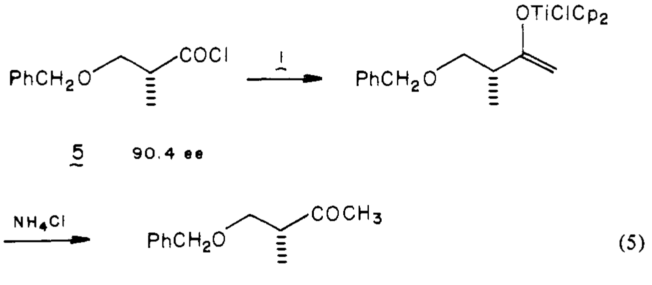
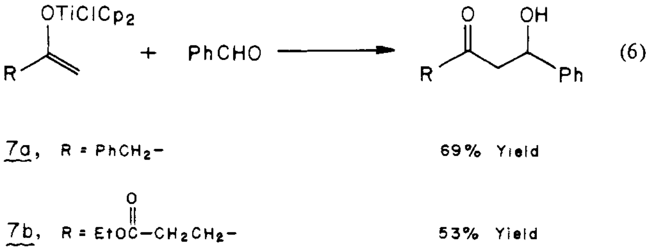


(5)

The optimum conditions for enolate formation with the acid chloride as the limiting reagent were determined by hydrolysis to the methyl ketone without prior isolation.[9] It is evident from Table I that the yields of ketone enolates are near 90% even with a bulky α-carbon or potentially reactive functionality present in the molecule.

These enolates undergo standard enolate reactions such as aldol condensation.[10] The reaction of the phenylacetone enolate, **7a**, with benzaldehyde demonstrates the regiostability of the enolate under the reaction conditions. A second example, **7b**, illustrates the selectivity of the reaction when another carbonyl functionality is present. The major byproduct of these reactions is the methyl ketone resulting from protonation of the enolate. In view of the recent development of methods for the synthesis of substituted alkylidenes,[12] this reaction provides a general new tool for organic synthesis.



(6)

Acknowledgment. We acknowledge the support of the National Science Foundation and helpful discussions of D. A. Evans.

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[8] The chiral carboxylic acid was obtained 99.2% optically pure from D. J. Mathre and D. A. Evans. The conversion to **5** by oxalyl chloride proceeded with slight epimerization resulting in 95.2% optically pure acid chloride. This was quantified by reaction with the lithium salt of (4*S*)-4-(2-propyl)oxazolidin-2-one and analysis of the resulting diastereomeric mixture by capillary gas chromatography. With correction for the enantiomeric impurity of the acid chloride, the methyl ketone produced an optical rotation $[\alpha]^{25}_{D}$ −19.3 (31 mg/mL). This is identical with that of an independently synthesized sample of the methyl ketone using the $(CH_3)_2CuLi$ reagent, shown not to epimerize the α chiral center of an acid chloride, and the procedure obtained from Posner et al. (Posner, G. H.; Whitten, C. E.; McFarland, P. E. *J. Am. Chem. Soc.* **1972**, *94*, 5106).

[9] Typically, 1.2 equiv of **1** was cooled to −20 °C and dissolved (0.4 M solution) in precooled toluene with stirring. The acid chloride was added via syringe, and the mixture was warmed to 0 °C. At this temperature, **1** dissociates into **2** and isobutylene, allowing the reaction to occur. After a short time, as recorded in Table I, the mixture was warmed to a higher temperature to ensure completion of the reaction. Hydrolysis was achieved by cooling the solution to −10 °C and introducing 1.5 equiv of HCl gas into the reaction vessel via syringe. All titanium precipitated from solution as titanocene dichloride. The supernatant was then removed for VPC analysis or isolation of the methyl ketone by silica gel chromatography.

