# Synthesis of 6-Hydroxy-5,5-dialkyl Substituted Cyclohexenones *via* (Bistrifluoroacetoxyiodo)benzene mediated Cyclization of 1,3-Dithiane and Ethyl Enol Ether

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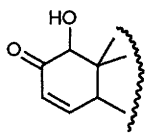
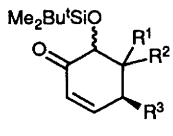
A novel type of intramolecular aldol reaction of 1,3-dithiane and ethyl enol ethers in the same molecule mediated by (bistrifluoroacetoxyiodo)benzene was used for synthesis of 6-hydroxy-5,5-dialkyl substituted cyclohexenones.

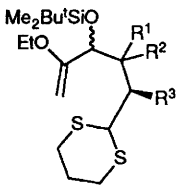
A number of compounds containing the 6-hydroxy-5,5-dialkyl substituted cyclohexenone ring system are present in biologically important terpenoids, *e.g.* triticones (spirostaphylotrichin)[1] and quassinoids,[2] this ring system being essential for potent activity.[3] The preparation of this ring is not easy by ordinary methods because of tautomerism of the α-hydroxyketone,[4] and the construction of the tertiary carbon centre at the 5-position would be difficult after ring formation.

We now describe a new preparation of 6-hydroxy-5,5-dialkyl substituted cyclohexenones (**1**) *via* a novel intramolecular reaction of 1,3-dithiane and ethyl enol ether units mediated by PIFA [(bistrifluoroacetoxyiodo)benzene] as the key carbon–carbon bond formation step. PIFA is an excellent reagent for various types of oxidation,[5] and is also effective for hydrolysis of dithioacetals and enol ethers.[6] When 1,3-dithiane and ethyl enol ether functionalities are both present at an appropriate position in the same molecule (**2**), the use of PIFA led to carbon–carbon bond formation. The γ-1,3-dithianyl ethyl enol ether (**2a**)† was treated with PIFA (1.2 equiv.) in anhydrous acetonitrile (0.05—0.08 M) at −20 °C for

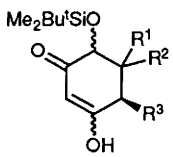




(1)



(2)



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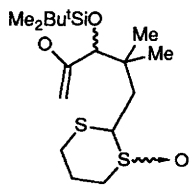
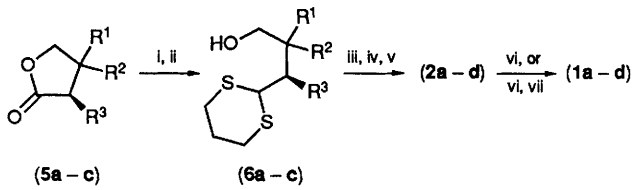


(4)

| | $R^1$ | $R^2$ | $R^3$ | $OSiBu^tMe_2$ |
|---|---|---|---|---|
| **a**; | $CH_2OCH_2Ph$ | $CH_2OSiBu^tMe_2$ | H | α : β (1 : 1) |
| **b**; | Me | Me | H | — |
| **c**; | Me | Me | $OCH_2Ph$ | α |
| **d**; | Me | Me | $OCH_2Ph$ | β |

† All new compounds reported here gave satisfactory spectroscopic data (NMR, IR, and mass), which were available as supplementary material to the referees.




**Scheme 1.** Chromatographic separation of the diastereoisomeric α and β alcohols. *Reagents and conditions* : i, $Bu^i_2AlH$, $CH_2Cl_2$, −78 °C; ii, propane-1,3-dithiol, $SnCl_4$, $CH_2Cl_2$, −20 °C; iii, pyridinium chlorochromate, molecular sieves, 4 Å, $CH_2Cl_2$, room temp., or $BaMnO_4$, $ClCH_2CH_2Cl$, 70 °C; iv, α-ethoxyvinyl-lithium, LiBr, ether, −78 °C; v, $Me_2Bu^tSiOSO_2CF_3$, 2,6-lutidine, $CH_2Cl_2$, −78 °C; vi, PIFA, MeCN, −20 °C then $H_2O$, 0 °C to room temp.; **vii**, $MeSO_2Cl$, $EtNPr^i_2$, $CH_2Cl_2$, 0 °C.

5 min then hydrolysed with water (100 equiv.) at 0 °C giving rise to the cyclohexenone (**1a**) in 67% yield. In the reaction of (**2b**), (**2c**), and (**2d**) with PIFA the aldol condensation stopped at the β-hydroxyketone stage, giving (**3b**), (**3c**), and (**3d**) in 35, 90, and 85% yields in a *ca.* 3 : 1 diastereoisomeric ratio. No significant amounts of by-products were isolated except in the case of (**2b**) in which the dithiane sulphoxide (**4**) was obtained in 54% yield. The β-hydroxyketones (**3**) were treated with methanesulphonyl chloride in the presence of *N*,*N*-di-isopropylethylamine, leading to the corresponding cyclohexenones (**1b**), (**1c**), and (**1d**) in 90—95% yields. This PIFA-promoted cyclization is mild and complete in several minutes in all cases.‡ This reaction is unusual because aldehyde and methyl ketone components masked as the 1,3-dithiane and ethyl enol ether respectively have both reacted intramolecularly without any deprotection.§

The substrates (**2a—d**) were efficiently derived from γ-butyrolactones (**5a—c**) as shown in Scheme 1. Reduction of the γ-butyrolactone (**5**) with di-isobutylaluminium hydride gave the lactol, treatment of which with propane-1,3-dithiol in the presence of $SnCl_4$ afforded the 1,3-dithianes (**6a—c**) in 70—85% yields in two steps. The primary alcohols (**6**) were transformed to the α-silyloxy ethyl enol ethers (**2a—d**) in three steps in 56—65% yields.

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‡ This reaction does not take place intermolecularly in which the simple hydrolysed product, having aldehyde and methyl ketone units, is obtained quantitatively.

§ Acetyl or benzoyl groups may also be used to protect the secondary alcohol; the corresponding cyclic aldol is obtained in 70—90% yield in 4 : 1 diastereoisomeric ratio.