

We are continuing to investigate the chemistry of **2** and related trans-fused bicyclo[*n*.1.0]alkanes.

Acknowledgment. We are indebted to the National Science Foundation for Grant CHE-8114772, which supported this investigation.

Registry No. **2**, 84194-54-7; **3a**, 29311-53-3; **3b**, 25126-93-6; **4**, 53389-31-4; **5**, 84194-49-0; **6**, 2345-85-9; **7**, 84194-50-3; **8**, 84194-51-4; **9**, 84194-52-5; **10**, 84194-53-6.

(15) In studying this facile isomerization, we were very concerned about the possibility of either acid-catalyzed or transition-metal-promoted rearrangement of **2**. This was of special concern in view of the large observed negative entropy of activation (-15.8 eu),¹⁶ which would more commonly be associated with a bimolecular process than with a unimolecular process. Because of our long-term experience with both acid-catalyzed and transition-metal-promoted rearrangements of highly strained ring systems, precautions were taken to avoid such complications from the start. Since all rates were measured by ¹H NMR, all tubes were carefully base treated prior to use. In addition, the NMR tubes used were new, and the rates were reproducible in different tubes. Any type of acid-catalyzed process could be rigorously excluded since treatment of **2** with *p*-toluenesulfonic acid in acetonitrile showed that **2** was only partially isomerized (40%) after 3 days at 75 °C. Under these acidic conditions, **2** did not yield **11** but instead gave an olefin that was identified as 1,3-cycloheptadiene. Pirkle and Lunsford had observed $\Delta S^\ddagger = -3.7$ eu for a related system^{3b} while Berson and co-workers have observed $\Delta S^\ddagger \approx -16$ eu for the unimolecular cleavage of the 1,4-carbon-carbon σ bond of 5-alkylidenebicyclo[2.1.0]pentanes followed by dimerization of the intermediate diradical.¹⁷ It was suggested in the latter work that the relatively large observed ΔS^\ddagger may signify a spin-forbidden transition state.

(16) The entropy of activation reported in Table I lists an error based on the reproducibility of the rates in several kinetic runs. If the uncertainty in ΔS^\ddagger is calculated by using the temperature variation of the NMR spectrometer which was used in the kinetic measurements, an uncertainty in ΔS^\ddagger of 15.6 eu is obtained. Thus, the reported ΔS^\ddagger should not be overinterpreted. Benson, S. W.; O'Neal, H. E. "Kinetic Data on Gas Phase Unimolecular Reactions"; *Natl. Stand. Ref. Data Ser., Natl. Bur. Stand.* **1970**, No. 21, p 8. We wish to thank Prof. J. Berson for bringing this reference to our attention.

(17) Rule, M.; Lazzara, M. G.; Berson, J. A. *J. Am. Chem. Soc.* **1979**, *101*, 7091.

Stereochemistry of Transmetalation in the Palladium-Catalyzed Coupling of Acid Chlorides and Organotins

Jeff W. Labadie and J. K. Stille*

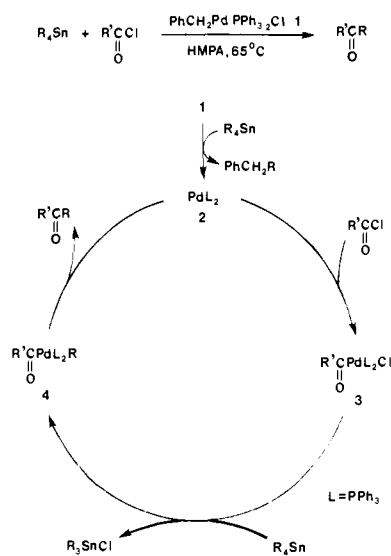
*Department of Chemistry, Colorado State University
Fort Collins, Colorado 80523*

Received October 26, 1982

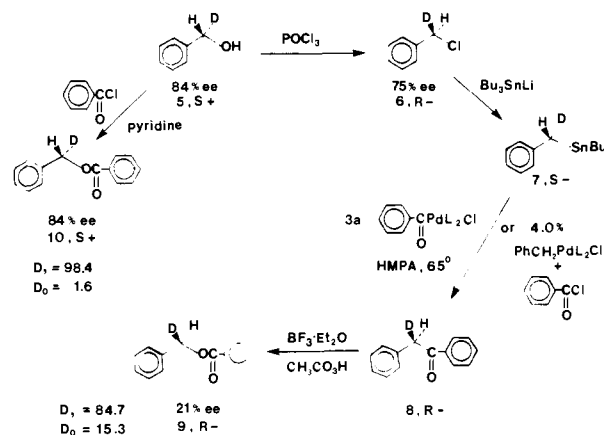
Although transmetalation reactions between organotin compounds and palladium halide complexes is an important step in the palladium-catalyzed cross-coupling of organic halides and organotin, there is essentially no mechanistic information available for this reaction. We report that this transmetalation occurs predominately with inversion of configuration at the saturated carbon being transferred.