[10] Yield of isolated product based on 1 mmol of acid chloride used for in situ formation of the enolate. Products were characterized by ^1H NMR, ^{13}C NMR, IR, and C,H analysis. The aldol product (67% yield), starting from pivaloyl chloride and pivaldehyde, was identified by comparison to literature spectra.[11]

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Aryl Isomerization during Aliphatic CH Bond Activation

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The transition-metal-stabilized benzyne or *o*-phenylene (η^2-C_6H_4) ligand has been shown to be both an interesting and reactive group.[1-7] The ligand is normally generated in mononuclear systems by β- (ortho-) hydrogen abstraction from an aryl group, and this synthetic approach has allowed a stable example to be isolated and structurally characterized.[8]

We report here our conclusive identification of a benzyne intermediate during the isomerization of a tantalum–aryl compound. The reaction is interesting in that the ortho hydrogen is transferred to the carbon atom of a cyclometalated chelate, the reverse (isomerization) step thus involving the activation of an aliphatic CH bond by the intermediate benzyne.

We recently reported that alkylation of $Ta(OAr')_2Cl_3$ (I) (OAr′ = 2,6-di-*tert*-butylphenoxide) with LiPh (3 equiv) leads to the room-temperature formation of $Ta(OC_6H_3\text{-}t\text{-}BuCMe_2CH_2)(OAr')(Ph)_2$ (II), in which one of the CH bonds of a *tert*-butyl group has been activated and cleaved.[9] Thermolysis of II (120 °C/toluene) leads to the loss of benzene and formation of $Ta(OC_6H_3\text{-}t\text{-}BuCMe_2CH_2)_2(Ph)$ (III), in which a further CH bond activation has taken place.[9] We have extended this chemistry to the use of the three tolyllithium reagents and have obtained the results shown in Table I.[10] The three products obtained at room temperature, IIo, IIm, and IIp, can be shown by ^1H NMR spectroscopy to be isomerically pure (>98%). However, the product of thermolysis of these compounds at 125 °C are mixtures of IIIm and IIIp. Hence, isomerization of the tolyl groups is taking place during the second step of the reaction. A possible pathway

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(10) The three isomeric tolyllithium reagents were synthesized from the corresponding bromotoluene and *n*-butyllithium in hexane/toluene. The compounds $Ta(OC_6H_3\text{-}t\text{-}BuCMe_2CH_2)(OAr')(tol)_2$, *o*-tolyl (IIo), *m*-tolyl (IIm), and *p*-tolyl (IIp) were obtained by treating $Ta(OAr')_2Cl_3$ with the corresponding lithium salts in benzene and isolated by using the same procedures outlined in ref 9 for the synthesis of II. In the case of IIo the yield was substantially lower than for the other isomers. The ^1H NMR spectra of the compounds showed them to be isomerically pure. In particular, the chemical shifts and pattern of the ortho protons was extremely characteristic. ^1H NMR spectra (470 MHz, toluene-d_8) (IIo) δ 8.62 (d, *o*-H); (IIm) δ 7.93 (s), 7.90 (d, *o*-H's); (IIp) δ 7.95 (d, *o*-H). The aryloxide resonances were very similar to those of II; see ref 9. Thermolysis of these compounds was carried out in sealed ^1H NMR tubes in toluene-d_8. Toluene was generated along with a mixture of IIIm and IIIp. No IIIo could be observed. Again, the ^1H NMR spectrum of the mixtures is distinctive in the aromatic region, allowing a determination of the isomer ratio. ^1H NMR spectrum (470 MHz, toluene-d_8) (IIIm) δ 7.97 (s), 7.95 (d, *o*-'s); (IIIp) δ 8.05 (d, *o*-H). The aliphatic chemical shifts of the metalated aryloxide ligands were very similar to those of III; see ref 9.

