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An Efficient Synthesis of *cis*-Hydroindan-5-ones by Novel Modified de Mayo Reaction Using 2,3-Dihydro-4-pyrones as the Enone Chromophore

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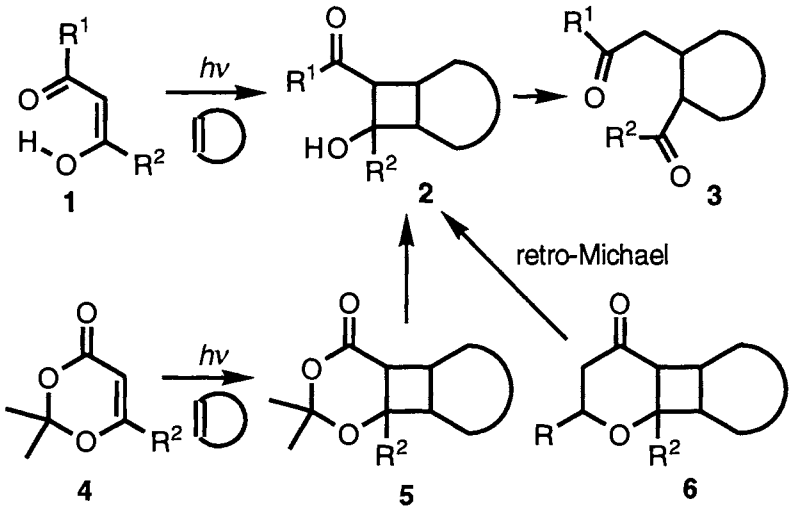
A de Mayo type cyclobutane ring opening of the photo[2+2]cycloadduct derived from 2,3-dihydro-4-pyrones and cyclopentene was effected by heating the adduct under an acid catalysis. The 1,2-disubstituted cyclopentanes thus formed spontaneously underwent intramolecular Michael addition to afford *cis*-hydroindan-5-ones in satisfactory yields.

The photo[2+2]cycloaddition of enones to alkenes has become an important reaction in the rapid construction of complex molecules.[1,2] Among the photo[2+2]cycloaddition reactions, the cycloaddition of enolized 1,3-diketones (**1**) to alkenes is often referred to as de Mayo reaction, in which the primary cycloadduct acylcyclobutanol (**2**) undergoes spontaneous retro-aldol cyclobutane cleavage to afford 1,5-diketone (**3**).[2,3]

Previously, we[4] and others[5] have reported a modified de Mayo method by using 1,3-dioxin-4-ones (**4**) as the enone chromophores. In this method, the photoadduct (**5**) is converted into the 5-oxoalkanoic acid (**3**: R^1= OH) by hydrolytic opening of 1,3-dioxane ring followed by the spontaneous cyclobutane cleavage. Based on this method, a variety of complex molecules[2,6] and chiral synthons[2,7] have been readily synthesized.



Scheme 1.

These results prompted us to investigate an alternative de Mayo variant which utilizes 2,3-dihydro-4-pyrones as the enone chromophores. The crucial step in this variant is the retro-Michael ring opening of the

