A Facile Preparation of 4-Alkylidene-3-tosyloxazolidin-2-ones from Propargylic Alcohols and *p*-Toluenesulfonyl Isocyanate Using a CuI/Et_3N Catalyst

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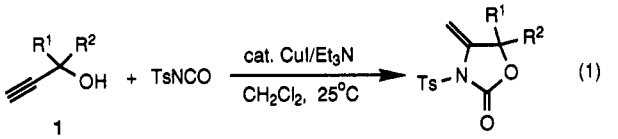
Oxazolidinones constitute an important class of heterocyclic compounds[1] that are widely used in the industrial,[2] pharmaceutical,[3] and agricultural[4] fields as well as in organic synthesis. In particular, the preparation of 4-alkylideneoxazolidinones has generated considerable interest since they generate useful heterocycles such as 3*H*-indoles, which are intermediates in the synthesis of dyestuffs.[2b] *N*-Alkyl- and -aryl-4-alkylideneoxazolidin-2-ones can be obtained from the base-catalyzed[5] and thermal[6] reactions of propargylic alcohols and isocyanates and from the reaction of propargylic alcohols, CO_2, and amines in the presence of copper salts[7] or phosphines[8] as catalysts, while oxazolidinones having an *N*-tosyl group have not been prepared except for one example.[9] For an on-going project,[10] we required oxazolidinones bearing various N-substituents including tosyl.

This paper describes a facile, one-pot preparation of 4-alkylideneoxazolidinones having an *N*-tosyl group under mild conditions in good yields starting from propargylic alcohols and *p*-toluenesulfonyl isocyanate in the presence of catalytic amounts of cuprous iodide and triethylamine (eq 1).

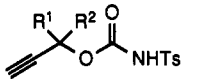
Reaction of propargyl alcohol (**1a**) (10 mmol) with *p*-toluenesulfonyl isocyanate (10 mmol) in dichloromethane (10 mL) containing catalytic amounts of cuprous iodide (1 mol %) and triethylamine (5 mol %) at room temperature afforded 4-methylene-3-tosyloxazolidin-2-one (**2a**), which was easily isolated by column chromatography in 80% yield. A variety of propargylic alcohols (**1b–f**) having terminal acetylene units reacted with *p*-toluenesulfonyl isocyanate under the same reaction conditions to give the corresponding oxazolidinones (**2b–f**) in good yields (Table I). The regioisomeric six-membered cyclic carbamates were not obtained in any case. In the absence of CuI as a catalyst, only simple addition to give an acyclic carbamate **3** was observed and cyclization leading to the desired oxazolidinone **2** did not occur. However, the cyclization of isolated acyclic carbamate **3** occurred easily in the presence of the catalyst CuI/Et_3N in CH_2Cl_2 to afford oxazolidinone **2**.



(1)

1 **2**

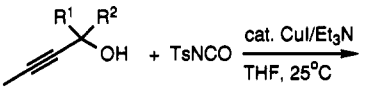
a; $R^1 = R^2 = H$
b; $R^1 = H$, $R^2 = Me$
c; $R^1 = R^2 = Me$
d; $R^1 = Me$, $R^2 = -(CH_2)_2CH{=}CH_2$
e; $R^1 = Me$, $R^2 = Ph$
f; $R^1, R^2 = -(CH_2)_5-$



3

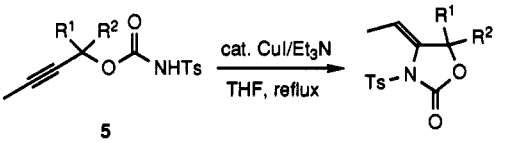
Ts = *p*-$CH_3C_6H_4SO_2$

The reaction of 3-substituted propargyl alcohol derivatives, such as 2-butyn-1-ol (**4a**) and 3-pentyn-2-ol (**4b**), with *p*-toluenesulfonyl isocyanate gave acyclic carbamates **5a** and **5b**, respectively, at room temperature even in the presence of CuI. However, one-pot addition/cyclization can be effected in refluxing THF containing CuI and Et_3N to afford 4-ethylideneoxazolidinones **6a** (73%) from **4a** and **6b** (79%) from **4b** (eq 2). This reaction gave exclusively



4

a; $R^1 = R^2 = H$
b; $R^1 = H$, $R^2 = Me$



(2)

5 **6**

a; 73 % (*Z* only)
b; 79 % (*Z* only)

a single stereoisomer as indicated by ^1H NMR and ^{13}C NMR. The *Z* stereochemistry depicted stems from a 9.3% NOE between methylene protons on C(5) and the olefinic proton in **6a**.

