stereochemical assignment of epoxy alcohols was made on the basis of the literature precedent[12,13] and later confirmed by NOE experiments. Additional evidence for this assignment was secured by subjecting the threo allylic alcohol to Sharpless asymmetric epoxidation conditions [(+)- or (−)-diethyl tartrate (DET)/t-BuO_2H/CH_2Cl_2/O °C].[14] In the case of (+)-DET conditions we observed a ratio greater than 100:1 of syn and anti products, whereas (−)-DET showed a decrease in this ratio (60:40).[15,16]

Treatment of the threo anti epoxide **4** with camphorsulfonic acid (CSA) in wet CH_2Cl_2 gave the desired cyclized product **5** in 89% yield. Supporting evidence for the stereochemical assignments was obtained from NOE experiments on the triol 5, its C2′ and C3′ stereoisomers,[17] and their triacetoxy derivatives. In particular, irradiation of H5′ in **5** showed an enhancement of H3′ and H1′, and irradiation of H3′ enhanced H5′ and H1′.[18]

It is interesting to note two points about the cyclization process. First, each of the four isomeric epoxides,[17] when treated with CSA, generated a different isomer of **5**. This result establishes that no stereochemical scrambling occurs during the cyclization, and therefore the stereochemistry of the cyclization products was solely dictated by the stereochemistry of the epoxy alcohols. Second, acetonide cleavage generates two free hydroxyl groups, either a priori could open the epoxide by attack at the quaternary center. Exclusive attack by the secondary hydroxyl is due to a combination of factors, the most important being the ability of the secondary hydroxyl to adopt a more favorable trajectory than the primary hydroxyl.

Hydrogenolysis of the triol **5** afforded C-sucrose **6**, which gave satisfactory spectroscopic data (^1H and ^{13}C NMR, MS, IR, $[\alpha]_D$).[19] The overall yield of C-sucrose from the vinyl iodide **1** was approximately 30%. Using the same sequence of reactions, all the C2′ and C3′ stereoisomers of C-sucrose were also obtained from the corresponding stereoisomers of **4**.[20]

In summary, we have developed a concise and efficient synthesis of C-sucrose and its C2′ and C3′ stereoisomers, which may also have interesting biological activity. Studies are currently in progress to define the preferred conformation of C-sucrose[21] and to test its effect on the sweetness receptor.

Acknowledgment. Financial support from the National Institutes of Health (NS 12108) is gratefully acknowledged.

Supplementary Material Available: ^1H NMR spectra of key compounds and tables listing NOE data of the triol **5** and its C2′ and C3′ stereoisomers and their triacetates (15 pages). Ordering information is given on any current masthead page.

Ulrich C. Dyer, Yoshito Kishi*
Department of Chemistry
Harvard University
12 Oxford Street
Cambridge, Massachusetts 02138
Received April 8, 1988

Construction of β-Lactams by Highly Selective Intramolecular C–H Insertion from Rhodium(II) Carboxylate Catalyzed Reactions of Diazoacetamides

Summary: Intramolecular β-C–H insertion occurs in high yield and with exceptional selectivity in rhodium(II) carboxylate catalyzed decompositions of diazoacetamides.

Sir: A wide variety of methods have been developed for the construction of the β-lactam ring.[1] Among them, intramolecular carbenoid processes involving carbon–hydrogen insertion initially appeared to be attractive versatile procedures,[2] but despite extensive investigations,[3-6] both low yields and low selectivities in the photochemical and thermal decomposition of diazo amides limited further development of this methodology. Diazo ketones have subsequently been shown to undergo preferential intramolecular γ-C–H insertion in catalytic decompositions,[7-10] which offer advantages in product yields and selectivities over photochemical and thermal methods, and rhodium(II) acetate has been demonstrated to be the catalyst of choice for these transformations.[7] However, a limited number of examples of competitive β-C–H insertions have also been reported for catalytic decompositions of diazo carbonyl compounds,[6,11-13] although the cause for this unexpected

