Toetab TÜ ja TTÜ doktorikool
"Funktsionaalsed materjalid ja tehnoloogiad" (FMTDK)

ESF projekt 1.2.0401.09-0079

3-ALKYLATION OF CYCLOPENTANE-1,2-DIONES

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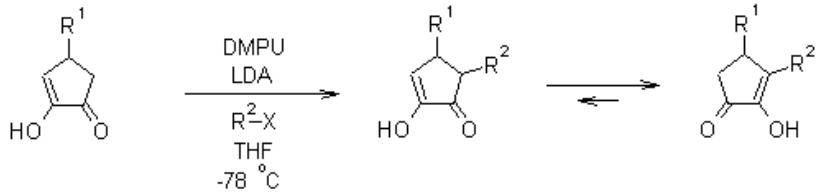
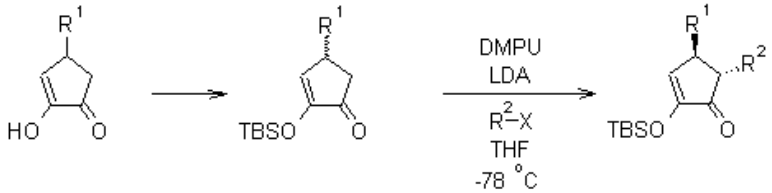
The cyclopentane template is very common among natural compounds and various synthetic analogues of natural compounds. 3-Alkyl-cyclopentane-1,2-diones can be converted to biologically active synthetic nucleoside analogues [1] that are developed as promising antiviral agents. Herein we present a novel alkylation method of cyclopentane-1,2-diones that provides a new synthetic route to 3-alkyl- and 3,4-dialkyl-cyclopetane diones that will allow to prepare the above mentioned compounds with structures previously unobtainable.



When subjected to LDA in -78 ºC the 4-substituted-cyclopentane-1,2-dione (R_1 = CH_2OBn), which exists exclusively in the depicted enolic form, can be electrophilically alkylated in the 3-position (R_2 = $CH_2COOtBu$). If DMPU is added to the reaction mixture, the selectivity and yield remain unchanged, but reaction time decreases from 2 h to 0,5 h. Under these conditions (LDA, DMPU, -78 ºC) both 4-substituted and unsubstituted cyclopentane-1,2-diones (R_1 = H, CH_2OBn) can be alkylated in the 3-position with various alkylating agents (R_2 = Me, Bn, Bz, CH_2COCH_3, $CH_2COOtBu$, CH(OH)Ph) in up to 55% isolated yield with up to 30% starting material recovered. The product is formed in the kinetic enol form which partially isomerises to the thermodynamic enol form under reaction conditions and during workup.

If the starting material (R_1 = CH_2OBn) is trapped into a single enol form by protecting the enolic OH with TBS group, the reaction exposes excellent diastereoselectivity towards *trans* alkylation when alkylated with stericly bulkier alkylating agents (R_2 = $CH_2COOtBu$, Bz). In our future research this could provide an access to enantiomerically enriched 3,4-disubstituted-cyclopentane-1,2-diones if the enol protection is performed asymmetrically [2].



References

1. A. Jõgi, M. Ilves, A. Paju, T: Pehk, T. Kailas, T. A.-M. Müürisepp, M. Lopp, *Tetrahedron: Asymmetry*, **19**, (2008), 628-634.

2. L. Ma, P. G. Williard, *Tetrahedron: Asymmetry* **17**, (2006), 3021-3029.