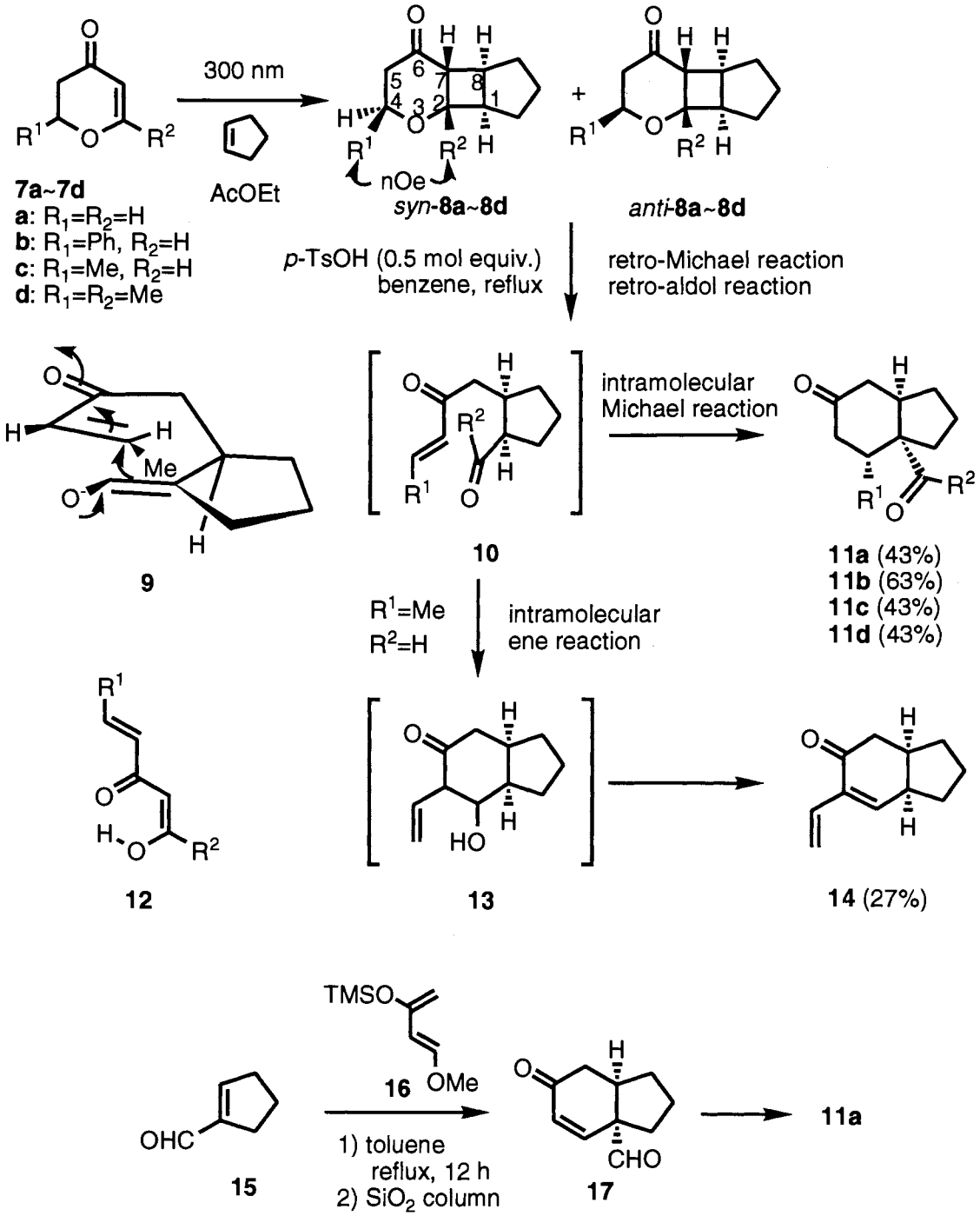
pyran ring of the photo[2+2]adduct (**6**) to generate the intermediate cyclobutanol (**2**: R^1 = CH=CHR) which inevitably produces the corresponding 1,5-diketone. In this communication, we report an efficient synthesis of *cis*-hydroindan-5-one derivatives based on this methodology.

It has been reported that 2,3-dihydro-4-pyrones efficiently undergo photo[2+2]cycloaddition to alkenes.[8] Thus, the unsubstituted pyrone (**7a**)[9] was irradiated at 300 nm[10] light in the presence of cyclopentene (20 mol equiv.) in ethyl acetate at room temperature to give the photo[2+2]adduct in 95% yield.[11] Gas chromatograph and 500 MHz ^{1}H NMR analyses revealed that this adduct consists of three diastereoisomers (*ca.* 10:4:1). The major diastereoisomer was assigned to *cis-anti-cis* adduct (**8a**) on the basis of the comparable coupling constants for the C_2-H (δ 4.090 ppm, dd, J = 6.5, 2.2 Hz) with the data for the dioxinone-cyclopentene adduct (**5**: R^2=H)[12] with the same configuration, while the configurations of the minor diastereoisomers were not determined. On irradiation under the similar conditions, substituted dihydropyrones (racemic **7b**,[13] **7c**,[13] and **7d**[14]) gave approximately equal amounts of *syn*-**8** and *anti*-**8** as the major products together with a small amount of four to six unidentified diastereoisomers (gas chromatography analysis) in total yields of 70-80%. The configuration of *syn*-**8** (less polar) and *anti*-**8** (more polar) both isolated in 30~35% yields by Lobar Column with hexane-ether (10:1) were assigned by ^{1}H NMR spectroscopic studies (nOe experiments between C_2-H or Me and C_4-H of *syn*-**8**).