(14) Katsuki, T.; Sharpless, K. B. *J. Am. Chem. Soc.* **1980**, *102*, 5974.
(15) Ratio of isomers determined by ^1H NMR analysis.
(16) For a review of double diastereodifferentiation, see: Masamune, S.; Choy, W.; Peterson, J. S.; Sita, L. R. *Angew. Chem., Int. Ed. Engl.* 1985, *24*, 1.
(17) All the four C2′ and C3′ stereoisomers of **5** were obtained from MCPBA epoxidation of either erythro or threo allylic alcohols, followed by chromatographic separation, and then treatment with CSA in wet CH_2Cl_2.
(18) The tables listing NOE observed for the triol **5** and its C2′ and C3′ stereoisomers and their triacetates are included in the supplementary material.
(19) ^1H NMR (500 MHz, CD_3OD) δ 2.05 (2 H, m), 3.28 (1 H, t, J = 8.8 Hz), 3.52 (1 H, dd, J = 8.9 and 7.9 Hz), 3.46 (1 H, dd, J = 8.9 and 5.4 Hz), 3.63–3.85 (8 H, m), 4.08–4.13 (2 H, m), 4.25 (1 H, m); ^{13}C NMR (125 MHz, CD_3OD) δ 31.69, 62.79, 62.79, 65.15, 72.12, 72.80, 72.86, 74.58, 75.73, 77.55, 81.86, 84.18, 84.93; $[\alpha]_D$ +21.6° (c 0.3, MeOH).
(20) The details of synthesis will be published in a full account.
(21) For NMR studies on the solution conformation of O-sucrose, see: (a) Bock, K.; Lemieux, R. U. *Carbohydr. Res.* **1982**, *100*, 63. (b) Cristofides, J. C.; Davies, D. B. *J. Chem. Soc., Chem. Commun.* **1985**, 1533. (c) McCain, D. C.; Markley, J. L. *Carbohydr. Res.* **1986**, *152*, 73. (d) Tyrell, P. M.; Prestegard, J. H. *J. Am. Chem. Soc.* **1986**, *108*, 3990.

(1) (a) Durckheimer, W.; Blumback, J.; Latrell, R.; Scheunemann, K. H. *Angew. Chem., Int. Ed. Engl.* **1985**, *14*, 180. (b) *Recent Advances in the Chemistry of β-Lactam Antibiotics*; Brown, A. G., Roberts, S. M., Eds.; Royal Society of Chemistry: London, 1985. (c) *Chemistry and Biology of β-Lactam Antibiotics*; Morin, R. B., Gorman, M., Eds.; Academic: New York, 1982.
(2) (a) Corey, E. J.; Felix, A. M. *J. Am. Chem. Soc.* **1965**, *87*, 2518. (b) Moll, F. *Z. Naturforsch., B: Anorg. Chem., Org. Chem., Biochem., Biophys., Biol.* **1966**, *21B*, 297. (c) Rando, R. R. *J. Am. Chem. Soc.* **1970**, *92*, 6706; **1972**, *94*, 1629.
(3) (a) Brunwin, D. M.; Lowe, G.; Parker, J. *J. Chem. Soc. C* **1971**, 3756. (b) Brunwin, D. M.; Lowe, G.; Parker, J. *J. Chem. Soc. D* **1971**, 865. (c) Lowe, G.; Parker, J. *J. Chem. Soc. D* 1971, 577. (d) Franich, R. A.; Lowe, G.; Parker, J. *J. Chem. Soc., Perkin Trans. 1* **1972**, 2034. (e) Lowe, G.; Ramsay, M. V. J. *J. Chem. Soc., Perkin Trans. 1* **1973**, 479.
(4) Golding, R. T.; Hall, D. R. *J. Chem. Soc., Perkin Trans. 1*, **1975**, 1517.
(5) (a) Tomioka, H.; Kitagawa, H.; Izawa, Y. *J. Org. Chem.* **1979**, *44*, 3072. (b) Tomioka, H.; Kondo, M.; Izawa, Y. *J. Org. Chem.* **1981**, *46*, 1090.
(6) Ponsford, R. J.; Southgate, R. *J. Chem. Soc., Chem. Commun.* **1979**, 846.
(7) (a) Taber, D. F.; Ruckle, R. E., Jr. *J. Am. Chem. Soc.* **1986**, *108*, 7686. (b) Taber, D. F.; Ruckle, R. E., Jr. *Tetrahedron Lett.* **1985**, *26*, 3059. (c) Taber, D. F.; Petty, E. H.; Raman, K. *J. Am. Chem. Soc.* **1985**, *107*, 196. (d) Taber, D. F.; Raman, K. *J. Am. Chem. Soc.* **1983**, *105*, 5935. (e) Taber, D. F.; Petty, E. H. *J. Org. Chem.* **1982**, *47*, 4808.
(8) Wenkert, E.; Davis, L. L.; Mylari, B. L.; Solomon, M. F.; da Silva, R. R.; Shulman, S.; Warnet, R. J.; Ceccherelli, P.; Curini, M.; Pellicciari, R. *J. Org. Chem.* **1982**, *47*, 3242.
(9) Chakraborti, A. K.; Ray, J. K.; Kundu, K. K.; Chakrabarty, S.; Mukherjee, D.; Ghatak, U. R. *J. Chem. Soc., Perkin Trans. 1*, **1984**, 261.
(10) (a) Sakai, K.; Fujimoto, T.; Yamashita, M.; Kondo, K. *Tetrahedron Lett.* **1985**, *26*, 2089. (b) Monteiro, H. J. *Tetrahedron Lett* **1987**, *28*, 3459. (c) Corbel, B.; Hernot, D.; Haelters, J.-P.; Sturtz, G. *Tetrahedron Lett.* **1987**, *28*, 6605.

