Synthesis and Catalytic Reactions of Chiral N-(Diazoacetyl)oxazolidones

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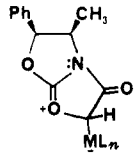
Received October 11, 1984

The chiral diazo compounds (4*R*,5*S*)-*N*-(diazoacetyl)-4-methyl-5-phenyloxazolidone (**3**) and (4*S*)-*N*-(diazoacetyl)-4-(2-propyl)oxazolidone (**4**) have been prepared from their corresponding parent oxazolidones. Catalytic cyclopropanation of styrene with **3** using rhodium(II) acetate gave, after oxazolidone exchange with ethanol, the trans and cis isomers ethyl 2-phenylcyclopropanecarboxylate (trans/cis = 1.8) with a 14% excess of the 1*R*,2*R* enantiomer and a 13% excess of the 1*R*,2*S* enantiomer. In reactions with **4**, the trans cyclopropane isomer was formed with a 13% excess of the 1*R*,2*R* enantiomer. A metal carbene that is not associated with the oxazolidone carbonyl group is implicated by the results. Diazo compound **3** is sensitive to acid-catalyzed rearrangement, and this process is competitive with catalytic cyclopropanation.

Asymmetric induction in catalytic cyclopropanation reactions of olefins with diazo compounds has been achieved with the use of chiral catalysts, particularly those of copper.[1-3] Few chiral diazo esters have been reported, and their use has been restricted to carbon–hydrogen insertion reactions.[4] Catalytic cyclopropanation reactions with chiral diazo compounds have not been reported. Recent demonstrations of the effectiveness of chiral alkanoyloxazolidones for diastereoselection in alkylation and aldol condensation reactions[5] and the potential directive influence of the oxazolidone carbonyl group for carbenoid transformations (eg., **1** and **2**) prompted us to construct *N*-(diazoacetyl) derivatives of chiral oxazolidones and to investigate their reactivity for transformations common to diazo compounds.



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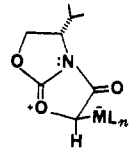

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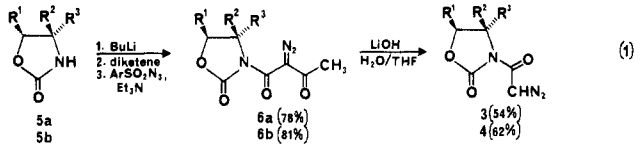
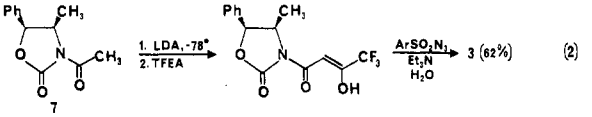
Results and Discussion

Synthesis. We have focused our efforts on the synthesis of **3** and **4** because of the generally recognized reactivity of diazoacetyl derivatives.[6] The scheme that was eventually successful for these constructions is presented in eq 1 (**a**, R^1 = Ph, R^2 = CH_3, R^3 = H; **b**, R^1 = R^2 = H, R^3 = $CH(CH_3)_2$). The production of **6** by condensation with diketene and diazo transfer[7] was straightforward, but, owing to difficulties encountered in the chromatographic separation of *p*-toluenesulfonamide from **6** following diazo transfer with *p*-toluenesulfonyl azide, *p*-(azidosulfonyl)-benzoic acid (eq 1, Ar = *p*-$HOOCC_6H_4$) was the preferred reagent for this transformation. However, because of the inherent sensitivity of *N*-acyloxazolidones to base hydrolysis,[5] deacylation of **6** presented a serious challenge. Reaction of **6a** with sodium methoxide (1 equiv of THF, −78 °C) gave only the original starting material **5a** in quantitative yield. In 70% aqueous acetonitrile at 0 °C, the use of a stoichiometric amount of potassium hydroxide gave **3** in only 15% yield. With an equivalent amount of phenol and lithium phenoxide in anhydrous THF at 25 °C, a 40% yield of **3** was realized. Optimum results were obtained with 1.0 equiv of lithium hydroxide in 65% aqueous THF at 0 °C, and hydrolysis to **5** was the only competing reaction.



