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HIGHLY EFFICIENT SYNSTHESIS OF γ-LACTONES WITH TITANIUM HOMOENOLATES

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The reaction of $TiCl_4$ with the cyclopropane 1 gives the trichlorotitanium homoenolate of alkyl propionate (2) in high yield. This titanium alkyl reacts with aldehydes to give γ-hydroxyesters or γ-chloroesters depending both on the reaction conditions and on the substrate. More nucleophilic dichloromonoalkoxytitanium homoenolate (3) is available by the reaction of 1 with 0.5--0.7 equiv of $Ti(OR)_4$. This homoenolate reacts smoothly with aldehydes and ketones to give γ-lactones. The yield ranges from 80--95% with common aliphatic and aromatic aldehydes and ketones. The new homoenolate species with RO = tert-butoxy is more reactive than the one with RO = isopropoxy. The titanium homoenolates show high equatorial selectivity (84--88%) in the reaction with substituted cyclohexanones. The selectivity is much higher than that of the related dilithium propionic acid homoenolate and comparable to the common titanium alkyl reagents. The reaction of 2 or 3 with α-substituted aldehydes gives γ-hydroxyester or γ-lactones resulting from a Cram-type transition state as a major product with over 80% selectivity. A synthetic scheme to obtain an anti-Cram compound has been devised.