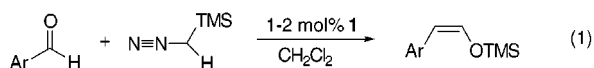# Rhodium(I)-Catalyzed Homologation of Aromatic Aldehydes with Trimethylsilyldiazomethane

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One-carbon homologation reactions are of broad utility in organic synthesis. In the case of aromatic aldehyes, homologation to the corresponding arylacetaldehydes has previously been accomplished via conversion to the epoxides[1] and subsequent rearrangement, or phosphorane transfer[2] followed by acid hydrolysis of the resulting alkyl enol ethers. In this communication, we report the single-step transformation of aromatic aldehydes to *cis*-1-aryl-2-trimethylsilyloxy ethylenes, that is the phenyl acetaldehydes protected as their *cis*-TMS-enol ethers, employing trimethylsilyldiazomethane and the rhodium(I) Lewis acid catalyst **1** (eq 1). This reaction is equivalent to *three* separate steps

$$Ar\overset{O}{\underset{H}{\bigvee}} + N\!\equiv\!\overset{TMS}{\underset{H}{N\!-\!}} \xrightarrow[\text{CH}_2\text{Cl}_2]{\text{1-2 mol\% }\mathbf{1}} Ar\diagdown\diagup OTMS \qquad (1)$$

employing standard organic techniques[3] and is selective for the *Z*-isomer. Furthermore, experimental evidence supports the involvement of a unique, *stable* rhodium(I)−trimethylsilyldiazomethane complex, **2**, which has been isolated and crystallized.

Treatment of an orange solution of the three-coordinate, 14-electron rhodium complex **1**[4] in dichloromethane at −78 °C with trimethylsilyldiazomethane (eq 1) produced a dark green solution, which upon addition to cold pentane gave a microcrystalline solid that was determined by spectroscopic and crystallographic methods to be the *N*-bound adduct of TMS-diazomethane, **2**.[5] Complex **2** is the first example of a transition metal η^1-*N*-bound diazoalkane complex that contains a proton at the α-carbon atom, and it is the only diazoalkane complex that lacks either the resonance stabilization provided by esters or aromatic groups,[5,6] or the additional steric and electronic stabilization provided by a second TMS group.[5,7] The isolated product **2** is moderately stable

(1) (a) Lemini, C.; Ordonez, M.; Perez-Flores, J.; Crus-Almanza, R. *Synth. Commun.* **1995**, *25*, 2695−2702. (b) Cannon, J. G.; True, C. D.; Long, J. P.; Bhatnagar, R. K.; Leonard, P.; Flynn, J. R. *J. Med. Chem.* **1989**, *32*, 2210−2214. (c) Haridas, K. *Indian J. Chem., Sect. B* **1987**, *26B*, 1018−1020. (d) Capon, R. J.; Ghisalberti, E. L.; Jefferies, P. R. *J. Chem. Res. Synop.* **1987**, 118−119. (e) Sinha, J.; Singh, R. P.; Srivastava, J. N. *J. Indian Chem. Soc.* **1986**, *63*, 907−909. (f) Hanlon, B.; John, D. I. *J. Chem. Soc., Perkin Trans. 1* **1986**, 2207−2212.

(2) (a) Sardessai, M. S.; Abramson, H. N. *Org. Prep. Proced. Int.* **1991**, *23*, 419−424. (b) Nair, M. G.; Murthy, B. R.; Patil, S. D.; Kisliuk, R. L.; Thorndike, J.; Gaumont, Y.; Ferone, R.; Duch, D. S.; Edelstein, M. P. *J. Med. Chem.* **1989**, *32*, 1277−1283. (c) Doad, J. G. S. *J. Chem. Res., Synop.* **1987**, 370−371.

(3) Two steps are required to homologate an aryl aldehyde (see refs 1 and 2) and a third to protect it as the silyl enol ether.

(4) Dias, E. L.; Brookhart, M.; White, P. S. *Chem. Commun.* In press.

(5) For a recent review of transition metal complexes of diazoalkanes, see: Dartiguenave, M.; Menu, M. J.; Deydier, E.; Dartiguenave, Y.; Siebald, H. *Coord. Chem. Rev.* **1998**, *180*, 623−663.

(6) (a) Werner, H.; Schneider, M. E.; Bosch, M.; Wolf, J. *et al. Chem. Eur. J.* **2000**, *6*, 3052−3059. (b) Wolf, J.; Lutz, B.; Fries, A.; Werner, H. *Angew. Chem., Int. Ed. Engl.* **1990**, *29*, 510−512.

(7) Menu, M. J.; Crocco, G.; Dartiguenave, M.; Dartiguenave, Y.; Bertrand, G. *J. Chem. Soc., Chem. Commun.* **1988**, 1598−1599.

(8) It should be noted that this distance may be somewhat artificially shortened by vibrational disorder about N(8).