(1)

An alternate approach (eq 2) that appears to be promising for the synthesis of these diazo compounds was briefly examined.[8] Condensation of *N*-acetyloxazolidone **7**[5a] with 2,2,2-trifluoroethyl trifluoroacetate (TFEA) followed by diazo transfer in the presence of no more than 1.0 equiv of water gave **3** directly without the need for a separate deacylation step. The enhanced reactivity of the trifluoroacetyl group toward nucleophilic addition and the superior leaving group ability of its hydroxyl adduct minimizes competition with hydrolytic cleavage of the oxazolidone, which is the major competing reaction in the deacylation of **6**.



(2)

Reactions. Rhodium(II) acetate catalyzed cyclopropanation of styrene with **3** was performed under previously described optimized reaction conditions.[10] Following conversion of the derivative oxazolidone to the corresponding ethyl ester (eq 3), the component ethyl 2-phenylcyclopropanecarboxylates were chromatographically separated and isolated. Product yields were unexpectedly low (35–40% of 8) for the cyclopropanation reaction, but control experiments established that neither

(1) (a) Nozaki, H.; Moriuti, S.; Takaya, H.; Noyori, R. *Tetrahedron Lett.* **1966**, 5239. (b) Noyori, R.; Takaya, H.; Nakanisi, Y.; Nozaki, H. *Can. J. Chem.* **1969**, *47*, 1242. (c) Nozaki, H.; Takaya, H.; Moriuti, S.; Noyori, R. *Tetrahedron* **1968**, *24*, 2655.

(2) Moser, W. R. *J. Am. Chem. Soc.* **1969**, *91*, 1135.

(3) Aratani, T.; Yoneyoshi, Y.; Nagase, T. *Tetrahedron Lett.* **1975**, 1707; **1977**, 2599.

(4) Taber, D. F.; Raman, K. *J. Am. Chem. Soc.* **1983**, *105*, 5935.

(5) (a) Evans, D. A.; Bartroli, J.; Shih, T. L. *J. Am. Chem. Soc.* **1981**, *103*, 2127. (b) Evans, D. A.; Ennis, M. D.; Mathre, D. J. *Ibid.* **1982**, *104*, 1737.

(6) (a) Dave, V.; Warnhoff, E. *Org. React.* (*N.Y.*) **1970**, *18*, 217. (b) Marchand, A. P.; MacBrockway, N. *Chem. Rev.* **1974**, *74*, 431.

(7) Regitz, M.; Hocker, J.; Leidhegener, A. "Organic Syntheses"; Wiley: New York, 1973; Collect. Vol. V, p 197.

(8) Direct diazo transfer with **7** was not successful, and treatment of the lithium salt of **5a** with diazoacetyl chloride[9] only resulted in the production of **5a**.

(9) Bestmann, H. J.; Soliman, F. M. *Angew. Chem., Int. Ed. Engl.* **1979**, *18*, 947.

(10) Doyle, M. P.; van Leusen, D.; Tamblyn, W. H. *Synthesis* **1981**, 787.

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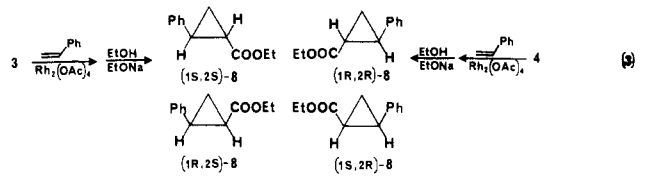
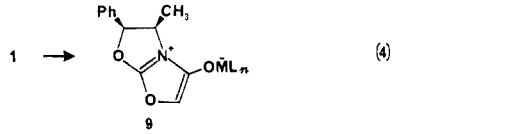


product loss nor isomerization occurred during exchange and isolation. The trans/cis isomer ratio was also surprisingly low at 1.8 (vs. 1.6 with ethyl diazoacetate[11] and 2.3 with *N,N*-dimethyldiazoacetamide) considering the size of the oxazolidone attachment. Optical rotations of the separated isomers showed a 14% ee of the 1*R*,2*R* enantiomer and a 13% ee of the 1*R*,2*S* enantiomer. Although low in absolute values, these enantiomeric excesses are greater than those previously observed with the chiral copper catalysts developed by Nozaki[1] and Moser.[2]