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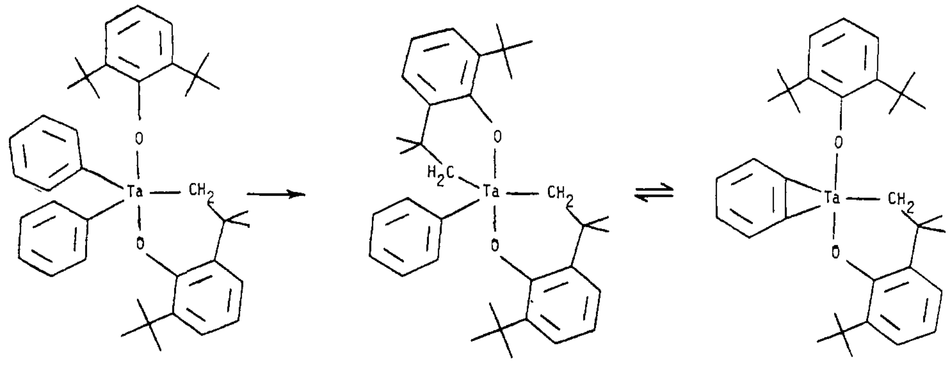
Table I[a–d]

$$\mathrm{Ta(OAr')_2Cl_3 + 3Li(tol)} \xrightarrow{25\ ^\circ\mathrm{C}} \underset{\mathrm{IIo\quad IIm\quad IIp}}{\mathrm{Ta(OC_6H_3\text{-}\mathit{t}\text{-}BuCMe_2CH_2)(OAr')(tol)_2}} \xrightarrow{125\ ^\circ\mathrm{C}} \underset{\mathrm{IIIo\quad IIIm\quad IIIp}}{\mathrm{Ta(OC_6H_3\text{-}\mathit{t}\text{-}BuCMe_2CH_2)_2(tol)}}$$

	IIo	IIm	IIp	IIIo	IIIm	IIIp
ortho, %	100				70	30
meta, %		100			60	40
para, %			100		25	75

[a] Products obtained by using *o*-, *m*-, or *p*-tolyl lithium. [b] IIo, IIm, and IIp refer to the monocyclometalated compounds containing two *o*-, *m*-, or *p*-tolyl groups. [c] IIIo, IIIm, and IIIp refer to the biscyclometalated compounds containing one *o*-, *m*-, or *p*-tolyl group. [d] Thermolysis was carried out at 125 °C for 24 h.

Scheme I



(II) (III)

for the second reaction is the initial formation of a benzyne group from the diaryl compound, which rapidly adds an aliphatic CH bond to give the product. However, this mechanism of isomerization cannot account for the formation of some of the para isomer (IIIp) from the ortho intermediate (IIo).[11] On heating the mixtures obtained in Table I to 170 °C for 12 h, an identical thermodynamic mixture of IIIm and IIIp (50:50 ± 5%) is given. Clearly this implies that isomerization can occur in the monoaryl products themselves.

The mechanism of this isomerization was conclusively identified by synthesis and thermolysis of the labeled compound $\mathrm{Ta(OC_6H_3\text{-}\mathit{t}\text{-}BuCMe_2CH_2)(OAr')(C_6D_5)_2}$ (II*).[12] On mild thermolysis (100 °C/toluene-d_8) the compound smoothly converts to III* with no detectable kinetic isotope effect on the rate of the reaction when compared with unlabeled II. Detailed analysis of the ^{1}H NMR spectrum of the product in the aromatic region showed the presence of a small signal at δ 8.05 due to less than 5% hydrogen in the ortho position. After the compound was heated at 170 °C for 12 h, analysis showed this signal to have increased significantly in intensity. Further monitoring of the solution spectra after various times at this temperature showed a gradual buildup of this signal and a smaller doublet building up at the meta position. After 72 h at 170 °C, the spectra showed a great deal of incorporation of hydrogen into the ortho, meta, and para positions of the phenyl group (see supplementary materials).

