Solvent Mediated Reactions of Diethylhex-1-ynylaluminium with 3,4-Epoxycyclopentene

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Summary Reaction of diethylhex-1-ynylaluminium with 3,4-epoxycyclopentene in an ether solvent resulted in predominant opening of the epoxide ring by attack at the allylic carbon, while use of a hydrocarbon solvent led to rearrangement of the epoxide to cyclopent-3-enone, followed by further reaction of the carbonyl group.

SEVERAL years ago we investigated a potential route (equation [1]) to prostaglandins (**2**) that required the regioselective opening of a 3,4-epoxycyclopentene system[1,2] (**1**, vinyl Z = carbonyl synthon[3]) by appropriate organometallic reagents (RM).[4] We report here the selectivity of epoxide ring opening of 3,4-epoxycyclopentene (**3**)[5] with a dialkylalkynylaluminium reagent. We have found that reaction at the desired allylic carbon can be accomplished with moderate selectivity in an appropriate ether solvent system. In contrast, rearrangement of the same epoxide to a carbonyl group followed by further reaction was the predominant pathway in a hydrocarbon solvent. Thus reaction of (**3**)

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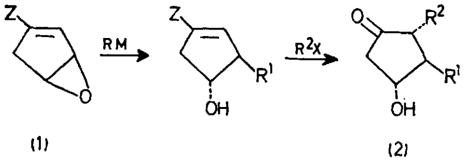
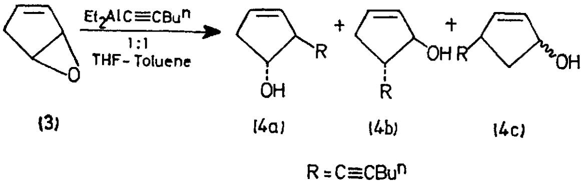
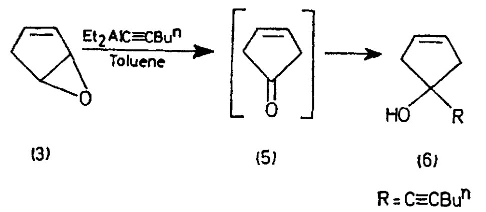
with diethylhex-1-ynylaluminium‡ (2 equiv.) in a 2:1·5:0·5 mixture of THF–toluene–hexane at −20°C, for 2 h, then overnight at room temperature, gave a 65% yield of products (equation [2]) after extraction and bulb-to-bulb distillation. Column chromatography on silica gel (50:1 weight ratio) using 10% ether in hexane as eluant gave a clean separation of four products (71% recovery). The structure of the major product (M^+ 164), comprising 75% of the mixture, was shown by n.m.r. spectroscopy (including decoupling experiments) to be the desired homoallylic alcohol (**4a**) [δ ($CDCl_3$) 3·56 (1H, m, O–CCHC≡), 4·34 (1H, m, CH–O), and 5·66 (2H, m, HC=CH)]. Smaller amounts of the products formed by attack at the homoallylic carbon (**4b**, 7%) [δ ($CDCl_3$) 3·36 (1H, m, O–C–CHC≡), 4·44 (1H, m, CH–O), and 5·68 (2H, m, HC=CH)], as well as conjugate addition (**4c**, 8%) [δ ($CDCl_3$) 3·68 (1H, m, O-CCHC≡), 4·92 (1H, m, CH–O), and 5·86 (2H, s, HC=CH)], were also identified. The structure of the remaining isomer (M^+ 164, 10%) was not clarified. The *trans* stereochemistry of (**4a**) and (**4b**) is assumed from the results of similar studies.[4a]



[1]



[2]



[3]

In striking contrast to these observations the same reaction (2 equiv. of the dialkylalkynylaluminium, −23 °C for 2 h, overnight at room temperature) in toluene§ produced (63% yield) the tertiary alcohol (**6**) [δ ($CDCl_3$) 2·76 (4H, s, $H_2CC{=}CCH_2$), and 5·68 (2H, s, HC=CH)], as the major product (84% of mixture) along with smaller amounts of (**4c**) (12%) and (**4a**) (4%). These results can be explained by the strong affinity of aluminium for oxygen. In the absence of an ether solvent the aluminium reagent apparently interacts with the epoxide oxygen and causes a highly selective rearrangement[2] of the epoxide (**3**) to cyclopent-3-enone (**5**), which then reacts further at the carbonyl group with diethyl-1-hexynylaluminium.

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‡ Generated *in situ* as follows: a solution of BuⁿLi (5·34 ml; 2·28 M) in hexane was added to anhydrous tetrahydrofuran (THF) (20 ml) and the mixture cooled to 0 °C and treated dropwise with hex-1-yne (1·4 ml; 1 mol. equiv.) followed by the slow addition of Et_2AlCl (16·24 ml; 0·75 M; 1 mol. equiv.; neat liquid[4] from Texas Alkyls) in toluene. The mixture was stirred at 0 °C for several minutes then allowed to warm to room temperature and stirred for 1·5 h. The resulting solution was treated with neat 3,4-epoxycyclopentene,[5] (0·49 ml; 0·5 mol. equiv.) at −20 °C.

§ Reaction as in ‡ footnote, except THF replaced by toluene. All reaction mixtures contained *ca.* 13% hexane (v/v) used as solvent for the BuⁿLi required for formation of hex-1-ynyl-lithium from hex-1-yne.

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