The palladium-catalyzed coupling of acid chlorides and organotin gives ketones in high yield.² The proposed catalytic cycle² (Scheme I) involves a transmetalation reaction between an organotin and an acylbis(triphenylphosphine)palladium(II) chloride complex, **3**, to afford an acylalkylbis(triphenylphosphine)palladium(II) chloride complex, **4**, which releases the desired ketone by reductive elimination. The presence of **3** is directly observable by ³¹P NMR in the coupling of phenyltributyltin and benzoyl chloride catalyzed by 25% of **1**. After 1.5 h at 65 °C in CDCl₃ the peak corresponding to **1** at δ 28.7 disappeared, and a new peak

Scheme I



Scheme II



appearing at δ 19.8 was shown by comparison to an independently prepared sample³ to be benzoylbis(triphenylphosphine)palladium(II)chloride, **3a**.

Since the reductive elimination of a saturated carbon is known to occur predominately with retention of configuration,⁴ the only step of unknown stereochemical consequence in the catalytic cycle is the transmetalation reaction. Thus, by conducting a catalytic reaction with benzoyl chloride and (*S*)-(-)-(α -deuteriobenzyl)-tributyltin, **7**, in the presence of **1** and observing the absolute configuration of the α -deuteriobenzyl phenyl ketone product, **8**, the stereochemistry of the transmetalation process could be unambiguously defined (Scheme II).

(*S*)-(+)-Benzyl- α -*d* alcohol (**5**, $[\alpha]_D^{20} +1.33^\circ$ (neat, $l = 1$ dm), 84.2% ee) was treated with POCl₃ in pyridine/CH₂Cl₂ to give (*R*)-(-)-benzyl- α -*d* chloride (**6**, $[\alpha]_D^{20} -1.15^\circ$ (neat, $l = 0.1$ dm), 75.0% ee).⁶ Tributyltin hydride was converted to lithium tributylstannate⁷ and added to a THF solution of **6** at 0 °C to yield (*S*)-(-)-(α -deuteriobenzyl)tributyltin (**7**, $[\alpha]_D^{20} -0.328^\circ$, $[\alpha]_{436}^{20} -0.790^\circ$ (neat, $l = 1$ dm)). The absolute configuration of **7** was not directly determined; however, it is known that displacement reactions with lithium triorganostannates under similar conditions proceed with predominate inversion of configuration at carbon.⁸

(1) Milstein, D.; Stille, J. K. *J. Am. Chem. Soc.* **1979**, *101*, 4992. Godschalx, J.; Stille, J. K. *Tetrahedron Lett.* **1980**, *21*, 2599. Kashin, A. N.; Bumagina, I. G.; Bumagin, N. A.; Beletskaya, I. P. *Zh. Org. Khim.* **1981**, *17*, 21. Kosugi, M.; Suzuki, M.; Hagiwara, I.; Goto, K.; Saitoh, K.; Migita, T. *Chem. Lett.* **1982**, 939.

(2) Milstein, D.; Stille, J. K. *J. Org. Chem.* **1979**, *44*, 1613.

(3) Suzuki, K.; Nishida, M. *Bull. Chem. Soc. Jpn.* **1973**, *46*, 2887.

(4) Milstein, D.; Stille, J. K. *J. Am. Chem. Soc.* **1979**, *101*, 4981.

(5) Midland, M. M.; Tramontano, A.; Zderic, S. A. *J. Am. Chem. Soc.* **1977**, *99*, 5211.

(6) Becker, Y.; Stille, J. K. *J. Am. Chem. Soc.* **1978**, *100*, 838.

(7) Still, W. C. *J. Am. Chem. Soc.* **1979**, *100*, 1481.

(8) San Filippo, J., Jr.; Silbermann, J. J. *J. Am. Chem. Soc.* **1982**, *104*, 2831.

The reaction of 1.03 equiv of **7** with 1.00 equiv of benzoyl chloride and 4.0 mol % **1** in HMPA was conducted at 65 °C for 16 h. The isolation of **8** by radial chromatography (10% ethyl acetate/hexane) afforded **8** (mp 50–52 °C; $[\alpha]_D^{20} -0.314^\circ$, $[\alpha]_{436}^{20} -0.772^\circ$ (CCl₄, *c* 30.0)), which had CD curves over a range of concentrations characteristic of the *R* isomer.⁹ Alternatively the reaction of **3a** with 1.04 equiv of **7** in HMPA at 65 °C afforded **8** with 54% of the stereospecificity as the catalytic reaction.

