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On the Stereochemical Outcome of the McMurry Coupling of Acetophenone. A Reinvestigation.

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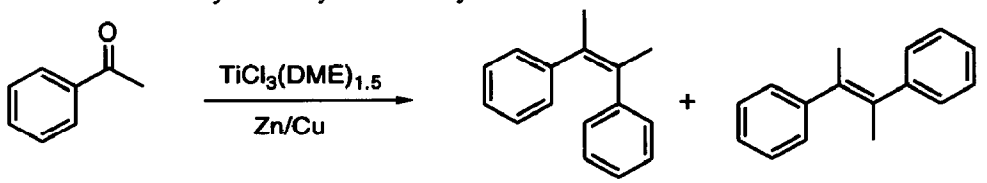
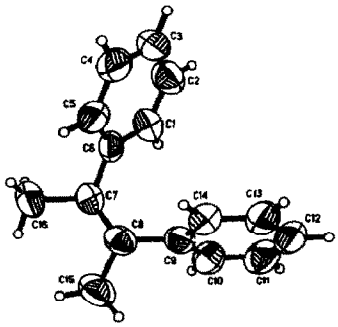
Abstract: In contrast to previous reports, the McMurry coupling reaction of acetophenone has been shown to give predominantly Z-2,3-diphenyl-2-butene.

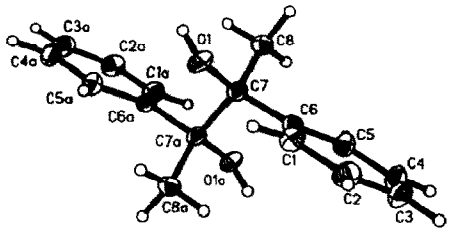
The titanium-induced reductive coupling of ketones and aldehydes has become an important method in the synthesis of olefins, especially when the target olefin is symmetrical. The stereoselectivity of the reaction depends on the substrate: aryl carbonyls often give predominantly *trans* olefins, but in the case of aliphatic carbonyls the stereoselectivity is usually considerably lower.



We recently reported on the catalytic/asymmetric dihydroxylation (AD) of tetra-substituted olefins,[1] and during this study we prepared some of the olefinic substrates via the McMurry coupling of ketones. One of the reactions tested was the coupling of acetophenone, a process well precedented in the literature and reported to give *trans*-2,3-diphenyl-2-butene. We followed the optimized procedure reported by McMurry *et. al.*[2] using $TiCl_3(DME)_{1.5}$/Zn-Cu as the source of low-valent titanium. Under these conditions the product isolated was a 92 : 8 mixture of the two double bond isomers. The isomers were separated by chromatography and the major isomer was assigned as *trans*-2,3-diphenyl-2-butene on the basis of its NMR spectrum.[3] This compound was then dihydroxylated under the optimized AD-conditions for tetra-substituted olefins and the corresponding diol was formed in 85% isolated yield. However, when the *ee* of this product was to be determined (with chiral HPLC and ^{1}H-NMR chiral shift reagents) it became obvious that it was a meso compound. Comparison of the ^{1}H-NMR spectrum with data from the literature[3b, 3c, 4] also suggested that the diol was a meso compound, which in turn would imply that the osmylation had taken place in an *anti* fashion over the double bond! In order to get an unambiguous answer to this problem the compound was subjected to X-ray crystallographic analysis,[5] which confirmed the meso structure. This left us with two alternatives, either an *anti* dihydroxylation or an incorrect assignment of the starting olefin. An osmium catalyzed dihydroxylation proceeding in an *anti* fashion is highly unlikely. In order to secure the assignment of the olefinic starting material, the 2,3-diphenyl-2-butene was subjected to X-ray crystallography.[5] The olefin did indeed have the Z-configuration, explaining why the *syn*-dihydroxylation had resulted in the meso diol. There has been a number of papers dealing with the reductive coupling of acetophenone to give 2,3-diphenyl-2-butene and in the majority of them[3a-d] use of incorrect literature data has led to a reversed assignment of the *E* and *Z* forms.



ORTEP drawing of the X-ray crystal structure of *Z*-2,3-diphenyl-2-butene



ORTEP drawing of the X-ray crystal structure of *erythro*-2,3-diphenyl-2,3-butadiol

It is also noteworthy that the predominant formation of *Z* olefin is probably not limited to the coupling of acetophenone, which might also mean that other assignments of tetra-substituted biaryl olefins are in error. For instance, it has been reported[6] that the homocoupling of *p*-bromoacetophenone and *p*-(triflouromethyl)-acetophenone, respectively, results in products with *E*-configuration. In a footnote, the author makes the comment that their assignment is in conflict with previous literature data since both melting points and ^{1}H-NMR spectroscopic data indicate that the products should be the *Z* isomers instead. In another case[7] the homocoupled products derived from *o*-(*p*-$CH_3C_6H_4SO_3$)-acetophenone, and *p*- and *m*-acetoxy acetophenone, respectively, have been tentatively assigned as *E*, on the basis of their UV-spectra.

In conclusion, it has been shown unambiguously by X-ray crystallography that the McMurry coupling of acetophenone gives predominantly *Z*-2,3-diphenyl-2-butene; earlier stereochemical assignments have thus been shown to be in error. Therefore, caution should be exercised in the assignment of the stereochemistry of tetrasubstituted olefins produced by the McMurry homocoupling reaction of ketones.

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5. Crystal data for olefin: $C_{16}H_{16}$,, crystal size=0.15x0.3x0.5 mm, monoclinic space group $P2_1$, a=10.224Å, b=8.713Å, c=14.349Å, β=95.65°, V=1272.1Å^3, Z=4, D_{calc}=1.088g/cm^3.Crystal data for diol: $C_{16}H_{18}O_2$, crystal size=0.5x0.5x0.5 mm, triclinic space group P1, a=7.939Å, b=8.996Å, c=9.755Å, α=68.60°, β=82.24°, χ=89.17°, V=642.3Å^3, Z=2, D_{calc}=1.253g/cm^3. Data were measured on a Siemens R3m/V diffractometer with graphite monochromated Mo-Kα radiation.
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