These results suggest that the role of the curpous iodide is to catalyze the cyclization of intermediate acyclic carbamates **3** and **5**. The formation of the *Z* isomers implies that trans addition of the carbamate across the triple bond occurs. This reaction provides a useful, convenient method for the synthesis of 4-alkylidene-3-tosyloxazolidin-2-ones (**2**) bearing a variety of substituents on the ring and the *exo*-methylene carbons.

Experimental Section

General Procedures. ^1H NMR spectra were recorded in $CDCl_3$. IR spectra were recorded as KBr pellets (for solids) or thin films (for liquids). GLC analyses (25 m × 0.2 mm CBP1-M25-025 capillary column) were performed with a flame-ionization detector and N_2 as carrier gas. Melting points are uncorrected. Column chromatography was performed with Wakogel C-200 (100–200 mesh) silica gel.

Materials. Propargylic alcohols (**1a–c,e,f** and **4a**) are commercially available. 3-Methyl-6-hepten-1-yn-3-ol (**1d**)[11] and 3-

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Table I. Synthesis of 4-Methylene-3-tosyloxazolidin-2-ones[a]

propargylic alcohol 1	product 2	isolated yield (%)
1a	2a	80
1b	2b	81
1c	2c	82
1d	2d	82
1e	2e	83
1f	2f	81

[a] Conditions: propargylic alcohol (10 mmol), *p*-toluenesulfonyl isocyanate (10 mmol), CuI (0.1 mmol), Et_3N (0.5 mmol), and CH_2Cl_2 (10 mL) at 25 °C for 20 h. Ts = *p*-toluenesulfonyl.

pentyn-2-ol (**4b**)[12] were prepared by the reported methods. THF and CH_2Cl_2 were freshly distilled from benzophenone ketyl and CaH_2, respectively, before use. Commercially available *p*-toluenesulfonyl isocyanate, cuprous iodide, and triethylamine were used without further purification.

Typical Procedure for Preparation of 4-Alkylidene-3-tosyloxazolidin-2-ones. In a 30-mL round-bottomed flask with a septum inlet was placed cuprous iodide (0.02 g, 0.1 mmol) under argon, and a dry dichloromethane (7 mL) solution of triethylamine (0.05 g, 0.5 mmol) and propargylic alcohol (10 mmol) was added. A dry dichloromethane (3 mL) solution of *p*-toluenesulfonyl isocyanate (1.97 g, 10 mmol) was added dropwise to the solution by syringe at 0 °C. After the mixture was stirred for 20 h at room temperature, a white solid was filtered. Evaporation of the filtrate left a crude product, which was subjected to column chromatography (EtOAc/hexane, 1:3) and recrystallized from CH_2Cl_2/hexane or EtOH.

4-Methylene-3-tosyloxazolidin-2-one (2a): yield 2.45 g (80%); white solid; mp 149–152 °C; IR 1796 (C=O) cm^{-1}; ^1H NMR (270 MHz) δ 2.46 (s, 3 H), 4.53 (dt, J = 2.2, 2.7 Hz, 1 H), 4.79 (t, J = 2.2 Hz, 2 H), 5.53 (dt, J = 2.4, 2.7 Hz, 1 H), 7.37 (d, J = 8.4 Hz, 2 H), 7.95 (d, J = 8.4 Hz, 2 H); ^{13}C NMR δ 21.8 (q), 67.1 (t), 90.8 (t), 128.2 (d, Ts, C(2)), 129.9 (d, Ts, C(3)), 134.2 (s, Ts, C(4)), 135.0 (s), 146.3 (s, Ts, C(1)), 151.7 (s, C=O). Anal. Calcd for $C_{11}H_{11}NO_4S$: C, 52.16; H, 4.38; N, 5.53; S, 12.66. Found: C, 52.09, H, 4.31; N, 5.46; S, 12.57.

