

STEREOCHEMISTRY AND MECHANISM OF THE COPPER(I) HALIDE CLEAVAGE OF THALLIUM-CARBON BONDS

Jan-E. Backvall\* and Mesbah U. Ahmad

Department of Organic Chemistry, Royal Institute of Technology, S-100 44 Stockholm, Sweden

Sakae Uemura\* and Akio Toshimitsu

Institute for Chemical Research, Kyoto University, Uji, Kyoto, Japan 611

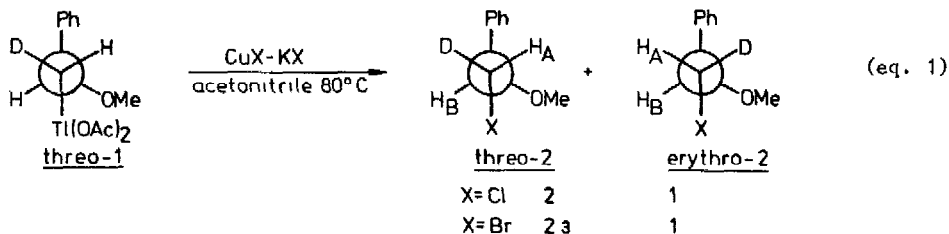
Takashi Kawamura

Department of Hydrocarbon Chemistry, Faculty of Engineering, Kyoto University, Kyoto, Japan 606

**Summary:** Stereochemical studies on the copper(I) halide cleavage of thallium-carbon bonds in acetonitrile indicate that at 80°C a radical path accounts for approximately 2/3 of the product, whereas at 60°C an ionic path predominates. The results are consistent with e.s.r. measurements by a spin trapping technique.

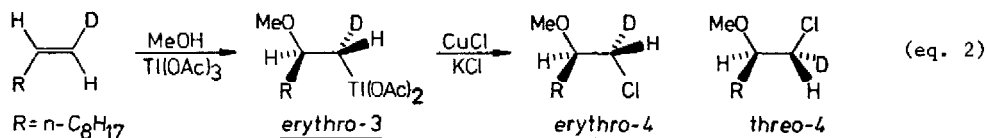
Although there are numerous studies on copper(II) halide cleavage<sup>1-4</sup> of metal-carbon bonds, relatively little is known about the action of copper(I) halides on metal-carbon bonds. It has been reported<sup>5</sup> that copper(I) halides induce cleavage of thallium-carbon bonds, replacing thallium with halide and it was recently shown<sup>6</sup> that alkyl radicals are involved in the cleavage process. We have now studied the stereochemistry of this cleavage reaction, using specifically deuterated thallium compounds 1 and 3, and found that a free radical mechanism is not the only pathway, an ionic pathway being a competitive process that becomes overwhelmingly predominant at lower temperature.

Reaction of thallium compounds, *threo-1* and *erythro-1*,<sup>7</sup> prepared by *trans*-methoxythallation of specifically deuterated styrenes, with copper(I) halide/potassium halide in acetonitrile for 5 hrs gave in each case a mixture of diastereoisomeric products (2), that was analysed by NMR spectroscopy. Reaction of *threo-1* with CuCl/KCl gave a mixture of *threo-2* (X = Cl) ( $\delta_A = 3.68$  ppm;  $J_{AB} = 8.1$  Hz) and *erythro-2* (X = Cl) ( $\delta_A = 3.59$  ppm,  $J_{AB} = 4.2$  Hz) in a ratio of 2:1, and the reaction of *threo-1* with CuBr/KBr gave *threo-2* (X = Br) ( $\delta_A = 3.45$  ppm;  $J_{AB} = 8.8$  Hz) and *erythro-2* (X = Br) ( $\delta_A = 3.40$  ppm;  $J_{AB} = 4.0$  Hz) in a ratio of 2.3:1<sup>8</sup> (eq. 1). Thus there is a slight preference for retention of configuration at carbon in the cleavage process. The configurational assignment of diastereoisomers 2 is based on NMR, and we have assigned the isomers with the larger coupling constants (8.1 and 8.8 Hz) as *threo* and the isomer with



the smaller coupling constants (4.2 and 4.0 Hz) as *erythro*, in agreement with a main conformation in which the phenyl and halide groups are *antiperiplanar* and the methoxy and halide groups are *gauche*.<sup>9,10</sup>

In order to determine the role of the phenyl group in the CuCl-cleavage of 1 (possible anchimeric assistance), we studied the analogous cleavage reaction of *erythro*-3 (eq. 2). The thallium-compound *erythro*-3, prepared by *trans*-methoxythallation of *E*-1-deuterio-1-decene<sup>11</sup> was a white semisolid mass that was identified by its NMR spectrum, and used without further purification. The results from some cleavage experiments, given in Table 1, show that at 80°C (reflux) a mixture of *erythro*- and *threo*-4 is formed in a ratio of 1:2. The configurational assignment of 4 was established by an independent synthesis of *erythro*-4 (cf. Table 1, note d). Thus there is a preference for inversion in this case which is in contrast to the preference for retention observed in the cleavage reaction of 1 (*vide supra*).