0022-3263/88/1953-3384$01.50/0

selectivity has not been determined. In our investigations of rhodium(II) carboxylate catalyzed decompositions of diazo amides, we have discovered highly effective general methods for the construction of the β-lactam ring by C–H insertion. This transformation can be made to occur in high yield and with exceptional selectivity, and we now report these results and the factors that influence their competition with alternative carbenoid processes.

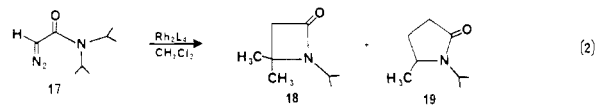
Treatment of *N*-benzyl-*N*-*tert*-butyldiazoacetoacetamide (**1**, S = H, R = CH_3CO), prepared from the corresponding secondary amine and diketene[14] followed by diazo transfer,[15] with rhodium(II) acetate (1.0 mol %) in refluxing benzene resulted in the exclusive production of β-lactam **2** (eq 1), which was isolated in 98% yield following chromatographic purification.[16] The trans stereochemical relationship of the acyl and phenyl substituents of **2** was established by ^1H NMR spectroscopy from the β-lactam ring coupling constants (J = 2.3 Hz),[17] and only the trans isomer was produced in these reactions. Identical results were obtained with a series of ring-substituted *N*-benzyl-*N*-*tert*-butyldiazoacetoacetamides from reactions performed under the same conditions (isolated yield of chromatographically pure **2** in parentheses): S = *p*-NO_2 (92%), S = *m*-Br (92%), S = *m*-CH_3O (90%), S = 3,4-$(CH_3O)_2$ (95%). In contrast, treatment of deacylated **1** (R = H)[18] with $Rh_2(OAc)_4$ in dichloromethane at room temperature formed the aromatic addition products **3** exclusively (eq 1) without a trace of the β-lactam insertion product.[19,20] The acetyl substituent of the diazo carbon obviously inhibits carbenoid addition to the electron-rich aromatic ring even when substituted with two methoxy groups to enhance its nucleophilic reactivity.

The bulky *tert*-butyl group is also essential to the success of this transformation. With *N*-benzyl-*N*-methyldiazoacetoacetamide, β-lactam **4** was produced in only 12% yield, and neither the corresponding aromatic addition product analogous to **3** nor the β-lactam from methyl C–H insertion was evident in the complex set of products formed in this reaction. Rhodium(II) acetate catalyzed decomposition of *N*-(*m*-methoxybenzyl)-*N*-ethyldiazoacetoacetamide in refluxing chloroform produced products from C–H insertion at all three aliphatic centers in 89% yield (Ar = *m*-$CH_3OC_6H_4$): **5** (22%, all trans), **6** (23%, trans/cis = 1.2), and **7** (55%). Similar mixtures were obtained with *N*-benzyl-*N*-isopropyldiazoacetoacetamide.

