Synthesis of Potentially Bioactive 2,6-Difluorobenzyl Derivatives of Cyclic Substances Obtained from Terpenoids

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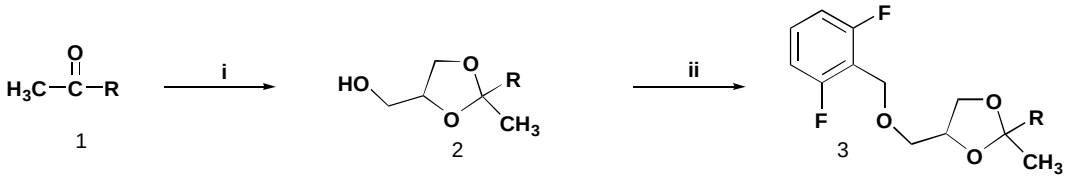
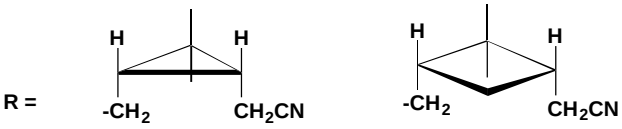
Some cyclic compounds, easily prepared from terpenoids, are versatile starting material for the synthesis of pesticides. On the other hand, 2,6-difluorobenzyl group also can be used as effective pharmacophoric building blocks. We report here the preparative synthesis of compounds containing both 2,6-difluorobenzyl group and natural framework derived from terpenoids.

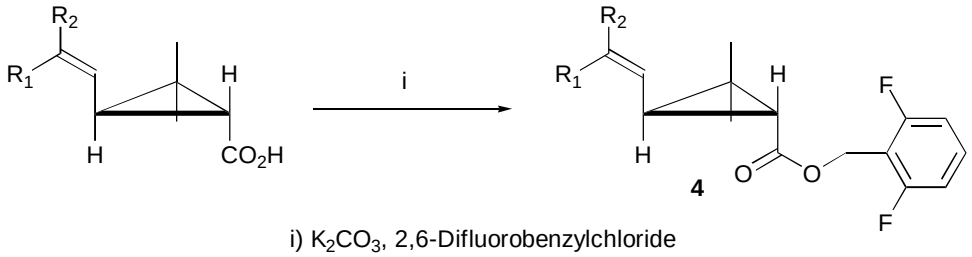
From *seco*-carene and *seco*-pinene derivatives **1** and glycerol were prepared 4-(hydroxymethyl)-1,3-dioxolanes **2**. The latter was stirred in liquid ammonia at -33°C successively with $NaNH_2$ and 2,6-difluorobenzylchloride to give 2,6-difluorobenzyl ethers **3** with good yields.



i) Glycerol, TsOH; ii) $NaNH_2$ / NH_3 (liq.), 2,6-Difluorobenzylchloride



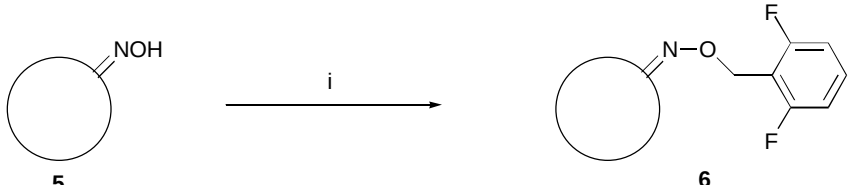
Because of the high reactivity chloro group in 2,6-difluorobenzylchloride, 2,6-difluorobenzyl esters of chrysanthemium acid derivatives **4** can be easily prepared.



i) K_2CO_3, 2,6-Difluorobenzylchloride

$R_1 = R_2 = CH_3$; $R_1 = Cl$, $R_2 = CH_3$; $R_1 = CH_3$, $R_2 = Cl$

2,6-Difluorobenzyl ethers of terpenoid ketoximes **6** were prepared in liquid ammonia at -33°C by stirring ketoximes **5** successively with $NaNH_2$ and 2,6-difluorobenzylchloride.



i) $NaNH_2$ / NH_3 (liq.), 2,6-Difluorobenzylchloride