A Baeyer–Villiger oxidation of **8** was carried out with 40% CH₃CO₃H/BF₃·Et₂O at 45 °C for 30 h¹⁰ in order to determine the absolute configuration of **8**. Following purification by medium-pressure liquid chromatography (5% ethyl acetate/hexane), **9** showed $[\alpha]_D^{20} -0.10^\circ$, $[\alpha]_{365}^{20} -0.310^\circ$ (CCl₄, *c* 9.0). The preparation of (*S*)-(+)- α -deuteriobenzyl benzoate, **10**, by acylation of **5** with benzoyl chloride/pyridine showed $[\alpha]_D^{20} +0.36^\circ$, $[\alpha]_{365}^{20} 26^\circ$ (CCl₄, *c* 9.0). The optical center of **5** is not affected by the acylation. Thus, **9** and **10** are enantiomers, and **9** must be (*R*)-(-)- α -deuteriobenzyl benzoate.

Since the Baeyer–Villiger oxidation is known to occur with retention of configuration at the saturated carbon of the ketone,¹¹ **8** must be of *R* configuration. Thus, the transmetalation occurs predominately with inversion of stereochemistry at the saturated carbon being transferred.

The optical purity of **9** is 21% (based on $[\alpha]_{365}^{20}$), which corresponds overall to 28% ee for the three reactions between **6** and **9**. There are points in the sequence between **6** and **9** where racemization is likely by processes other than the transmetalation step. The enolization of **8** as well as deuterium loss in a protic environment would lead to loss of optical purity. The loss of optical activity due to deuterium loss alone can be estimated from the deuterium content (mass spectrum): D₁:D₀ for **9** = 84.7:15.3 (= 98.4:1.6 for **10**). By assuming a deuterium isotope effect of 2 for the enolization process, then 42% of **8** racemized in the reactions from **7** to **9**.¹² Consequently, the highest possible optical purity that could have been realized for **8** was 43% ee, and therefore the transmetalation must have occurred with $\geq 65\%$ stereospecificity. By using α -dideuteriobenzyl phenyl ketone as a model, it was observed that 2.3% deuterium loss occurred in the radial chromatography, while no deuterium loss occurred in the Baeyer–Villiger reaction.

Other points in the reaction scheme where racemization could occur include the displacement of chloride from **6** by Bu₃SnLi. Although this occurs with >90% inversion with (*S*)-(+)-octyl chloride,⁸ the displacement of a benzyl chloride by lithium triorganostannates is more likely to be accompanied by nonstereospecific free-radical processes, which would lower the optical purity of **7**.¹³ Further, only a 52.6% stereospecificity for the reductive elimination of a methyl and an α -deuteriobenzyl group from palladium has been reported.⁴ Taking these possibilities into account, it is likely that the amount of inversion occurring in the transmetalation step is relatively high.

In a polar solvent such as HMPA, inversion of configuration at carbon bonded to tin in transmetalation is analogous to the stereochemistry observed in acetonitrile for the bromine cleavage of a saturated carbon bonded to tin.¹⁴ Accordingly, the trans-

metalation in this catalytic reaction can be compared to an electrophilic cleavage reaction in which the catalytic intermediate, **3**, is behaving as the electrophile.

Acknowledgment. This research was supported by Grant CHE-8003336 from the National Science Foundation. ³¹P spectra were obtained from the Colorado State University Regional NMR Center funded by the National Science Foundation, Grant CHE-78-18581. Palladium chloride was provided under the Johnson-Matthey Metal Loan Program.

Fast Intramolecular Electron Transfer in Radical Ions over Long Distances across Rigid Saturated Hydrocarbon Spacers¹

L. T. Calcaterra, G. L. Closs,*† and J. R. Miller*‡

Chemistry Division, Argonne National Laboratory
Argonne, Illinois 60439
Department of Chemistry, The University of Chicago
Chicago, Illinois 60637

Received October 20, 1982

Measurements²⁻¹¹ of electron-transfer rates in systems with donor and acceptor (D and A) groups linked by spacers (S) have tended to confirm the traditional notion that fast ET requires contact or near contact between the reactants. But fast long-distance intermolecular ET occurs in solids when reaction energetics are optimized.^{12,13} We have embarked on a program of building molecules of the general structure D–S–A to test dependence of ET rates on distance, reaction energetics, and molecular structure, and report here the first results.

