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REGIOSELECTIVITY IN THE CONJUGATE ADDITION OF LITHIUM DIMETHYLCOPPER TO CYCLOHEXADIENONES

James A. Marshall, Ronald A. Ruden[1], Larry K. Hirsch[2]
and Mark Phillippe[3]

Department of Chemistry, Northwestern University

Evanston, Illinois 60201 USA

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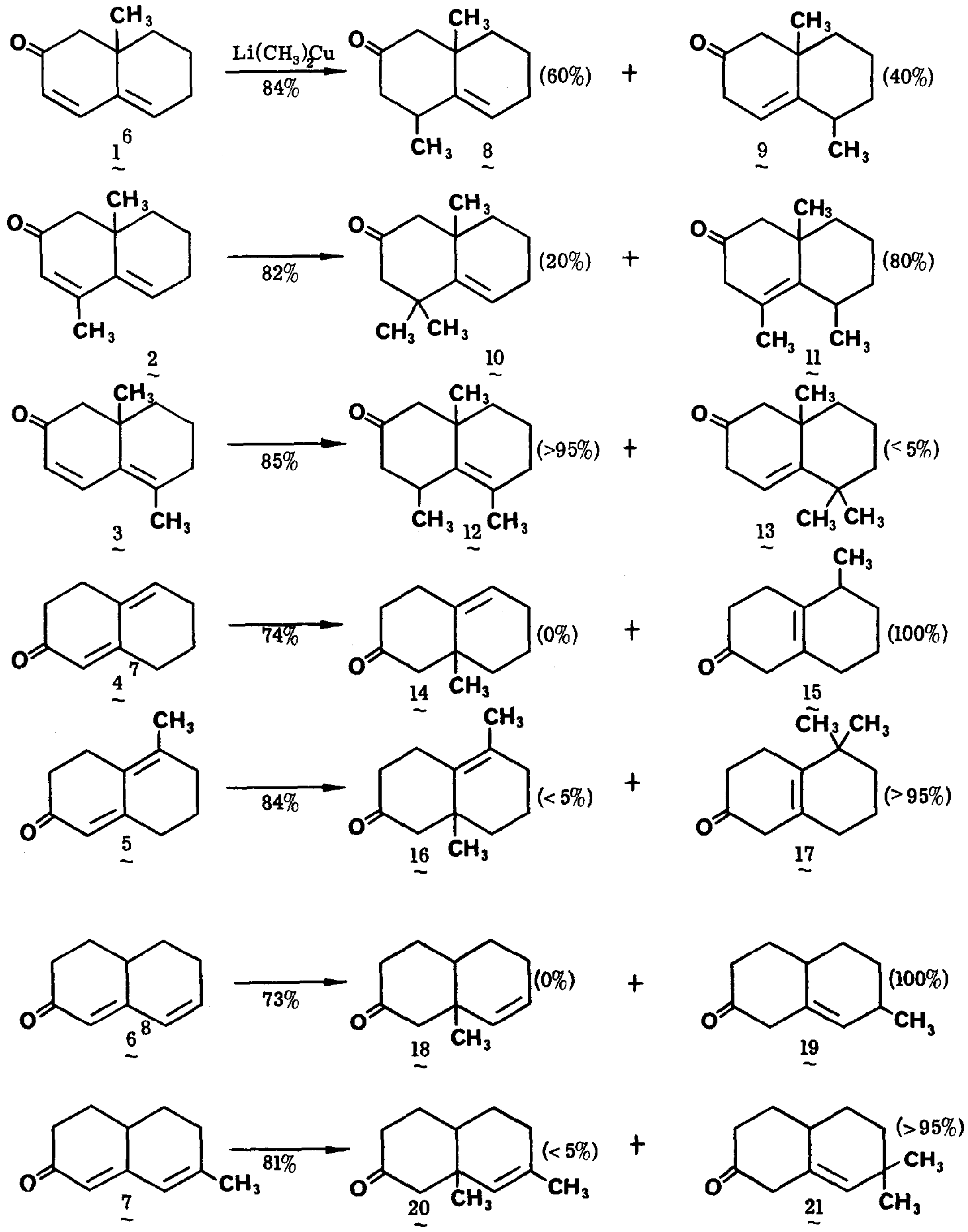
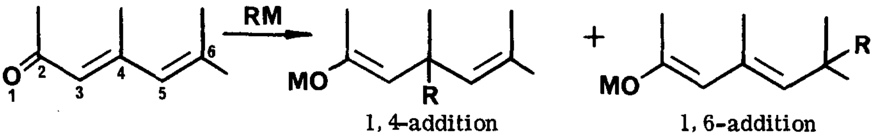
The conjugate addition of organometallic reagents to enones constitutes a useful, and often highly selective alkylation method. A number of studies have been carried out on conjugated enones and organocopper reagents with the aim of discovering the factors which control the selectivity of this reaction.[4] The situation with conjugated dienones is slightly more complicated in that 1, 6 as well as 1, 4-addition can take place (equation 1). A priori, one might expect a product-like transition state to favor the 1, 6-pathway owing to the preservation of conjugation. The 1, 4-addition, on the other hand, disrupts conjugation and thus introduces an unfavorable situation in an advanced transition state. If, however, the conjugate addition reaction proceeds through a reactant-like transition state one might expect steric factors to play a more important part such that the ratio of 1, 4 to 1, 6 adduct may be determined by the steric accessibility of the 4 vs 6 position. Of course, the most likely situation is one somewhere between these two mechanistic extremes. The study reported herein was undertaken in an effort to gain some insight regarding regioselectivity in organocopper additions to conjugated dienones.

