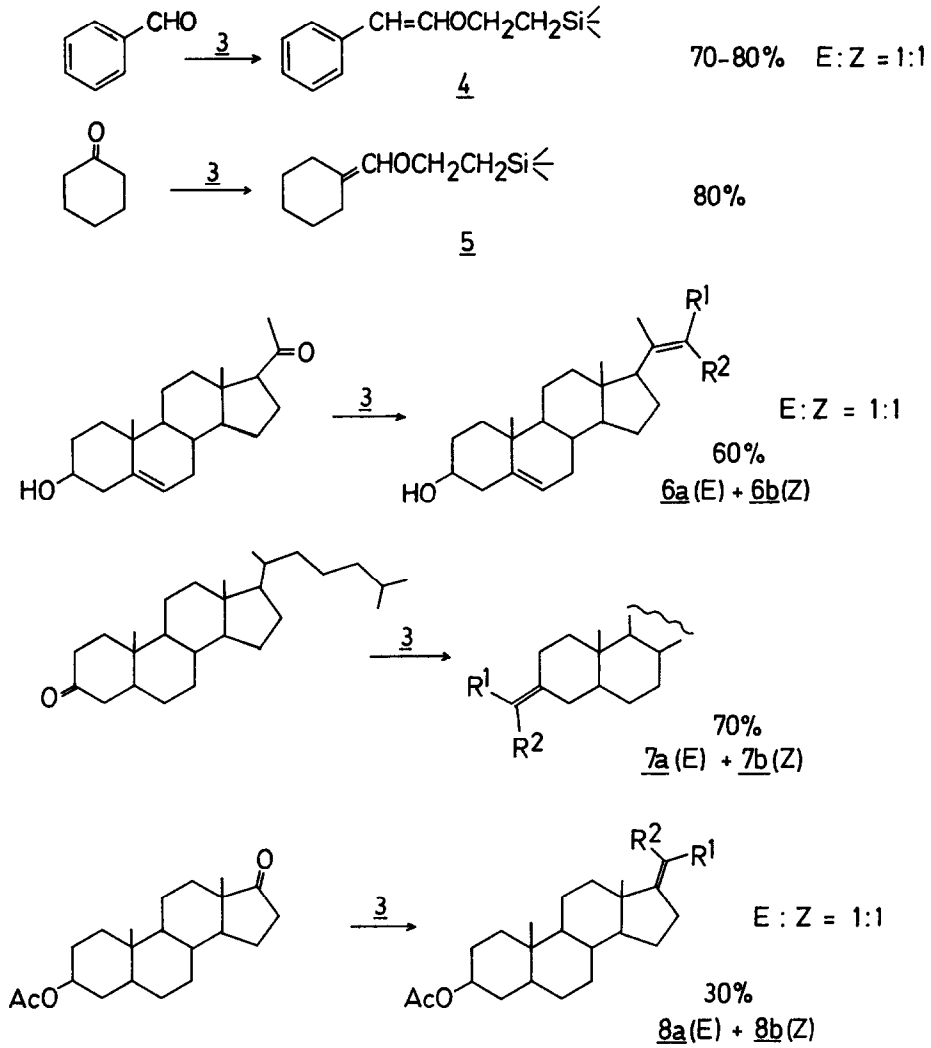
1 2

$$\xrightarrow{DMSO/NaH} (C_6H_5)_3P^+CH^-OCH_2CH_2Si(CH_3)_3$$

3

This salt can easily be transformed to the ylid 3 by means of DMSO-NaH[3] at 0-20°C. The ylid 3 functions as a donor of the formaldehyde carbon and produces with various carbonyl compounds the expected enolether derivatives (4-8) in good yields (scheme 1). Usually two equivalents of 3 per one equivalent of the carbonyl compound have been used. The compounds 4 and 5, isolated according lit.cit. 3, were destilled in a bulb to bulb apparatus (0.01 Torr, 90-110°C). All the analytic data are satisfactory. The other products 6-8 were isolated by removing DMSO at 0.01 Torr and chromatography on silica gel with petrolether-ethyl acetate (3:7) either as an E/Z-mixture (7a+7b) or even as the pure E- and Z-forms 6a, 6b, 8a, 8b, respectively. MS- and 250-MHz-PMR-spectra correspond to the expected structures. This method offers a more convenient procedure of homologation of carbonyl compounds than the hitherto practised transformation of ketones and aldehydes. The derivatives 4-8 are