Radical anions of molecules I–III (Figure 1) were generated by reactions with solvated electrons (e_s⁻) formed by a 30ps pulse of electrons from the Argonne Linac in 2-methyltetrahydrofuran (MTHF) at room temperature (296 ± 2 K) with a bimolecular rate constant of 1 × 10¹¹ M⁻¹ s⁻¹.¹⁴ In each case the donor is

* To whom correspondence should be addressed at The University of Chicago.

† To whom correspondence should be addressed at Argonne National Laboratory.

(1) This work was supported by the Office of Basic Energy Sciences, Division of Chemical Science, US-DOE under Contract W-31-109-ENG-38 and by National Science Foundation Grant CHE7821789.

(2) Taube, H. In "Tunneling in Biological Systems"; Chance, B., et al., Eds.; Academic Press: New York, 1979; p 173.

(3) Okada, T.; Fujita, T.; Kubota, M.; Masuki, S.; Mataga, N.; Ide, R.; Sakata, M.; Misumi, S. *Chem. Phys. Lett.* **1972**, *14*, 563.

(4) Mataga, N.; Ottolenghi, M. In "Molecular Association"; Foster, Roy, Ed.; Academic Press: London, 1979; pp 1–78.

(5) Chang, T. J.; Eisenthal, K. B. *J. Am. Chem. Soc.* **1974**, *96*, 6828.

(6) Wang, Y.; Crawford, M.; Eisenthal, K. B. *J. Phys. Chem.* **1980**, *84*, 2696.

(7) Mazur, S.; Dixit, V. M.; Gerson, F. *J. Am. Chem. Soc.* **1980**, *102*, 5343.

(8) Creutz, C.; Kroger, P.; Matsubara, T.; Netzel, T.; Stuin, N. *J. Am. Chem. Soc.* **1979**, *101*, 5442.

(9) Shimada, K.; Szwarc, M. *Chem. Phys. Lett.* **1974**, *28*, 540; **1975**, *34*, 503.

(10) De Schryver, F.; Boens, N.; Put, J. *Adv. Photochem.* **1977**, *10*, 359.

(11) Borkent, J.; DeJong, A.; Verhoeven, J.; De Boer, Th. *Chem. Phys. Lett.* **1978**, *57*, 530.

(12) Passman, P.; Verhoeven, J.; De Boer, Th. *Chem. Phys. Lett.* **1978**, *57*, 530. Passman, P.; Koper, N. W.; Verhoeven, J. W. *Recl. Trav. Chim. Pays-Bas* **1982**, *101*, 363. In contrast to other work these authors used rigid bichromophoric molecules with 3.8- and 5.8-Å edge separations, which gave complete fluorescence quenching.

(13) Miller, J. R. *Science (Washington, D.C.)* **1975**, *189*, 221. Beitz, J.; Miller, J. J. *Chem. Phys.* **1979**, *71*, 4579. Miller, J.; Beitz, J. *Ibid.* **1981**, *74*, 6746.

(14) Miller, J.; Beitz, J.; Huddleston, R. K., submitted for publication.

(9) The CD spectra of a 16.4 × 10⁻³ M methanol solution of **8** was a negative curve; $[\theta] = -10.3^\circ$ (312 nm). A methanol solution of (*S*)-(+)- α -methyldeoxybenzoin also gave a negative curve. Since deuterium behaves in a dissignate manner, **8** is of *R* configuration by correlation. See: Sundaraman, P.; Gunter, B.; Djerassi, C. *J. Org. Chem.* **1980**, *45*, 4231. The use of a chiral shift reagent tris[3-(trifluoromethyl)hydroxymethylene]-*d*-camphorato]europium(III) did not provide a method of determining the enantiomeric excess of **8**. Others (Numan, H.; Wynberg, H. *J. Org. Chem.* **1978**, *43*, 2232) have reported that the direct determination of the optical purity of a ketone in which optical activity is solely due to deuterium substitution has never been realized.

(10) Kaiser, R.; Lampar, D. *Helv. Chim. Acta* **1978**, *61*, 2671.

(11) Mislow, K.; Brenner, J. *J. Am. Chem. Soc.* **1953**, *75*, 2318.

(12) The percentage of **8** racemized due to deuterium loss in enolization = (98.4 – 84.7)/0.984 = 13.9%. If the deuterium isotope effect (*k_H*/*k_D*) is approximately 2, then the percentage of racemization due to proton loss in enolization = 2 × 13.9% = 27.8%, and the overall percentage of **8** racemized through enolization is 42%.

(13) San Filippo, J., Jr.; Silbermann, J.; Fagan, P. *J. Am. Chem. Soc.* **1978**, *100*, 4834.

(14) McGahey, L. F.; Jensen, F. R. *J. Am. Chem. Soc.* **1979**, *101*, 4397.