The selectivity that is observed in these reactions does not appear to be a function of electronic influences by substituents. Rather, these results can be explained by insertion into C–H bonds that are locked in close proximity to the reactive carbenoid center. Overlap of the nitrogen nonbonded electrons with the carbonyl π system fixes the amide conformation so that the larger nitrogen substituent is oriented toward the carbonyl group (**8**). Steric effects by the carbenoid substituents on benzylic substituents force the aryl group away from the acetyl group and coordinated metal and place the benzylic hydrogens within the reactive environment of the carbenoid center. As a test of this hypothesis, *N*-benzyl-*N*-(3,4-dimethoxybenzyl)-diazoacetoacetamide (**9**) was subjected to $Rh_2(OAc)_4$-catalyzed decomposition. If **10a** and **10b** represent the reactive intermediates, we anticipated that preferential insertion would occur at the unsubstituted benzylic carbon. The model system, *N*,*N*-dibenzyldiazoacetoacetamide, formed only β-lactam **11** after catalytic decomposition in refluxing chloroform. As expected, **9** yielded both **12** (60%) and **13** (22%) and a minor amount (18%) of two cycloheptatriene regioisomers from addition to the 3,4-dimethoxybenzene ring so that the ratio of products from **10b**/**10a** was 1.5.

Application of this methodology to aliphatic systems in which both β- and γ-C–H insertion are possible demonstrates its broad suitability for the construction of β-lactams. Rhodium(II) acetate catalyzed decomposition of the diazoacetoacetamides derived from diisopropylamine, dicyclohexylamine, and *trans*-2,6-dimethylpiperidine in benzene at room temperature formed the corresponding β-lactam products **14**–**16** exclusively and in high yield: **14** (89%), **15** (100%), and **16** (90%, isomer ratio = 1.4). The corresponding diazoacetamides also formed β-lactam products, but in these systems, competition between β-C–H and γ-C–H insertion occurred. However, enhancement of the relative yield of the β-lactam product can be achieved by catalyst modification. Thus, treatment of *N*,*N*-diisopropyldiazoacetamide (**17**) with $Rh_2(OAc)_4$ (1.0 mol %) in dichloromethane at room temperature afforded lactams **18** and **19** in 95% isolated yield and a 4.2:1.0 ratio (eq 2). With rhodium(II) perfluorobutyrate,[21] the **18**/**19**

(11) Tresca, J. P.; Fourrey, J. L.; Polonsky, J.; Wenkert, E. *Tetrahedron Lett.* **1973**, 895.
(12) Cane, D. E.; Thomas, P. J. *J. Am. Chem. Soc.* **1984**, *106*, 5295.
(13) (a) Smale, T. C. *Tetrahedron Lett.* **1984**, *25*, 2913. (b) Brown, P.; Southgate, R. *Tetrahedron Lett.* **1986**, *27*, 247.
(14) Clemens, R. J. *Chem. Rev.* **1986**, *86*, 241.
(15) Taber, D F.; Ruckle, R. E., Jr.; Hennessy, M. J. *J. Org. Chem.* **1986**, *51*, 4077.
(16) Compound **2** (S = H): ^1H NMR ($CDCl_3$, 300 MHz) δ 7.43–7.30 (m, Ph), 5.02 (d, J = 2.3 Hz, CHN), 3.91 (d, J = 2.3 Hz, CHCO), 2.29 (s, CH_3CO), and 1.25 (s, *t*-Bu); ^{13}C NMR ($CDCl_3$) δ 199.7 ($COCH_3$), 163.0 (CON), 139.4, 129.0, 128.6, 126.7, 70.9, 54.5, 30.0, and 20.1; IR (KBr) 1746 (C=O) and 1707 (C=O) cm^{-1}.
(17) (a) Barrow, K. D.; Spotswood, T. M. *Tetrahedron Lett.* **1965**, 3325. (b) Kagan, H. B.; Basselier, J. J.; Luche, J. L. *Tetrahedron Lett.* **1964**, 941. J_{trans} is in the range 2.2–2.8 Hz, and J_{cis} is 4.9–5.9 Hz.
(18) Doyle, M. P.; Dorow, R. L.; Terpstra, J. W.; Rodenhouse, R. A. *J. Org. Chem.* **1985**, *50*, 1663.
(19) Doyle, M. P.; Shanklin, M. S.; Pho, H. Q. *Tetrahedron Lett.*, in press. McKervey, M. A.; Tuladhar, S. M.; Twohig, M. F. *J. Chem. Soc., Chem. Commun.* **1984**, 129.
(20) The only exception is **1** (R = H, S = *p*-NO_2), which forms the corresponding β-lactam **2** (R = H) exclusively and suggests a general methodology for the construction of these β-lactams.



