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Lithiated Cyclopropanone Ketals

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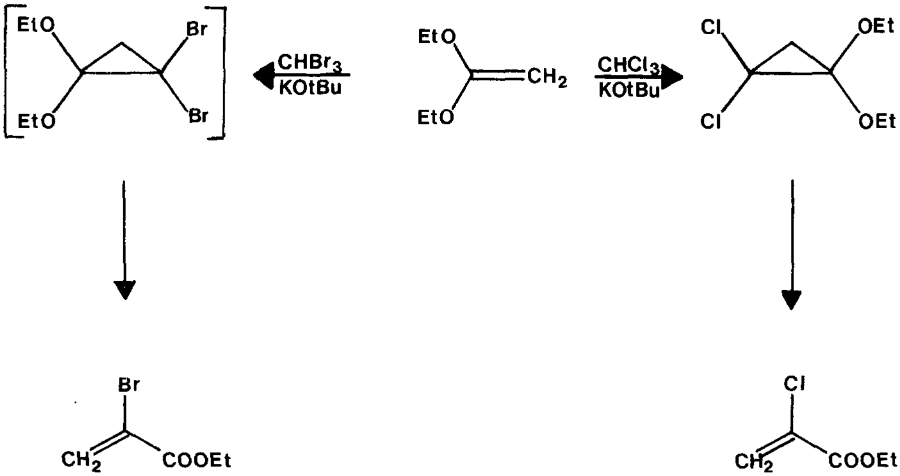
Abstract: The ketene acetal I reacted with dibromocarbene yielding the dibromocyclopropanone ketal II, which was reduced to the monobromide III by treatment with tri-n-butyltin hydride. Reaction of III with n-butyllithium at -78°C yielded the lithiated cyclopropanone ketal IV, which yielded adducts with acetone, cyclohexanone, cyclohexenone, 3,3,3-trimethoxybutan-2-one, 2-butanone, and 3-pentanone.

The cyclopropanone hydrates[1] have unusual and potentially useful functionality. However, because of their exceptional reactivity, protected cyclopropanones with attached functional groups are difficult to synthesize. For example, reaction of ethyl diazoacetate with ketene diethylacetal yielded only ring-opened product.[2] In the halogen series, the dichlorocarbene adduct with ketene diethylacetal was isolated by McElvain and Weyna,[3] who found that it rearranged (Scheme 1) to ethyl α-chloroacrylate above 100°. Dull and

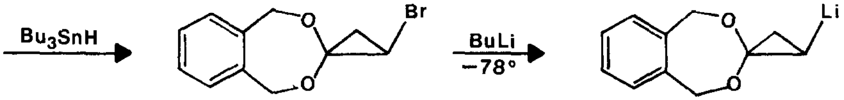


SCHEME 1

Abend[2] observed that the corresponding dibromide was too unstable to be isolated; it rearranged following preparation or on attempted distillation at 72°C to ethyl α-bromoacrylate (Scheme 1).

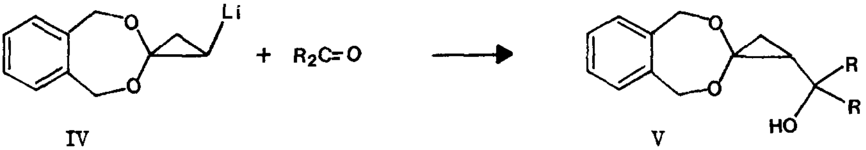
We have now found that use of a cyclic ketal dampens the reactivity of the product cyclopropane with the result that reaction of the ketene acetal I[4] with bromoform and potassium t-butoxide[5] yields the stable dibromide II, mp 135-136. The dibromide II is useful for further development because tri-n-butyltin hydride reduction of chlorocyclopropanes requires temperatures near 140°C[6] conditions too severe for the McElvain dichloride. Thus, II was readily converted to the monobromide III, mp 75-75.5°C, by treatment at room temperature with tri-n-butyltin hydride.[7,8] The lithium derivative IV was formed upon reaction of III with n-BuLi at -78°.

I II



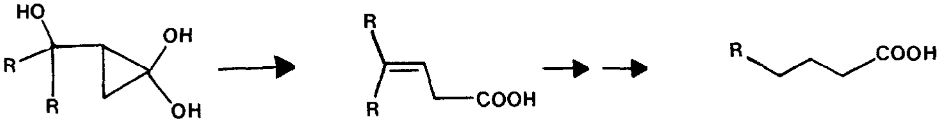
III IV

The lithiated ketal IV[10] opens many avenues for elaboration of the cyclopropanone hydrate ring system. Here, it is demonstrated that the lithiated cyclopropanone ketal IV reacts smoothly with carbonyl compounds yielding the carbinols Va-f (Table).

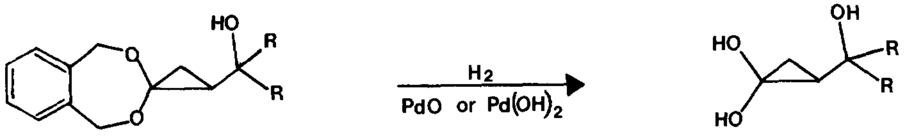


IV V

The protecting o-xylyl group may be removed by hydrogenolysis with PdO[11] in ethyl acetate or Pd(OH)$_2$[12] in MeOH with K_2CO_3. We found this reduction to be sensitive to conditions. The reactive cyclopropanone hydrate group tends to undergo ring opening followed by reduction of the resulting olefin. If the hydrogenation reaction is kept ice cold and



is carried out rapidly, the cyclopropanone hydrate can be isolated. However, each compound required some experimentation with catalyst washing and reaction time and temperature to produce optinum conditions for cyclopropanone hydrate formation.



V

VI

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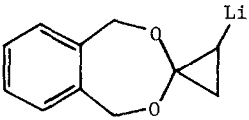
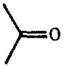
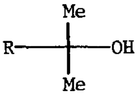
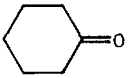
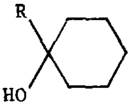
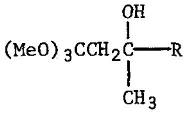
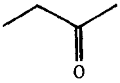
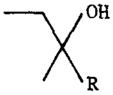
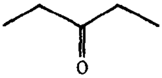
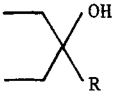
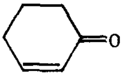
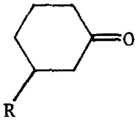
TABLE. Reaction of  (R-Li) with carbonyl compounds

Starting Materials	Products Va-f	Yield %[b]	mp °C
	 Va	66	63-65
	 Vb	67	102-103
$(MeO)_3CCH_2COCH_3$	 $(MeO)_3CCH_2\overset{OH}{\underset{CH_3}{C}}-R$ Vc	45	
	 Vd	36	
	 Ve	50	53-55
 with $Cu-C\equiv CCH_2OMe$[a]	 Vf	45	

(a) Reference 9.

(b) Isolated by chromatography on silica gel in the presence of 0.1% Hünig's base.

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