Carrying out the thermolysis of II* in toluene and monitoring the reaction by ^{2}D NMR gave complementary results.[13] Initially at 100 °C, the deuterium label was entirely contained in the ortho, meta, and para positions of the Ta–Ph function of III*. On extended heating at 170 °C, this label scrambled from the aromatic region and signals built up in the aliphatic region at the same chemical shifts as those of the *t*-Bu, $\mathrm{CMe_2}$, and $\mathrm{CH_2}$ groups. Hence the label scrambles over the 39 possible sites in the Ta*Ph* and $\mathrm{Ta(OC_6H_3\text{-}\mathit{t\text{-}BuCMe_2CH_2})}$ functions.

These results are consistent with the pathway indicated in Scheme I, in which the ortho proton (or deuterium) is transferred to the Ta–$\mathrm{CH_2}$ function to cause an opening of the metalated ring and formation of a benzyne ligand. Readdition of one of the aliphatic CH bonds can now take place allowing isomerization (in the tolyl case) or H/D exchange into the aliphatic groups of the metalated aryloxide. The fact that the deuterium label can also scramble with the nonmetalated *t*-Bu group implies that the intermediate benzyne complex $\mathrm{[Ta(OC_6H_3\text{-}\mathit{t}\text{-}BuCMe_2CH_2)(OAr')(\eta^2\text{-}C_6H_4)]}$ has a sufficient lifetime to allow rotation of the aryl oxide to present a new *t*-Bu group for activation.

However, although these results clearly imply the intermediacy of a benzyne during the isomerization of the final products, it is not yet clear if the lack of formation of any IIIo from IIo at 125 °C is due to the fact that isomerization is very fast in IIIo, leading to IIIm and then IIIp, or whether the metalation step in the more sterically crowded IIo involves the direct formation of an intermediate benzyne as outlined earlier.[11]

Acknowledgment. We thank the donors of the Petroleum Research Fund, administered by the American Chemical Society, and Research Corp. for support of this work.

Supplementary Material Available: 470-MHz ^{1}H NMR spectra showing the gradual increase of proton resonances in the aromatic region (1 page). Ordering information is given on any current masthead page.

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(11) (a) Only two isomers of the benzyne ligand $\eta^2\text{-}\mathrm{C_6H_3Me}$ can exist, 2-methylbenzyne and 3-methylbenzyne. The ortho-tolyl group can only form 2-methylbenzyne by abstraction of an ortho hydrogen, and readdition of a hydrogen can lead either back to the ortho-tolyl (presumably less sterically favored) or to the meta-tolyl group. A one-step ortho- to para-tolyl isomerization is therefore not possible by this process. The meta-tolyl group has the option to form both methylbenzynes, depending on which ortho hydrogen is removed, and hence can theoretically isomerize directly to a mixture of ortho-, meta-, and para-tolyl groups. (b) We note that facile isomerization of methylbenzyne ligands has been observed on triosmium clusters; see: Arce, A. J.; Deeming, A. J. *J. Chem. Soc., Dalton Trans.* **1982**, 1155.

(12) $\mathrm{LiC_6D_5}$ was synthesized from $\mathrm{C_6D_5Br}$ (99.59% deuteriated; Merck and Co.) and *n*-butyllithium in hexane/toluene. The syntheses of II* and III* were identical with those of the unlabeled compounds.

(13) The ^{2}D NMR spectra of II* and III* were obtained on a Varian XL-200 spectrometer in sealed 5-mm NMR tubes with purified toluene as solvent. The initial spectrum of III* showed δ 8.10 (*o*-D), 7.8 (br, *m*- and *p*-D). After extended heating these signals decreased in intensity and new peaks at δ 1.6 (*t*-Bu), 1.3 ($Me_2\mathrm{CH_2}$), and a small peak at δ 2.3 due to deuterium in one of the diastereotopic $\mathrm{CMe_2}CH_2$ positions. The ratio of these peaks was approximately the same as those seen in the ^{1}H NMR of III, showing that the H/D scrambling is statistical over the aliphatic groups.