5-Methyl-4-methylene-3-tosyloxazolidin-2-one (2b): yield 2.45 g (81%); white solid; mp 100–104 °C; IR 1791 (C=O) cm^{-1}; ^1H NMR (270 MHz) δ 1.47 (d, J = 6.3 Hz, 3 H), 2.46 (s, 3 H), 4.47 (dd, J = 2.2, 2.2 Hz, 1 H), 4.99 (ddq, J = 2.2, 2.2, 6.3 Hz, 1 H), 5.53 (dd, J = 2.2, 2.2 Hz, 1 H), 7.36 (d, J = 8.2 Hz, 2 H), 7.95 (d, J = 8.2 Hz, 2 H); ^{13}C NMR δ 20.8 (q), 21.7 (q), 75.3 (d), 90.8 (t), 128.1 (d, Ts, C(2)), 129.6 (s), 129.8 (d, Ts, C(3)), 134.2 (s, Ts, C(4)), 140.8 (s), 146.2 (s, Ts, C(1)). Anal. Calcd for $C_{12}H_{13}NO_4S$: C, 53.92; H, 4.90; N, 5.24; S, 12.00. Found: C, 53.86; H, 4.78; N, 5.20; S, 12.01.

5,5-Dimethyl-4-methylene-3-tosyloxazolidin-2-one (2c): yield 2.31 g (82%); white crystalline solid; mp 82–84 °C; IR 1786 (C=O) cm^{-1}; ^1H NMR (270 MHz) δ 1.46 (s, 6 H), 2.46 (s, 3 H), 4.46 (d, J = 3.0 Hz, 1 H), 5.51 (d, J = 3.0 Hz, 1 H), 7.36 (d, J = 8.1 Hz, 2 H), 7.95 (d, J = 8.1 Hz, 2 H); ^{13}C NMR δ 21.8 (q), 27.8 (q), 83.3 (s), 90.2 (t), 128.1 (d, Ts, C(2)), 129.6 (d, Ts, C(3)), 134.4 (s, Ts, C(4)), 145.1 (s), 146.1 (s, Ts, C(1)), 150.2 (s, C=O). Anal. Calcd for $C_{13}H_{15}NO_4S$: C, 55.50; H, 5.37; N, 4.98; S, 11.40. Found: C, 55.11; H, 5.27; N, 4.97; S, 11.35.

5-(3-Butenyl)-5-methyl-4-methylene-3-tosyloxazolidin-2-one (2d): yield 2.64 g (82%); pale yellow oil; IR 1798 (C=O) cm^{-1}; ^1H NMR (270 MHz) δ 1.44 (s, 3 H), 1.67–1.91 (m, 4 H), 2.45 (s, 3 H), 4.43 (d, J = 3.0 Hz, 1 H), 4.88 (ddt, J = 10.7, 1.5, 1.5 Hz, 1 H), 4.90 (ddt, J = 16.6, 1.5, 1.5 Hz, 1 H), 5.56 (d, J = 3.0 Hz, 1 H), 5.64 (ddt, J = 16.6, 10.7, 5.9 Hz, 1 H), 7.36 (d, J = 8.6 Hz, 2 H), 7.94 (d, J = 8.6 Hz, 2 H); ^{13}C NMR ($CDCl_3$) δ 21.6 (q), 26.8 (q), 26.9 (t), 39.7 (t), 85.0 (s), 90.3 (t), 115.3 (t), 127.9 (d, Ts, C(2)), 129.8 (d, Ts, C(3)), 136.4 (d), 143.4 (s, Ts, C(4)), 146.1 (s, Ts, C(1)), 150.3 (s, C=O). Anal. Calcd for $C_{16}H_{19}NO_4S$: C, 59.79; H, 5.96; N, 4.36; S, 9.98. Found: C, 60.19; H, 6.01; N, 4.29; S, 9.69.

5-Methyl-4-methylene-5-phenyl-3-tosyloxazolidin-2-one (2e): yield 2.85 g (83%); pale yellow solid; mp 91–92 °C (CH_2Cl_2/hexane); IR 1800 (C=O) cm^{-1}; ^1H NMR (270 MHz) δ 1.81 (s, 3 H), 2.43 (s, 3 H), 4.60 (d, J = 2.8 Hz, 1 H), 5.64 (d, J = 2.8 Hz, 1 H), 7.26–7.32 (m, 7 H), 7.86 (d, J = 8.4 Hz, 2 H); ^{13}C NMR δ 21.7 (q), 26.9 (q), 85.6 (s), 93.7 (t), 124.8 (d, Ph, C(2)), 128.1 (d, Ts, C(2)), 128.7 (d, Ph, C(4)) 128.8 (d, Ph, C(3)), 129.8 (d, Ts, C(3)), 134.3 (s, Ts, C(4)), 140.0 (s, Ph, C(1)), 144.1 (s), 146.1 (s, Ts, C(1)), 150.6 (s, C=O). Anal. Calcd for $C_{18}H_{17}NO_4S$: C, 62.96; H, 4.99; N, 4.08; S, 9.34. Found: C, 62.62; H, 4.92; N, 4.11; S, 9.33.

