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STEREOSELECTIVE α-ALKYLATION OF KETONES AND ESTERS USING CHROMIUMTRICARBONYL-COMPLEXED BENZYL ACETATES

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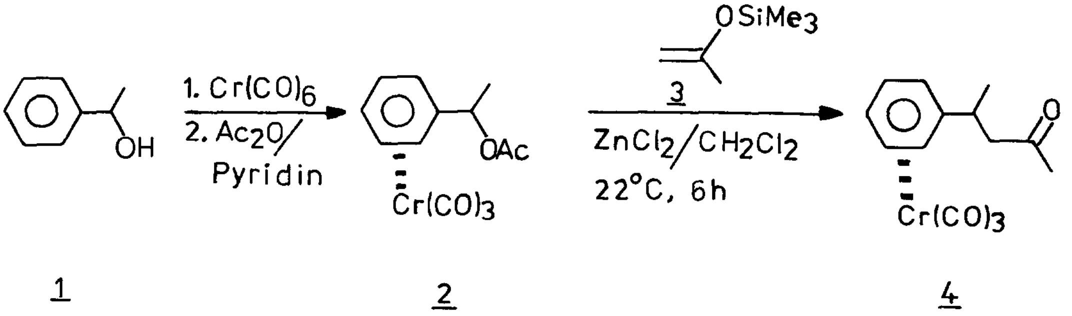
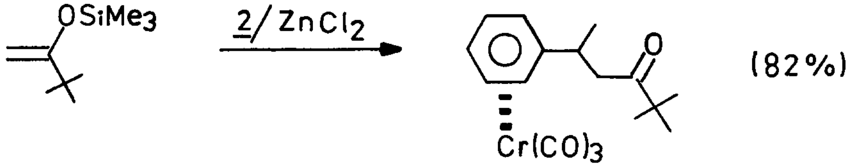
Summary: Secondary benzyl acetates complexed by $Cr(CO)_3$ react 100% stereoselectively with silyl enol ethers in the presence of $ZnCl_2$.

The complexation of aromatic compounds with $Cr(CO)_6$ to form arene-$Cr(CO)_3$ adducts alters the electronic properties of the organic substrate[1)], allowing for a number of synthetically useful manipulations[2)]. One consequence is the increased rate of S_N1 solvolysis of benzyl halides, alcohols and acetates, which occurs in such a way that typical O- and N-nucleophiles of the kind ROH, H_2O or RCN (Ritter-Reaction) trap the intermediate carbocations 72-100% anti-stereoselectively with respect to the $Cr(CO)_3$ moiety, which can then be cleaved oxidatively[1,3)]. We wish to report that carbon nucleophiles can be induced to react similarly, making 100% stereoselective C-C-bond formation possible.

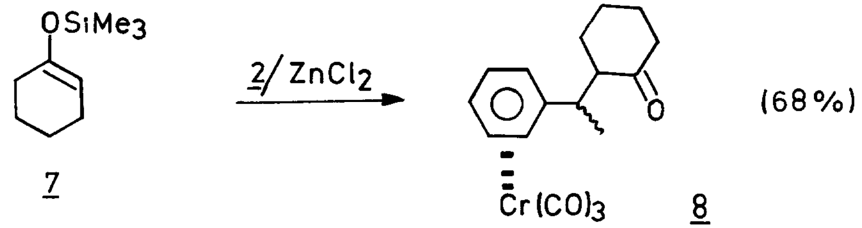
Since S_N1-active acetates alkylate silyl enol ethers in the presence of ZnX_2[4)], it seemed possible that Cr-complexed benzyl acetates such as 2[5)] could also be effective alkylating agents. Indeed, equivalent amounts of $ZnCl_2$ mediate smooth alkylation of the type 2 + 3 → 4 (∿95% conversion; 84% isolated):



The procedure is general, as shown by the formation of 6 and 8.