(9) One methyl of the TMS group does in fact have van der Waals contacts with an isopropyl group of the neighboring molecule, which is manifested in an uncharacteristic twisting of the isopropyl group with respect to the plane of the aromatic ring.
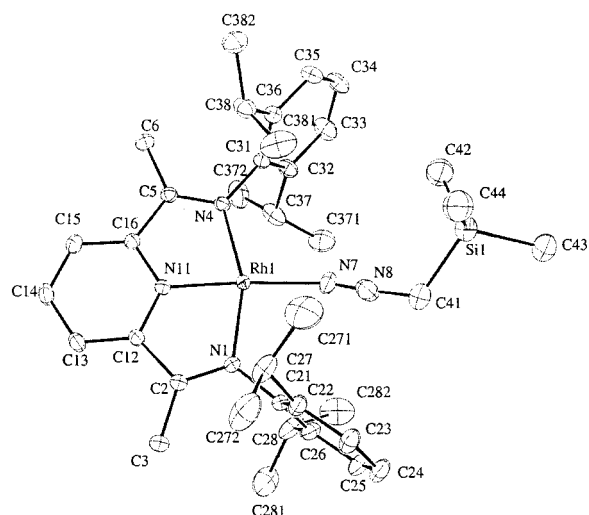
Figure 1. X-ray crystal structure of **2**. Thermal ellipsoids are drawn at the 50% probability level. Selected bond lengths and angles are: Rh-(1)−N(7), 2.007(3); Rh(1)−N(1), 2.0203(25); Rh(1)−N(11), 1.0952(24); N(7)−N(8), 1.067(5); N(8)−C(41), 1.348(6); Rh(1)−N(7)−N(8), 142.1-(3); N(7)−N(8)−C(41), 176.2(4); N(11)−Rh(1)−N(7), 175.56(12).

in dichloromethane solution at room temperature, decomposing to unidentified products with a half-life of approximately 12 h.
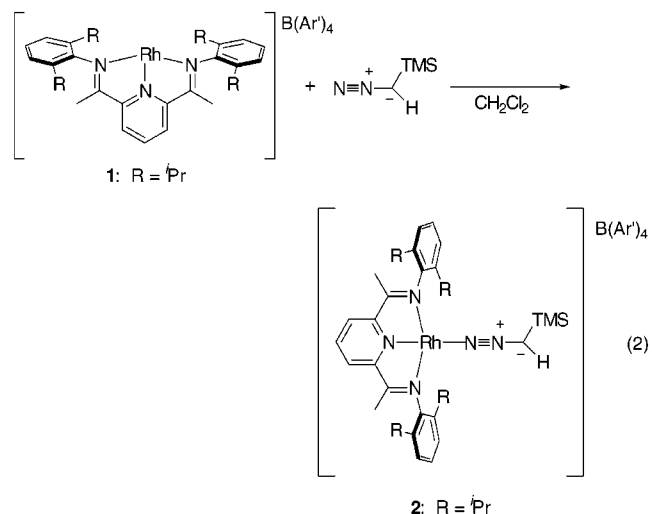
On the basis of spectroscopic data, the resonance structure depicted in eq 2 is the more accurate description of **2**. In the infrared spectrum, ν(N−N) = 2057 cm^{-1} in dichloromethane (2030 cm^{-1} KBr), as compared with 2069 cm^{-1} for free TMS-diazomethane. Not only does this confirm the triply bonded structure, but it also suggests that there is little to no back-bonding from rhodium to nitrogen. In the ^{1}H NMR spectrum (CD$_2$Cl$_2$), the TMS-diazomethane proton appears as a doublet at δ = 2.44 ppm, with a surprising $^4J_{Rh-H}$ = 2 Hz. The α-carbon resonance appears as a broad singlet at δ = 38.2 ppm in the ^{13}C NMR spectrum, comparable to chemical shifts observed for the two bis-trimethylsilyldiazomethane complexes that have been previously reported.[7]

The X-ray crystal structure of **2** (Figure 1) reinforces these observations. The Rh(1)−N(7) distance of 2.01 Å is comparable to that for the imine nitrogens (∼2.03 Å), indicating that the TMS-diazomethane acts as a simple two-electron donor ligand. The N(7)−N(8) distance of 1.07 Å confirms the triple bond character, and is by far the shortest N−N bond length observed for this type of complex (∼1.16 Å for other structures).[5−7,8] While

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Table 1. Aryl Aldehydes and TMS-Enol Ether Products[a]

| Substrate	X (sub)	Product	X (prod)	Yield (%)[b]	E:Z[c]
	3a: H		**4a:** H	62	1:3.7
	3b: Cl		**4b:** Cl	63	1:5.1
	3c: OCH$_3$		**4c:** OCH$_3$	80	1:8.7
	3d: NMe$_2$		**4d:** NMe$_2$	(82)	1:4.5
	5a: CH$_3$		**6a:** CH$_3$	56	1:3.0
	5b: NO$_2$		**6b:** NO$_2$	(54)	1:5.3
	7a: CH$_3$		**8a:** CH$_3$	47	1:2.9
	7b: OH		**8b:** OTMS[d]	36[d]	——[e]
	9a: O		**10a:** O	(60)	1:2.4
	9b: S		**10b:** S	74	1:6.2