CHART I


1⁶
Li(CH$_3$)$_2$Cu
84%
8 (60%)
9 (40%)
2
82%
10 (20%)
11 (80%)
3
85%
12 (>95%)
13 (< 5%)
4⁷
74%
14 (0%)
15 (100%)
5
84%
16 (< 5%)
17 (> 95%)
6⁸
73%
18 (0%)
19 (100%)
7
81%
20 (< 5%)
21 (> 95%)
O
CH$_3$

(1)

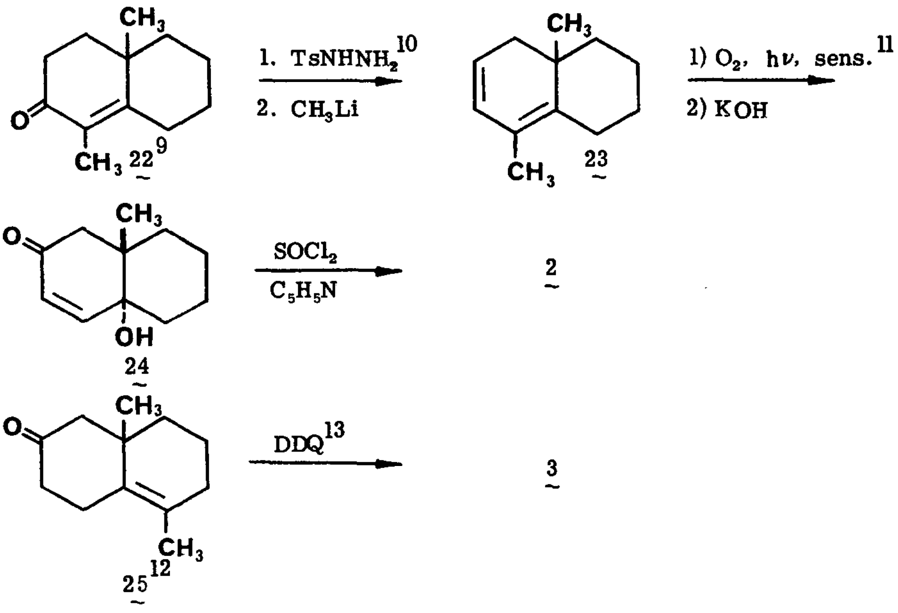


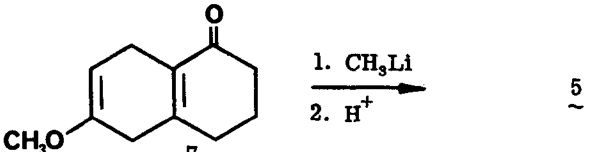
Dienones 1 - 7 were treated in ether at 0° with ethereal lithium dimethylcopper for 45 min and the resulting mixture was quenched with aqueous ammonium chloride to give the indicated addition products (Chart I).[5] Analyses of mixtures were carried out by repeated integration of the nmr spectra or by gas chromatography. In cases where 1, 6-adducts were formed, the resulting β, γ-unsaturated ketone or mixture of adducts was treated with acid (HCl-acetone) to afford the corresponding α, β-unsaturated isomer.

Our findings (Chart I) indicate that conjugation in the transition state does not exert a strong directing effect on the reaction. Thus, with dienones 1, 2 and 3 in particular, steric factors can easily be envisioned as the primary directors of regioselectivity. The most striking finding with the remaining dienones (4 - 7) is the virtual absence of angular methylation products. Again, steric control would best seem to account for this result.

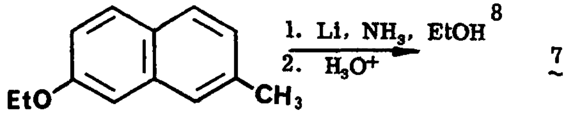
Previously unreported dienones were prepared as indicated in Chart II.

CHART II





26[7]



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