4-Methylene-5,5-pentamethylene-3-tosyloxazolidin-2-one (2f): yield 2.59 g (81%); white solid; mp 87–89 °C (EtOH); IR 1779 (C=O) cm^{-1}; ^1H NMR (270 MHz) δ 1.51–1.79 (m, 10 H), 2.45 (s, 3 H), 4.42 (d, J = 2.8 Hz, 1 H), 5.51 (d, J = 2.8 Hz, 1 H), 7.35 (d, J = 8.0 Hz, 2 H), 7.94 (d, J = 8.0 Hz, 2 H); ^{13}C NMR δ 21.1 (t), 21.6 (q), 24.2 (t), 36.6 (t), 84.8 (s), 90.1 (t), 127.9 (d, Ts, C(2)), 129.7 (d, Ts, C(3)), 134.3 (s, Ts, C(4)), 144.9 (s), 145.9 (s, Ts, C(1)), 150.2 (C=O). Anal. Calcd for $C_{16}H_{19}NO_4S$: C, 59.79; H, 5.96; N, 4.36; S, 9.98. Found: C, 59.63; H, 5.99; N, 4.41; S, 9.92.

(*Z*)-4-Ethylidene-3-tosyloxazolidin-2-one (6a): yield 1.95 g (73% based on **4a**); white solid; mp 84–85 °C (CH_2Cl_2/hexane); IR 1782 (C=O) cm^{-1}; ^1H NMR (270 MHz) δ 1.88 (dt, J = 7.2, 1.7 Hz, 3 H), 2.46 (s, 3 H), 4.66 (dq, J = 1.7, 1.7 Hz, 2 H), 5.27 (tq, J = 7.2, 1.7, 1 H), 7.36 (d, J = 8.2 Hz, 2 H), 7.96 (d, J = 8.2 Hz, 2 H); ^{13}C NMR δ 14.5 (q), 21.7 (q), 70.1 (t), 112.3 (d), 128.1 (s), 128.2 (d, Ts, C(2)), 129.8 (d, Ts, C(3)), 135.3 (s, Ts, C(4)), 145.7 (s, Ts, C(1)), 153.5 (s, C=O). Anal. Calcd for $C_{12}H_{13}NO_4S$: C, 53.92; H, 4.90; N, 5.24; S, 11.99. Found: C, 53.78; H, 4.85; N, 5.23; S, 12.18.

(*Z*)-4-Ethylidene-5-methyl-3-tosyloxazolidin-2-one (6b): yield 2.22 g (79% based on **4b**); white solid; mp 103–105 °C (CH_2Cl_2/hexane); IR 1790 (C=O) cm^{-1}; ^1H NMR (270 MHz) δ 1.46 (d, J = 6.4 Hz, 3 H), 1.87 (dd, J = 7.3, 1.7 Hz, 3 H), 2.45 (s, 3 H), 4.91 (dqq, J = 6.4, 1.7, 1.7 Hz, 1 H), 5.21 (dq, J = 7.3, 1.7 Hz, 1 H), 7.36 (d, J = 8.3 Hz, 2 H), 7.97 (d, J = 8.3 Hz, 2 H); ^{13}C NMR δ 14.7 (q), 19.4 (q), 21.7 (q), 78.1 (d), 111.6 (d), 127.0 (s), 128.5 (d, Ts, C(2)), 129.7 (d, Ts, C(3)), 133.7 (s, Ts, C(4)), 135.2 (s, Ts, C(1)), 145.6 (s, C=O). Anal. Calcd for $C_{13}H_{15}NO_4S$: C, 55.50; H, 5.37; N, 4.98; S, 11.40. Found: C, 55.40; H, 5.39; N, 4.93; S, 11.52.

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Studies on Polycyclic Azaarenes. 3.[1] Stereoselective Synthesis of *trans*-10,11-Dihydroxy-10,11-dihydrodibenz[*a*,*h*]-acridine and *trans*-10,11-Dihydroxy-10,11-dihydroacenaphtho-[1,2-*b*]quinoline

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Dibenz[*a*,*h*]acridines are found to be mutagenic and carcinogenic.[2] There is substantial evidence that they are metabolically activated to reactive diol epoxide intermediates that bind to DNA in vivo. The diastereomeric 10,11-diol 8,9-epoxide is 20–40 times more mutagenic than the related 3,4-diol 1,2-epoxide.[2,3]

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