(2)

ratio was only 2.4, but the use of rhodium(II) 2-phenoxybenzoate provided an increase in this product ratio to 6.2. The diazoacetamide derived from *trans*-2,6-dimethylpiperidine also formed products from both β-C–H and γ-C–H (methyl) insertion, but because of piperidine ring constraints, the β-lactam/γ-lactam product ratio was already 16 in the $Rh_2(OAc)_4$-catalyzed reaction (92% isolated yield).

Acknowledgment. We are grateful to the National Science Foundation for support of this research and to both the National Science Foundation and the Keck Foundation for partial funding to purchase the high-field NMR spectrometer employed for these investigations. We thank the Johnson Matthey Co. for their loan of rhodium(III) chloride.

(21) Doyle, M. P.; Mahapatro, S. N.; Caughey, A. C.; Chinn, M. S.; Colsman, M. R.; Harn, N. K.; Redwine, A. E. *Inorg. Chem.* **1987**, *26*, 3070.

Michael P. Doyle,* Michael S. Shanklin, Su-Min Oon Hoan Q. Pho, Feike R. van der Heide[†] William R. Veal

Department of Chemistry
Trinity University
San Antonio, Texas 78284

Received March 29, 1988

[†]Predoctoral exchange student from the University of Leiden, The Netherlands.

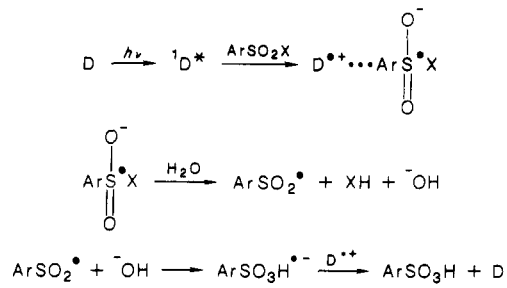
Hydrolysis of Tosyl Esters Initiated by an Electron Transfer from Photoexcited Electron-Rich Aromatic Compounds

Summary: Selective hydrolysis of tosyl esters was realized by irradiation of UV light (>300 nm) in the presence of electron-rich aromatic compounds and the reaction proceeds via an electron-transfer process.

Sir: The tosyl group is a unique protecting group for sugar and nucleic acid synthesis because of its ability to provide regioselective protection of hydroxy groups by means of the dibutylstannylene derivaties and its stability under solvolytic conditions.[1] However, the drastic conditions that have been employed for the detosylation step reduce the utility of this group.[2] Thus, development of a mild and selective method for the hydrolysis of the tosyl ester is still required.

Direct photolysis of tosyl esters in the presence of sodium methoxide has been reported,[3] and, recently, Masnovi showed that the mechanism of this type of reactions[4] involves an electron-transfer process. Unfortunately, utilization of 254-nm light limits the applicability of this reaction to substrates that have no chromophore other than the tosyl group.[5] Recently, we reported that the photohydrolysis of tosylamides[6] proceeds smoothly via electron-transfer from the excited electron-donating aromatic compounds such as *p*-dimethoxybenzene or 1,5-dimethoxynaphthalene (Scheme I, X = NRR′) and now we have extended this process to the hydrolysis of tosyl esters as shown in Scheme I (X = OR).