Initial attempt to open the pyran ring of **8a** in retro-Michael manner by a base catalysis (*t*-BuOK in refluxing benzene) resulted in recovery of **8a**. However, the desired reaction and the concomitant cyclobutane cleavage took place under an acid catalysis followed by intramolecular Michael reaction of the unsaturated 1,5-diketone intermediate (**10**) to furnish the *cis*-fused hydroindan-5-one derivatives (**11a-d**).

Thus, refluxing a solution of **8a~d** (stereomixture) and *p*-toluenesulphonic acid (0.5 mol equiv.) in benzene for 30 min afforded **11a~d** all as a single diastereoisomer.[15] The reaction of **8c** afforded 6-vinyl-indanone **14** as the by-product.[16] Clearly, compound **14** is formed by intramolecular hetero-ene reaction at the formyl group of **10c** followed by elimination of water from the intermediate **13**. Overall yields of **11** and **14** from dihydropyrone **7** are shown in scheme 2. Both compounds **11** and **14** are deduced to have *cis*-configuration at the ring juncture on account of the transition structure **9** whose cyclization to *cis*-fused products is much more favorable than that to the *trans*-fused products. This assignment was confirmed by an alternative synthesis of **11a**. Diels-Alder reaction of 1-cyclopentene-1-carboxaldehyde (**15**) with Danishefsky's diene (**16**) in toluene (reflux, 12 h) followed by chromatography on silica gel gave the *cis*-indanone (**17**, 21% from **15**),[17] which on hydrogenation with 10% Pd-C catalyst gave **11a**. The configuration of phenyl and methyl substituents in **11b~d** is also deduced to be as depicted based on **9** with thermodynamically stable *rans*-configuration at the enone moiety. The nOe (7.6%) observed between formyl and 7-methyl protons of **11c** well supports this stereochemistry.

In conclusion, 2,3-dihydro-4-pyrones served as photochemical equivalents of enolized unsaturated 1,3-diketone (**12**)[18] whose application to de Mayo method seems to be unsuitable due to its possible prototropic tautomerism. This modified de Mayo method provides an efficient method for preparing *cis*-hydroindan skeleton. This method seems to be equally applicable to synthesis of other cyclohexanone derivatives, since the 2,3-dihydro-4-pyrones efficiently undergoes photp[2+2]cycloaddition to a variety of alkenes.[8] Further studies on this methodology including asymmetric cyclohexanone annulation using none-racemic dihydropyrones as the enone component are in progress.



Scheme 2.

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References

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10) Photoreactions were carried out using Rayonet Photochemical Reactor with RPR 3000 Å lamps. Purification by silica gel chromatography with mixture of hexane-ethyl acetate (10:1~5:1 v/v) gave oily [2+2]adduct **8** as a mixture of diastereomers, which was used directly for the next reaction.
11) All new compounds exhibited satisfactory spectroscopic (300 or 500 MHz ^{1}H NMR, IR) and high resolution mass spectral analytical data.
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15) Selected ^{1}H NMR (300 MHz, $CDCl_3$, δ) data. **11a**: 9.578 (1H, d, J = 0.8 Hz). **11b**: 2.463 (1H, dd, J = 16.6, 3.8 Hz), 2.696 (1H, dd, J 16.6, 14.0 Hz), 3.252 (1H, dd, J = 14.0, 3.8 Hz), 7.141~7.368 (5H, m), 9.435 (1H, s). **11c**: 1.228 (3H, d, J = 7.0 Hz), 9.698 (1H, d, J = 1.0 Hz). 11d: 1.012 (3H, d, J = 7.1 Hz), 2.212 (3H, s).
16) Selected ^{1}H NMR (300 MHz, $CDCl_3$, δ) of **14**: 5.152 (1H, dd, J 11.5, 1.5 Hz), 5.652 (1H, dd, J = 18.1, 1.5 Hz), 6.483 (1H, dd, J = 18.1, 11.5 Hz), 6.747 (1H, d, J = 4.0 Hz).
17) Selected ^{1}H NMR (300 MHz, $CDCl_3$, δ) data of **17**: 2.472 (1H, dd, J = 16.8, 4.0 Hz), 2.580 (1H, dd, J = 16.8, 5.9 Hz), 2.750~2.857 (1H, m), 6.150 (1H, d, J = 10.4 Hz), 6.616 (1H, dd, J = 10.4, 1.8 Hz), 9.574 (1H, s).
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