[a] Conditions: [aldehyde] = [TMS-diazomethane] = 0.33 M, [**1**] = 5.3 mM. [b] Yields in parentheses are conversions determined in NMR scale experiments; all others are isolated yields. [c] E:Z ratios determined from NMR scale experiments. [d] The other product of the reaction was an insoluble polymer resulting from self-deprotection. [e] Undetermined.

the N(7)−N(8)−C(41) bond angle of 176° is the most linear geometry that has been observed, one puzzling aspect of this structure is the nonlinear Rh(1)−N(7)−N(8) bond angle of 142°. Although it is impossible to definitively identify the cause of this anomaly, crystal-packing forces appear to be at least partly responsible.[9]

Adding benzaldehyde to a solution of **2** in an NMR scale reaction results in the transformation depicted in eq 1. In addition to the *Z*-isomer which is produced in 80% conversion, the *E*-isomer (∼15%) and 1-phenyl-1-(trimethylsilyloxy)ethylene (<5%) are also observed as minor reaction products. When the reaction is performed catalytically in CH$_2$Cl$_2$, using 1−2 mol % of **1** generated in situ, vigorous nitrogen evolution occurs accompanied by an exotherm large enough to cause the solvent to boil. Best results were obtained when the aldehyde was added dropwise either as a neat liquid, or as a dichloromethane solution for solids, and a cold water bath was used to control the temperature. The *cis*-TMS-enol ethers are readily separated from the catalyst and minor isomers via flash chromatography on silica gel.

The reaction in eq 1 is fairly general in terms of substrates (see Table 1), with yields typically ranging from 50 to 80%, and proceeds in the manner described above with a few exceptions. While aldehydes with electron-donating substituents react the fastest, those with electron-withdrawing substituents react much slower, or in some cases not at all. For instance, the best substrates are 4-anisaldehyde and thiophene-2-carboxaldehyde, while 4-tri-fluoromethyl benzaldehyde does not react, and 3-nitrobenzalde-hyde reacts very slowly. Selectivity for the *Z*-isomer over the other two reaction products also varies with the electronic and steric nature the aryl group, with electron-donating substituents providing better selectivities. For example, an *E/Z* ratio of 1:8.7 is observed for 4-anisaldehyde, while it is 1:3.7 for benzaldehyde and 1:2.9 for 2-tolualdehyde.[10]

On the basis of these results and the presence of 1-aryl-1-trimethylsilyloxy ethylene as an observed product, we believe that the reaction likely proceeds through epoxide intermediates (eq 3).[11] When electron-donating substituents are present, opening

$$(3)$$
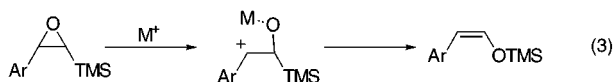
of the epoxide to the *E/Z* products is favored via stabilization of the incipient carbocation,[12] whereas electron-withdrawing substituents have a destabilizing effect.

In addition, our evidence also suggests that epoxide formation does *not* proceed through a Lewis acid-catalyzed activation of

the aldehydes toward the addition of TMS-diazomethane, and that complex **2** is the more likely intermediate in this reaction rather than the analogous aldehyde complex of **1** (which we have previously isolated and characterized[4]). For example, the order of addition of reagents dramatically affects the rate, with the reaction proceeding *much* faster when TMS-diazomethane is added first. If the aldehyde is initially added, thus preforming the aldehyde complex,[4] the reaction is extremely sluggish, often taking 12−24 h to reach completion. Coupled with the observation that aldehydes with electron-donating substituents, that is those *least* activated toward nucleophilic attack, are the most reactive, and that the solution color during reaction closely resembles that of complex **2**, it is unlikely that an aldehyde complex plays a significant role.

In summary, the rhodium-catalyzed transformation reported here is a new and effective strategy for synthesizing *cis*-TMS-enol ethers of aryl acetaldehydes directly from the corresponding aryl aldehydes and TMS-diazomethane. Not only can this reaction ultimately be used as a simple one-carbon homologation of aryl aldehydes, but the TMS-enol ethers themselves can also be used directly in subsequent transformations if desired, and are available without having to isolate the aryl acetaldehydes. The evidence from our initial studies suggests that the unique TMS-diaz-omethane rhodium complex **2**, which we have isolated and characterized, is intimately involved in this transformation, possibly via activation of the dinitrogen moiety for nucleophilic displacement by the carbonyl oxygen of the aldehyde. Further studies to extend the scope of this reaction with different substrates and different catalysts are currently underway.

(10) Product distributions were determined in NMR scale experiments.

(11) Previous examples of epoxide formation from aldehydes and TMS-diazomethane are (a) Maruoka, K.; Concepcion, A. B.; Yamamoto, H. *Synlett* **1994**, 663−664. (b) Hashimoto, N.; Aoyama, T.; Shioiri, T. *Heterocycles* **1981**, *15*, 975−979.

(12) For a similar Lewis acid-catalyzed rearrangement of silyl epoxides, see Fleming, I.; Newton, T. W. *J. Chem. Soc., Perkin Trans. 1* **1984**, 119−123.