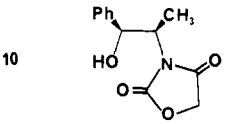
If **1** or **2** were to play a role in orienting the carbenoid intermediate for olefin addition, catalytic cyclopropanation of styrene with **4** would be expected to result in enantiomeric excesses of cyclopropane products opposite to those observed with **3**. If, on the other hand, the carbene center is not subject to a fixed orientation by the oxazolidone, either stereochemical result could be obtained. Treatment of **4** with styrene in the presence of $Rh_2(OAc)_4$ under the same conditions and with the identical isolation procedures as those employed with **3** gave the component ethyl 2-phenylcyclopropanecarboxylates in even lower yield (20–24%) and with the same trans/cis ratio (1.8). Because of the low product yield only the trans isomer was isolated, but its optical rotation, which corresponded to a 13% ee of the 1*R*,2*R* enantiomer, clearly demonstrated the absence of stereocontrol such as is suggested by **2**. Preferential approach of styrene to the *si* face of the metal carbenes derived from both **3** and **4** suggests that the (4*R*)-methyl substituent of **3** and the oxazolidone ring of **4** (and not its (4*S*)-isopropyl group) are oriented to hinder addition to the *re* face.

Oxazolidones **5a** and **5b** were not observed following catalytic cyclopropanation, and there was no apparent modification of the rhodium catalyst during these transformations. As a control experiment, 1.0 equiv of **6a** was combined with $Rh_2(OAc)_4$ in chloroform and, after gas evolution was complete, the green supernatant liquid was added to styrene. Ethyl diazoacetate was then transferred into this solution, and gas evolution ensued immediately. The stereoselectivity of this cyclopropanation reaction (trans/cis = 1.6) was identical with that performed with unmodified $Rh_2(OAc)_4$,[11] and the component ethyl 2-phenylcyclopropanecarboxylates did not exhibit measurable optical activity.

The unexpected low yields of cyclopropane products obtained from reactions of **3** and **4** with styrene in the presence of $Rh_2(OAc)_4$ caused us to investigate these reactions in greater detail. Intramolecular carbon–hydrogen insertion,[4,12,13] the Wolff rearrangement,[14] and reorganization of **1** (eq 4) were considered to be potential com-

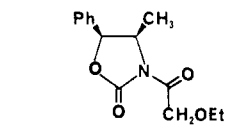


peting reactions. Treatment of **3** with $Rh_2(OAc)_4$ in chloroform resulted in rapid and quantitative gas evolution and in the production of a complex mixture of products of which **10** was the only volatile product. When the same



reaction was performed in chloroform or ether with 1.0 equiv of water, based on **3**, **10** was the sole reaction product. This same compound was identified in product mixtures obtained from reactions of **3** with styrene in the presence of $Rh_2(OAc)_4$ in yields ranging from 15% to 32% of the molar amount of reactant employed. Neither products resulting from carbon–hydrogen insertion[15] nor the product from the Wolff rearrangement was evident.

The origin of **10** is not straightforward. Addition of the elements of water to **9** could produce **10** but so could mechanisms involving initial protonation of **3** or oxygen–hydrogen insertion by the carbenoid generated from **3** into water with subsequent rearrangement. When the $Rh_2(OAc)_4$-catalyzed decomposition of **3** was performed in the presence of 1.0 equiv of ethanol, the resulting product mixture was composed of only the ethanol insertion product **11**. The use of $BF_3{\cdot}Et_2O$ in place of $Rh_2(OAc)_4$



gave **10** and a minor product that was not identified. The same result was obtained when this reaction was performed in the presence of ethanol. Attempts to trap **9** or its structural analogue from **4** by 1,3-dipolar addition[16] to ethyl acrylate were unsuccessful, and analogous products from reactions with styrene were not evident.