Furthermore, the stereochemistry of the cleavage reaction of *erythro*-3 was strongly temperature dependent. At 60°C the ratio *erythro*-4:*threo*-4 was 1:10 indicating an overwhelming predominance of inversion product. No significant change in the stereochemical outcome could be observed by running the reaction under nitrogen or by omitting or changing the amount of potassium chloride. In a control experiment *threo*-4 was refluxed in acetonitrile in the presence of CuCl/KCl for 12 hrs. From this experiment *threo*-4 was quantitatively recovered, indicating that *threo*-4 is stable under the reaction conditions. Thus the lower stereospecificity at higher temperature cannot be explained by isomerization *via* S<sub>N</sub>2-exchange of chloride.

In a previous study<sup>6</sup> it was shown by the spin trapping technique that the copper(I) halide/potassium halide cleavage reaction of 1 in acetonitrile involved free alkyl radicals, and it was suggested that this was the main path. The stereochemical outcome of the present study on the cleavage reactions of 1 and 3 indicates that there are also other pathways, but confirms the earlier conclusion that the reaction proceeds mainly *via* a radical path at 80°C. Thus the stereochemical results obtained at 80°C for both 1 and 3 are consistent with a mechanism in which approximately 2/3 reacts *via* a free radical path and 1/3 *via* an ionic path with thallium(III) as a leaving group (Scheme 1). For 1, the ionic path would involve anchimeric assistance by the phenyl group<sup>14</sup> (retention), and for 3, the ionic path would be nucleophilic displacement (inversion). At lower temperature the ionic path predominates and in the cleavage of 3 at 60°C more than 4/5 of the product 4 is formed by nucleophilic displacement of thallium(III) and only a minor part through free radicals. The rate of the reaction at this temperature, however, was quite slow compared with the rate at reflux<sup>15</sup> (cf. Table 1).

To obtain further evidence for a radical path in the reaction of 3 with copper(I) halide, undeuterated 3 was treated with copper(I) chloride or bromide (in the presence or absence of

Table 1. Reaction of *erythro*-3 with CuCl/KCl in acetonitrile<sup>a</sup>

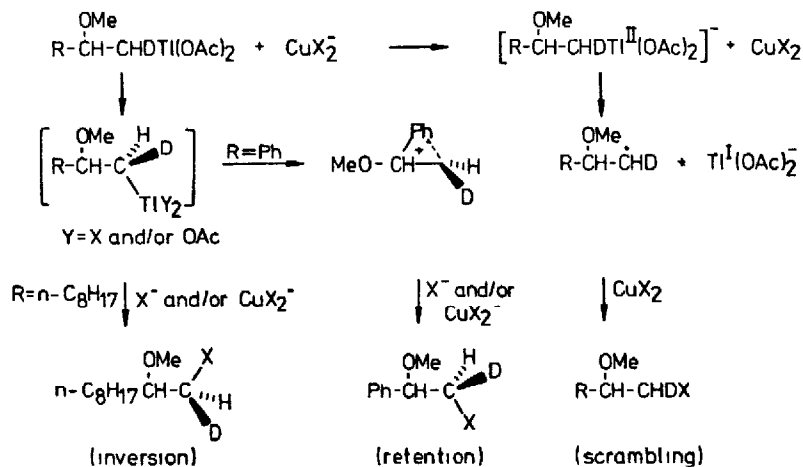
Temperature °C	Yield of <u>4</u> <sup>b</sup> %	Relative yield <sup>c</sup>	
		<i>erythro</i> - <u>4</u> <sup>d</sup>	<i>threo</i> - <u>4</u>
80	48	33	67
70	28	25	75
60	22	9	91

a. *Erythro*-3 (1 mmol), CuCl (2 mmol), KCl (2 mmol) was allowed to react in acetonitrile (5 ml) for 5 hrs. b. Based on the amount of Tl(OAc)<sub>3</sub> used in the oxythallation. c. The relative yield was determined by NMR spectroscopy (200 MHz instrument, acetone-d<sub>6</sub>), *erythro*-4: δ<sub>1</sub> = 3.65 ppm (J<sub>12</sub> = 5.1 Hz), *threo*-4: δ<sub>1</sub> = 3.60 ppm (J<sub>12</sub> = 4.6 Hz). d. Independently prepared by methylation of <sup>13</sup>*erythro*-1-chloro-1-deuterio-2-decanol<sup>4b,12</sup> with diazomethane using BF<sub>3</sub> as a catalyst.