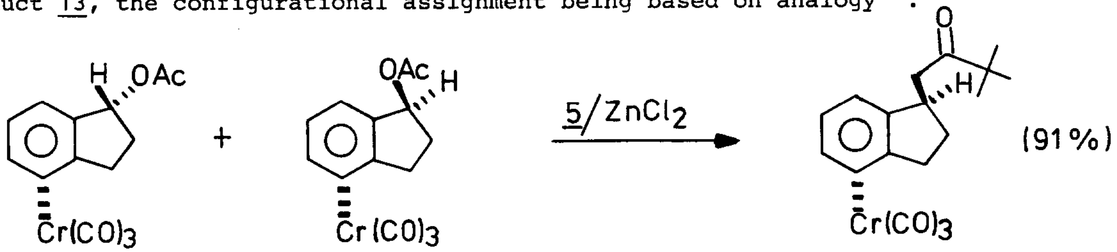


5 6



7 8

Since racemic 2 was used in all cases, no conclusion as to the stereochemistry of these unusual C-C-bond forming reactions was possible. Initial information regarding this question became available upon reacting a 40:60 diastereomeric mixture of racemic 9 and 10[5] (only the S,R- and S,S-enantiomers [6] are arbitrarily shown) with 5. The reaction produced a single (racemic) product 11. This stereoconvergent process very likely proceeds via the corresponding metal-stabilized carbocation, which is attacked in an anti manner. Indeed, use of 9[5] alone led to the same result[7]. Similarly, the ketene ketal 12 also afforded only the anti-adduct 13, the configurational assignment being based on analogy[7].



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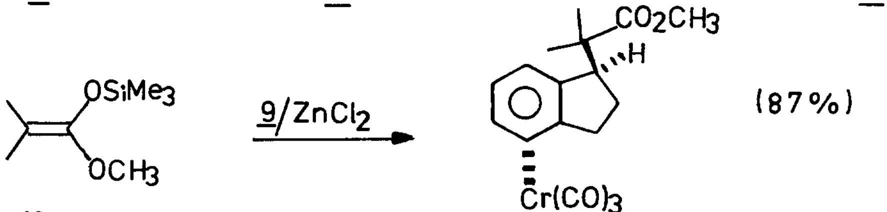
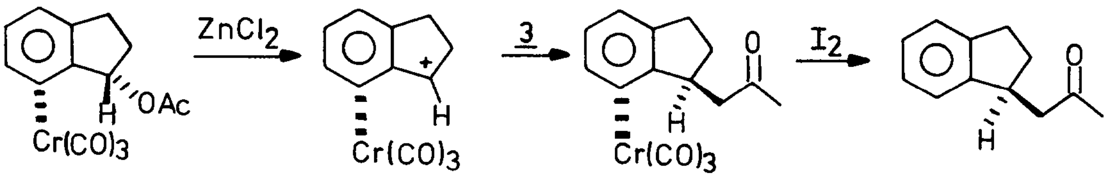


12 13

If the above assignments and conclusions are correct, use of optically active chromium complexes should result in optically active products with predictable absolute configuration. After having performed an antipode separation as described by Jaouen[8)], we reacted R,S-(-) 14 ($[\alpha]_D^{22}$ = -267°, c 1.90, $CHCl_3$; corresponding to 100% optical purity) with 3 and isolated 90% of 16 ($[\alpha]_D^{22}$ = -55°, c 1.75, $CHCl_3$). Here we employed a 50% excess of 3, in all other cases the equivalent amounts of silyl enol ethers were used. The expectation that 16 corresponds to the R,S-configuration with 100% optical purity was demonstrated by I_2-induced cleavage[9)] to form 17 (82% isolated). 17 turned out to have the S-configuration and to be 100% optically pure ($[\alpha]_D^{22}$ = -32°, c 2.24, acetone). This conclusion is based on the reported R-enantiomer which has the corresponding positive rotation[10)]. Thus, the process of alkylation described above occurs with 100% stereoselectivity anti to the metal. In this particular reaction the substitution process is one of inversion of configuration. However, in view of the previously mentioned stereoconvergence, this is simply a formality. Optically active carbocations 15 having planar chirality (in this case R-configuration) are involved.



14 15 16 17

In summary, the chiral chromium complexes described here serve as vehicles for 100% stereoselective C-C-bond formation. They are complementary to other transition-metal templates, e.g., synthetically highly useful allylic palladium complexes[11)] and cationic tricarbonyl(dienyl)iron reagents[12)] which also react with carbon nucleophiles.

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