The results described here suggest that $Rh_2(OAc)_4$-catalyzed cyclopropanation reactions with **3** or **4** occur from unassociated metal carbenes rather than from the dipolar arrangement of **1** or **2**. However, the presence of the oxazolidone carbonyl group does provide a competing pathway to the desired cyclopropanation that is not overcome by the use of alternative catalysts such as $Cu(OTF)_2$[17] or $CuCl{\cdot}P(O\text{-}i\text{-}Pr)_3$.[2] Although preliminary results of ylide generation and rearrangement with allyl methyl sulfide[18] and **3** show that these competing reactions can be minimized with the use of relatively strong nucleophiles, the present results do not suggest any advantage for the use of chiral diazo compounds for intermolecular carbenoid reactions.

Experimental Section

General Procedures. Instrumentation has been previously described.[19] Commercially available (1*S*,2*R*)-norephedrine (Aldrich Chemical Co., hydrochloride salt: $[\alpha]_D$ +33.4°, *c* 7 in H_2O) was converted into oxazolidone **5a** ($[\alpha]_D$ +163.7°, *c* 1.0 in $CHCl_3$) with the use of diphenyl carbonate according to the procedure of Evans.[5a] Similarly, oxazolidone **5b** ($[\alpha]_D$ +14.8°, *c* 7.0 in $CHCl_3$)[5a] was prepared from (*S*)-valinol (Sigma Chemical

(11) Doyle, M. P.; Dorow, R. L.; Buhro, W. E.; Griffin, J. H.; Tamblyn, W. H.; Trudell, M. L. *Organometallics* **1984**, *3*, 44.
(12) Burke, S. D.; Grieco, P. A. *Org. React.* (*N.Y.*) **1979**, *26*, 361.
(13) Taber, D. F.; Petty, E. H. *J. Org. Chem.* **1982**, *47*, 4808.
(14) Meier, H.; Zeller, K. *Angew. Chem., Int. Ed. Engl.* **1975**, *14*, 32.
(15) Decomposition of **6b** in anhydrous dichloromethane using $Rh_2(OOCCF_3)_4$ catalysis resulted in the production of four major products which included **5a** and the formal carbenic water insertion product. Carbon–hydrogen insertion products were not observed.
(16) Huisgen, R. *Angew Chem., Int. Ed. Engl.* **1963**, *2*, 565.
(17) Doyle, M. P.; Trudell, M. L. *J. Org. Chem.* **1984**, *49*, 1196.
(18) Doyle, M. P.; Tamblyn, W. H.; Bagheri, V. *J. Org. Chem.* **1981**, *46*, 5094.
(19) Doyle, M. P.; Griffin, J. H.; Chinn, M. S.; van Leusen, D. *J. Org. Chem.* **1984**, *49*, 1917.

Co.) and diethyl carbonate.[20] The synthesis of N-acetyloxazolidone 7 followed the Evans procedure.[5a] Tetrahydrofuran (THF) was distilled from sodium benzophenone ketyl immediately before use. Copper(II) trifluoromethanesulfonate,[21] the rhodium(II) trifluoroacetate dimer,[22] and (triisopropyl phosphite)-copper(II) chloride[2] were prepared by standard procedures.

Synthesis of 6a. n-Butyllithium (40 mmol of the 1.6 M solution in hexane) was added dropwise to a solution of oxazolidone **5a** (6.68 g, 38 mmol) in 80 mL of anhydrous THF that was maintained under nitrogen at −78 °C. At the completion of the addition, the THF solution turned orange and, after warming to −40 °C, became dark red. After the mixture was cooled to −78 °C, diketene (3.5 mL, 44 mmol) in 20 mL of THF was slowly added to the lithiated oxazolidone. After this addition was complete, the resultant light yellow solution was maintained at −78 °C for an additional 30 min, then allowed to warm to 0 °C over a 30-min period, mixed with 18 mL of a saturated ammonium chloride solution, and concentrated under reduced pressure. Dichloromethane and water were added to the residue, and, following removal of the water layer, the dichloromethane solution was washed twice with a saturated sodium bicarbonate solution, washed once with saturated sodium chloride, dried over anhydrous magnesium sulfate, and concentrated under reduced pressure. The residual viscous red oil was chromatographed (silica gel), and the ether eluent was concentrated to give 8.40 g of the white crystalline N-(acetoacetyl) derivative of **5a** (32.2 mmol, 85% yield): mp 84.5–85.5 °C; $[\alpha]^{30}_D$ 62.7° (*c* 1.98 in $CHCl_3$); ^1H NMR ($CDCl_3$) δ 7.5–7.2 (m, 5 H), 5.70 (d, *J* = 7.3 Hz, OC*H*Ph), 4.80 (d of q, *J* = 7 .3, 6.6 Hz, C*H*CH_3), 4.06 (s, $COCH_2CO$), 2.30 (s, CH_3CO), 0.94 (d, *J* = 6.6 Hz, CHC*H*$_3$). Anal. Calcd for $C_{14}H_{15}NO_4$: C, 64.35; H, 5.85. Found: C, 64.40; H, 5.85.