Scheme I[a]



[a] D, donor (dimethoxybenzenes, dimethoxynaphthalenes); X, NRR′ or OR.

The free energy change (ΔG) in the electron-transfer process from the singlet excited state of 1,5-dimethoxynaphthalene to methyl tosylate, calculated by the Weller equation,[7] was −14.5 kcal/mol in ethanol. This is obviously more negative than that for *N*-tosyl-*N*-methylphenethylamine (−5.79 kcal/mol).[6] Actually, fluorescence quenching experiments of 1,5-dimethoxynaphthalene by methyl tosylate gave a $k_q\tau$ from the linear Stern–Volmer plot of 43.8 M^{-1}. Hence, the k_q value was calculated to be 3.5×10^9 M^{-1} s^{-1} (τ = 12.6 ns), which means the process is occurring at nearly the diffusion-controlled rate and almost five times that of the rate of quenching by a tosylamide (MeNHTs). All of these results suggested that the hydrolysis of tosyl esters should be possible via a photosensitized electron-transfer process similar to that for tosylamides.

When tosyl esters of phenethyl alcohol, cyclohexanol, cholesterol, and cholestanol were irradiated under the conditions that were successful for the photosensitized cleavage of tosylamides,[6] the corresponding alcohols were obtained in good yield (Table I).[8] The reaction proceeded considerably slower in aqueous ethanol compared to the reactions of tosylamides, which were completed within 2 h.[9] However, employing acetonitrile as a solvent increased the rate of the reaction. As a coreductant,[10] hydrazine was

(1) (a) For the selective protection of the 2′-hydroxy group of nucleosides: Wagner, D.; Verheyden, J. P. H.; Moffatt, J. G. *J. Org. Chem.* **1974**, *39*, 24. (b) The protection of hexopyranosides: Munavu, R. M.; Szmant, H. H. *J. Org. Chem.* **1976**, *41*, 1932.

(2) Detosylation of 2′-*O*-tosyladenosine derivative using sodium amalgam has been reported: Ranganathan, R.; Larwood, F. *Tetrahedron Lett.* **1978**, 4341. However, this reaction is only applicable to purine nucleosides.

(3) (a) Zen, S.; Tashima, S.; Koto, S. *Bull. Chem. Soc. Jpn.* **1968**, *41*, 3025. (b) Izawa Y.; Kuromiya, N. *Bull. Chem. Soc. Jpn.* **1975**, *48*, 3197. (c) Pete, J. P.; Portella, C. *Bull. Soc. Chim. Fr.* **1980**, 275.

(4) Masnovi, J.; Koholic, D. J.; Binkley, R. *J. Am. Chem. Soc.* **1987**, *109*, 2851.

(5) Attempts to sensitize the detosylation reaction by using electron-transfer sensitizers such as phenothiazine, 9,10-dimethoxyanthracene, and *p*-dimethoxybenzene were reported to be unsuccessful.[4]

(6) (a) Hamada, H.; Nishida, A.; Matsumoto, Y.; Yonemitsu, O. *J. Am. Chem. Soc.* **1980**, *102*, 3978. (b) Hamada, T.; Nishida, A.; Yonemitsu, O. *J. Am. Chem. Soc.* **1986**, *108*, 140.

(7) Rehm, D.; Weller, A. *Isr. J. Chem.* **1970**, *8*, 259.

(8) Without donor, no reaction occurred.

(9) The efficiency of the photolysis of methyl tosylate (10 mM) in the presence of DMN (10 mM) and ammonia borane (10 mM) in 95% ethanol was measured and the quantum yield was ϕ = 0.003 (extrapolated to infinite concentration of methyl tosylate, ϕ_{lim} = 0.26) which is considerably smaller when compared to that of methyl tosylamide (ϕ_{lim} = 0.83). The reason for this low efficiency may be due to the presence of competing electron back-donation from the cation radical to the anion radical (Scheme I).

(10) The presence of coreductant was required for efficient reaction. The role of the coreductant may be the reduction of radical species, such as $D^{\bullet+}$ or the tolyl sulfonyl radical.

0022-3263/88/1953-3386$01.50/0