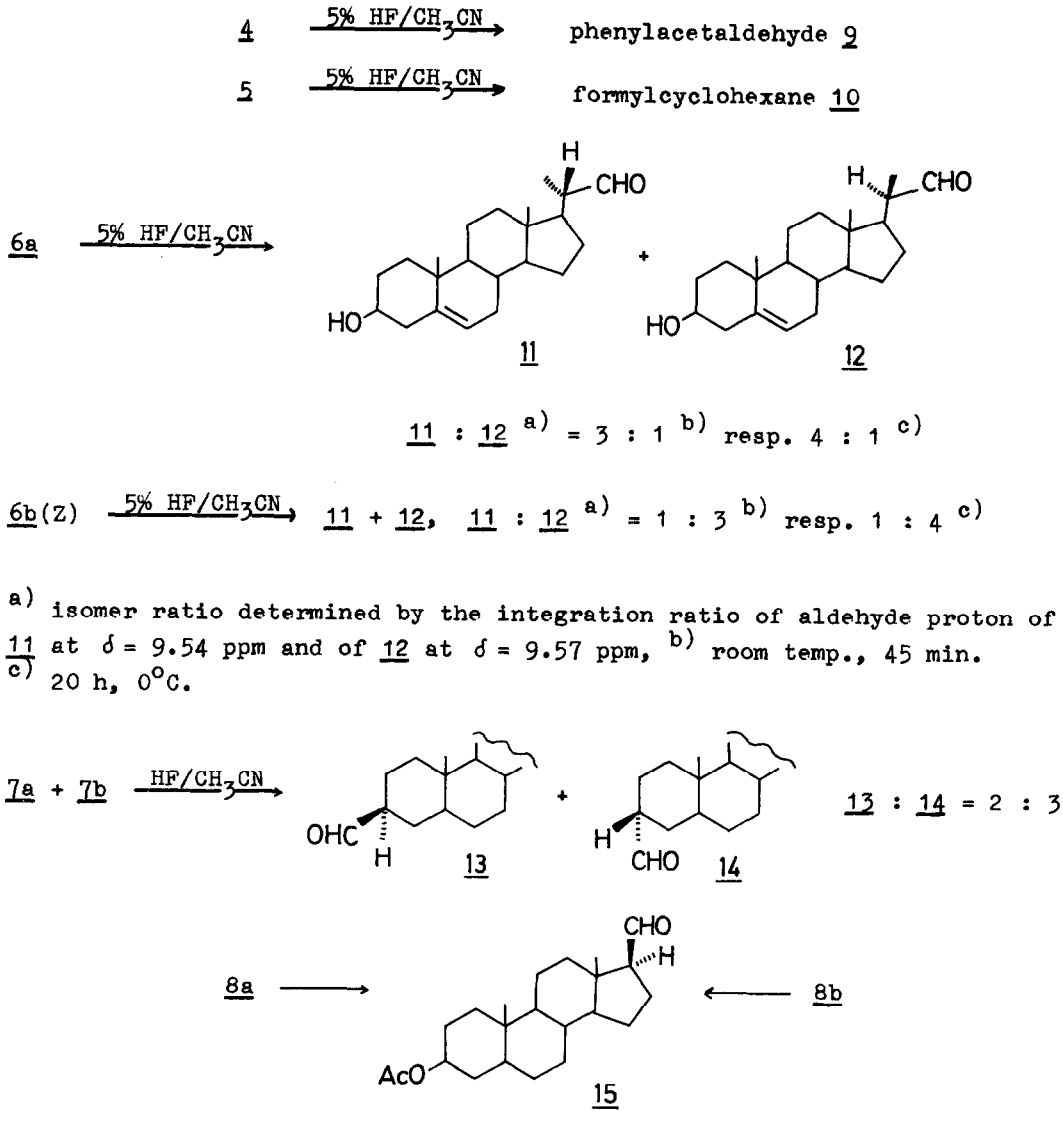
Scheme 1



(E, R^1 = OCH_2CH_2Si, R^2 = H)

(Z, R^1 = H, R^2 = OCH_2CH_2Si)

Scheme 2


4
5% HF/CH3CN
phenylacetaldehyde 9
5
5% HF/CH3CN
formylcyclohexane 10
6a
5% HF/CH3CN
H
CHO
HO
11
H
CHO
HO
12
11 : 12 a) = 3 : 1 b) resp. 4 : 1 c)
6b(Z)
5% HF/CH3CN
11 + 12, 11 : 12 a) = 1 : 3 b) resp. 1 : 4 c)
a) isomer ratio determined by the integration ratio of aldehyde proton of 11 at δ = 9.54 ppm and of 12 at δ = 9.57 ppm, b) room temp., 45 min.
c) 20 h, 0°C.
7a + 7b
HF/CH3CN
OHC
H
13
H
CHO
14
13 : 14 = 2 : 3
8a
8b
CHO
H
AcO
15

easily transformed to the corresponding carbonyl compounds by HF (5%) in CH_3CN [5] (scheme 2) according to the already mentioned fragmentation pattern, whereas the transformation of alkyl enol ethers [4] to the homologous aldehydes often meets with difficulties. Neutralisation of HF (solution of $NaHCO_3$, Na_2CO_3, 0-20°C) leads to phase separation. Freeze drying of the organic layer results in a crude mixture, containing the homologous carbonyl compound, which is isolated by chromatography. It should be mentioned that the desired cleavage could neither be realized with tetrabutylammonium fluoride [2,6] nor with $(C_2H_5)_3N \cdot 2HF$ [7a] or $(C_2H_5)_3N \cdot 3HF$ [7b].

The steroidal aldehydes 11 and 12 are formed in reciprocal amounts from their precursors 6a [8] and 6b [8], respectively. This fact suggests a kinetically controlled reaction. The stereochemistry of 11 was proved by an independent synthesis of the tert.-butyldimethylsilyl ether of 11 by Pfitzner-Moffat oxidation of 22-tosyloxycholest-5-en-3-ß-ol-tert.-butyldimethylsilyl ether [9]. Moreover this kind of formation of 11 and 12 represents a new methodology to create (S)- and (R)-chirality at C-20.

The mixture of 7a and 7b yields 3α- and 3ß-formylcholestene 13 and 14 (3:2). Correlating the integrations of the PMR signals of the 3α-proton (δ= 2.25, $W_{1/2}$= 32 Hz) and the 3ß-proton (δ= 2.40, $W_{1/2}$= 13 Hz) with the two aldehyde protons (α:δ = 9.67; ß:δ = 9.58) permits the assignment of 13 and 14.

In case of 8 both isomers yield the same ß-configurated C-20 aldehyde 15. Obviously the protonation of C-17 only takes place from the α-side.

References and notes

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