The acetoacetyl derivative of **5a** (4.64 g, 17.8 mmol) was dissolved in 22 mL of anhydrous acetonitrile, and triethylamine (1.98 g, 20 mmol) and p-(azidosulfonyl)benzoic acid (4.05 g, 17.8 mmol)[23] were subsequently added. Precipitation of p-(amidosulfonyl)-benzoate began within 10 min of the initial azide addition. After 20 h at room temperature, ether was added and the white precipitate was filtered. After removal of the solvent under reduced pressure, the resulting red oil was chromatographed (silica gel) using 1:3 ethyl acetate/hexane to give, after solvent evaporation, 4.68 g of a yellow oil (16.3 mmol, 92% yield) identified as **6a**: $[\alpha]^{30}_D$ +48.3° (*c* 0.62 in $CHCl_3$); ^1H NMR ($CDCl_3$) δ 7.55–7.25 (m, 5 H), 5.70 (d, *J* = 7.7 Hz, OC*H*Ph), 4.82 (d of q, *J* = 7.7, 6.5 Hz, C*H*CH_3), 2.49 (s, CH_3CO), 0.99 (d, *J* = 6.5 Hz, CHC*H*$_3$); IR (film) $\bar{\nu}_{C=N_2}$ 2128 cm^{-1}. Repeated attempts to crystallize **6a** were not successful. Anal. Calcd for $C_{14}H_{13}N_3O_4$: C, 58.53; H, 4.56. Found: C, 58.68; H, 4.49.

(4*R*,5*S*)-*N*-(Diazoacetyl)-4-methyl-5-phenyloxazolidone (3). Diazo compound **6a** (2.61 g, 9.2 mmol) was dissolved in 40 mL of THF, and, after cooling to 0 °C, 21 mL of water and $LiOH·H_2O$ (0.40 g, 9.5 mmol) were added sequentially. The initially clear yellow solution turned cloudy within 10 min after the addition of lithium hydroxide. After an additional 10 min, the reaction was terminated by dilution with water and extraction with ether. The ether solution was washed with water, dried over anhydrous magnesium sulfate, and concentrated under reduced pressure. NMR analysis showed only two products: **5a** and **3**. Following chromatography (silica gel) with 1:3 ethyl acetate/hexane and recrystallization from ether, 1.20 g of **3** (4.9 mmol, 54% yield) was obtained as yellow needles: mp 71–72 °C; $[\alpha]^{34}_D$ 14.0° (*c* 0.57 in $CHCl_3$); ^1H NMR ($CDCl_3$) δ 7.55–7.25 (m, 5 H), 6.62 (s, CHN_2), 5.69 (d, *J* = 7.4 Hz, OC*H*Ph), 4.82 (d of q, *J* = 7.4, 6.6 Hz, C*H*CH_3), 0.94 (d, *J* = 6.6 Hz, CHC*H*$_3$); IR (CCl_4) $\bar{\nu}_{C=N_2}$ 2113 cm^{-1}. Anal. Calcd for $C_{12}H_{11}N_3O_3$: C, 58.76; H, 4.53; N, 17.14. Found: C, 58.73; H, 4.58; N, 17.04.