potassium halide) in deoxygenated acetonitrile at 80°C for 1 min in the presence of the spin trap perdeuterionitrosodurene. Immediate measurement of the e s r spectrum at -35°C shows a spectrum similar to that observed in the case of PhCH(OMe)CH<sub>2</sub>Tl(OAc)<sub>2</sub><sup>6</sup> consisting of two sets of doublets (0.444 and 1.47 mT) further split into a 1:1:1 triplet (1.35 mT), g factor 2.0060. At 60°C the same spectrum, but with about 1/4 intensity (the quantity of 1/4 has only semi-quantitative significance), was observed. In agreement with these observations, the yield of the product n-C<sub>8</sub>H<sub>17</sub>CH(OMe)CH<sub>2</sub>Br in the reaction of n-C<sub>8</sub>H<sub>17</sub>CH(OMe)CH<sub>2</sub>Tl(OAc)<sub>2</sub> with equimolar amounts of CuBr and KBr in acetonitrile at reflux for 2 hrs was 59% but only 22% in the presence of nitrosobenzene. At 60°C the yield was almost the same in either the presence or absence of nitrosobenzene (14% after 2 hrs). Clearly, the addition of nitrosobenzene stops the free radical reaction pathway by trapping a free alkyl radical.

The role of copper(I) in these cleavage reactions is not wholly understood. However, in the radical pathway it is likely that the copper(I) halide acts as a reducing agent by transferring one electron to thallium, producing a labile thallium(II) compound. This intermediate

Scheme 1 (X=Cl, Br)



would undergo fast homolysis to an alkyl radical and thallium(I). Reaction of the alkyl radical with the copper(II) halide formed would give the organic halide. A similar electron transfer mechanism was recently proposed to account for the free radicals formed in the reductant induced cleavage of thallium-carbon bonds by ascorbic acid and N-benzyl-1,4-dihydrinicotinamide.<sup>16</sup> In the nucleophilic displacement of the thallium(III) moiety by halide the attacking species seem to be both  $X^-$  and  $CuX_2^-$ , since we have found that the reaction of  $n-C_8H_{17}CH(OMe)CH_2Tl(OAc)_2$  with KBr in acetonitrile at 60°C for 5 hrs gave 12% of the corresponding alkyl bromide, whereas the reaction with CuBr/KBr gave 24% of the alkyl bromide

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- The same stereochemical result was obtained from the cleavage reaction of *erythro-1* with CuBr/KBr
- (a) *Gauche* orientation between phenyl and halide (Cl, Br) is known to be less stable ( $\sim 0.35$  kcal)<sup>9b</sup> than *anti* orientation, whereas *gauche* orientation between a halide and an alkoxy group is at least as stable<sup>9b,9c</sup> as *anti* orientation. (b) W.C. Lin, *J. Chem. Phys.*, **52**, 2805 (1970). (c) S. Wolfe, *Acc. Chem. Res.*, **5**, 102 (1972).
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- Analogous phenyl participation has recently been observed in the  $CuCl_2-LiCl$  induced cleavage of  $\beta$ -phenethylpalladium bonds<sup>4a</sup>
- For example, the yield of the product  $n-C_8H_{17}CH(OMe)CH_2Br$ <sup>15b</sup> in the reaction of  $n-C_8H_{17}CH(OMe)CH_2Tl(OAc)_2$  with CuBr/KBr in acetonitrile was 59%<sup>2</sup> (for 2 hrs) and 24% (for 5 hrs) at reflux and at 60°C, respectively. Similarly, the reaction of **1** with CuBr/KBr in acetonitrile at 60°C for 5 hrs afforded only 7% yield of **2** (compare with the yield of 87% at reflux)<sup>5</sup> (b) Authentic sample prepared from 1-decene, NBS, and MeOH (reflux 2 hrs).
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