Synthesis of 6b. The same procedure for the reaction of the lithium salt of **5b** with diketene as previously reported for **5a** was employed, and the acetoacetyl derivative of **5b** was isolated as a yellow oil in 89% yield: ^1H NMR ($CDCl_3$) δ 4.6–4.2 (m, C*H*CH_2), 4.03 (d, *J* = 4.2 Hz, $COCH_2CO$), 2.60–2.15 (m, C*H*Me_2), 2.27 (s, CH_3CO), 0.93 (d, *J* = 7.0 Hz, CHC*H*$_3$), 0.92 (d, *J* = 6.8 Hz, CHC*H*$_3$).

This crude product was immediately subjected to diazo transfer with p-(azidosulfonyl)benzoic acid to give **6b** as a yellow oil in 91% yield: $[\alpha]^{25}_D$ +292° (*c* 1.8 in $CHCl_3$); ^1H NMR ($CDCl_3$) δ 4.8–4.2 (m, C*H*CH_2), 2.60–2.15 (m, C*H*Me_2), 2.47 (s, CH_3CO), 0.93 (d, *J* = 7.0 Hz, CHC*H*$_3$), 0.91 (d, *J* = 6.8 Hz, CHC*H*$_3$). Anal. Calcd for $C_{10}H_{13}N_3O_4$: C, 50.21; H, 5.48; N, 17.56. Found: C, 50.01; H, 5.56; N, 17.25.

(4*S*)-*N*-(Diazoacetyl)-4-(2-propyl)oxazolidone (4). With the procedure employed for the synthesis of **3**, **4** was prepared from **6b** as a yellow oil in 62% isolated yield: $[\alpha]^{25}_D$ 45.8° (*c* 1.8 in $CHCl_3$); ^1H NMR ($CDCl_3$) δ 6.62 (s, CHN_2), 4.70–4.35 (m, C*H*CH_2), 4.40–4.15 (m, C*H*CH_2), 2.65–2.25 (m, C*H*Me_2), 0.93 (d, *J* = 7.0 Hz, CHC*H*$_3$), 0.89 (d, *J* = 6.9 Hz, CHC*H*$_3$). Anal. Calcd for $C_8H_{11}N_3O_3$: C, 48.72; H, 5.62; N, 21.31. Found: C, 49.00; H, 5.52; N, 21.19.

Preparation of 3 from (4*R*,5*S*)-*N*-Acetyl-4-methyl-5-phenyloxazolidone (7). To 0.38 g of **7** (1.8 mmol) dissolved in 3 mL of anhydrous THF that was cooled to −78 °C was added a freshly prepared solution of lithium diisopropylamide (1.8 mmol) in 4 mL of THF over a 30-min period. The solution was stirred for an additional 30 min whereupon 2,2,2-trifluoroethyl trifluoroacetate (0.70 g, 3.6 mmol) was added all at once. Saturated aqueous ammonium chloride was added 5 min after the ester addition, and the reaction mixture was allowed to warm to room temperature. This solution was then diluted with water and extracted three times with ethyl ether. The ether extractions were combined, washed with 50% aqueous acetic acid, dried over anhydrous magnesium sulfate, and concentrated to afford a yellow oil[24] which was immediately subjected to the diazo transfer procedure of Regitz[7] using p-toluenesulfonyl azide, 1.0 equiv of water, and a 1.5 molar excess of triethylamine. Product isolation and chromatographic purification (silica gel) with 1:3 ethyl acetate/hexane gave 0.26 g of **3** (1.13 mmol, 62% yield).

Catalytic Cyclopropanation Reactions of 3 and 4 with Styrene. In a typical experiment **3** (0.24 g, 1.0 mmol) was dissolved in 0.52 g of styrene (5.0 mmol) and added by Sage syringe pump over a 4-h period to a mixture of $Rh_2(OAc)_4$ (8.8 mg, 2.0 mol %) in 0.52 g of styrene (5.0 mmol) maintained under nitrogen at 22 °C. After addition was complete, stirring was continued for an additional 8 h. The reaction mixture was diluted with ether, washed once with 10% aqueous hydrochloric acid and once with water, dried over anhydrous magnesium sulfate, and concentrated. The NMR spectrum of this reaction mixture clearly exhibited absorptions for the cyclopropane products derived from **3** at δ 3.7–2.5.

The cyclopropane product mixture was dissolved in 5 mL of 50:50 ether/ethanol and added to 2 mL of ethanol containing 10 mmol of sodium ethoxide at 0 °C. After the reaction solution was stirred for 10 min, water was added and the mixture was extracted with ether. The ether solution was dried over anhydrous magnesium sulfate and concentrated. Individual cyclopropane isomers were isolated by GC without evident isomerization from a packed 15% Carbowax 20M column as previously reported.[1c,25] The trans isomer exhibited $[\alpha]^{33}_D$ −42.7° (*c* 0.30 in $CHCl_3$), which corresponded to a 14% ee of (1*R*,2*R*)-**8**,[25] whereas the cis isomer exhibited $[\alpha]^{33}_D$ −2.4° (*c* 0.21 in $CHCl_3$), which corresponded to a 13% ee of (1*R*,2*S*)-**8**. Control experiments with the optically active mixture of **8** in which these cyclopropanes were subjected to the same reaction conditions used for their preparation from the corresponding oxazolidone derivatives showed neither geometrical isomerization nor racemization.

Decomposition of 3 by Rhodium(II) Acetate in the Presence of Water. To 0.073 g of **3** (0.30 mmol) dissolved in 5.0 mL of chloroform-*d* and containing 5.4 mg of water (0.30 mmol)

(20) Newman, M. S.; Kutner, A. *J. Am. Chem. Soc.* **1951**, *73*, 4199.
(21) Salomon, R. G.; Salomon, M. F.; Heyne, T. R. *J. Org. Chem.* **1975**, *40*, 756.
(22) Neumann, H. M.; Johnson, S. A.; Hunt, H. R. *Inorg. Chem.* **1963**, *2*, 960.
(23) p-Toluenesulfonyl azide was also employed for this transformation, but p-toluenesulfonamide contamination of the diazo product could not be conveniently resolved by chromatographic separation. Product yields were less than 82%.
(24) The NMR spectrum ($CDCl_3$) of this product mixture confirmed the presence of both enol forms: δ 7.5–7.2 (m, Ph), 5.74 and 5.71 (d, *J* = 7.3 Hz, OC*H*Ph), 4.85 and 4.81 (d of q, *J* = 7.3, 6.5 Hz, C*H*CH_3), 4.35 and 4.30 (s, CH=C(OH)CF_3), 0.96 and 0.94 (d, *J* = 6.5 Hz, CHC*H*$_3$).
(25) Nakamura, A.; Konishi, A.; Tatsuno, Y.; Otsuka, S. *J. Am. Chem. Soc.* **1978**, *100*, 3443, 6544.

was added 2.6 mg of $Rh_2(OAc)_4$ (2 mol %), and the resulting solution was stirred vigorously for 60 min. Gas evolution was immediate and continuous at room temperature. NMR analysis after 60 min showed that **3** had been completely converted to a new product which, after chromatographic isolation as a colorless oil from a silica gel column, was identified as **10** (0.069 g, 98% yield): $[\alpha]^{25}_D$ +3.2°; ^{1}H NMR ($CDCl_3$) δ 7.34 (s, Ph), 5.12 (d of d, J = 6.5, 2.8 Hz, PhC*H*OH), 4.46 (inner lines of AB pattern with separation of 0.7 Hz), 4.35 (d of q, J = 6.9, 6.5 Hz, C*H*CH_3), 2.92 (d, J = 2.8 Hz, CHO*H*), 1.52 (d, J = 6.9 Hz, CHC*H*$_3$) [upon addition of D_2O, absorption at δ 2.92 disappears and absorption at δ 5.12 becomes a doublet (J = 6.5 Hz)]; IR (CCl_4) $\tilde{\nu}_{OH}$ 3625 (s), 3502 (br) cm^{-1}, $\tilde{\nu}_{C=O}$ 1823 (m), 1796 (w), 1744 (s) cm^{-1}. Anal. Calcd for $C_{12}H_{13}NO_4$: C, 61.27; H, 5.57; N, 5.95. Found: C, 61.04; H, 5.62; N, 5.92.

Decomposition of 3 by Rhodium(II) Acetate in the Presence of Ethanol. The reaction was performed with 0.30 mmol of **3** and 0.30 mmol of ethanol in chloroform according to the previously described procedure for reaction with water. Compound **11** was isolated in 97% yield: ^{1}H NMR ($CDCl_3$) δ 7.50-7.15 (m, Ph), 5.49 (d, J = 7.2 Hz, OC*H*Ph), 4.63 (s, CH_2), 4.22 (quin, J = 7.1 Hz, C*H*CH_3), 3.76 (d of q, J = 7.1, 1.4 Hz, O*CH*$_2$CH$_3$), 1.29 (t, J = 7.1 Hz, OCH$_2$C*H*$_3$), 1.12 (d, J = 7.0 Hz, CHC*H*$_3$); mass spectrum, m/e (relative abundance) 218 (19, M - C_2H_5O), 158 (10), 157 (100), 135 (12), 130 (24), 129 (34), 128 (77), 118 (14), 117 (47), 116 (16), 115 (19), 107 (15), 105 (19), 101 (12), 91 (26), 77 (30), 70 (53). Anal. Calcd for $C_{14}H_{17}NO_4$: C, 63.87; H, 6.51. Found: C, 63.76; H, 6.81.

Decomposition of 3 by Boron Trifluoride Etherate in the Presence of Ethanol. Boron trifluoride etherate (1.0 mg) was added to a chloroform solution containing **3** (88 mg, 0.35 mmol) and 1.0 mL of ethanol. The reaction mixture was stirred for 1 h at room temperature after which the solvent was removed under reduced pressure. Spectral analysis showed **10** and at least one other oxazolidone product formed in less than 15% yield.

Acknowledgment. We are grateful to the National Science Foundation for their financial support of this work and to David A. Evans for generous samples of **5** and for helpful discussions concerning the syntheses of these diazo compounds.

Annulation to the Quinazoline Ring Utilizing Mesoionic Ring Systems[1a]

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Received August 21, 1984

anhydro-3-Hydroxythiazolo[3,2-*c*]quinazolin-4-ium hydroxides, prepared from the corresponding thioglycolic acid with cyclodehydrating agents and also from 4(3*H*)-quinazolinethiones and α-bromophenylacetyl chloride, were hydrolyzed at the 5-position of the quinazoline ring with hot water. Alkynic and alkenic dipolarophiles cycloadded readily in hot benzene; the former gave pyrido[1,2-*c*]quinazolines and the latter 1:1 cycloadducts which lost H_2S to give the above ring system. These procedures provided convenient annulation of a pyridinone to the *c* side of quinazoline. With ethyl acrylate, in addition to the normal 1:1 cycloadduct, a rearranged pyrrolo[1,2-*c*]quinazoline was obtained depending on the reaction conditions; analogous products were obtained with dimethyl fumarate. *anhydro*-1-Hydroxythiazolo[3,2-*a*]quinazolinium hydroxides, preferably generated in situ from the corresponding thioglycolic acid and dicyclohexylcarbodiimide (DCC), and alkynic dipolarophiles in refluxing benzene readily gave pyrido[1,2-*a*]quinazolines. Alkenic dipolarophiles also gave 1:1 cycloadducts, which lost H_2S to form pyrido[1,2-*a*]quinazolines, resulting in annulation of a pyridinone ring to the *a* side of quinazoline.

Annulation to a heterocyclic ring can often be satisfactorily effected by using the "masked" ylidic system present in mesoionic ring systems,[2,3] and in studies establishing the scope of this approach, we describe the annulation of the pyridinone ring to the *a* and *c* sides of the quinazoline nucleus utilizing appropriate mesoionic precursors.

anhydro-3-Hydroxythiazolo[3,2-*c*]quinazolin-4-ium Hydroxides

The ease of preparation, stability, and reactivity of the *anhydro*-3-hydroxythiazolo[3,2-*c*]quinazolin-4-ium hydroxide system depends markedly on the nature of the 2-substituent and to a lesser degree of the 5-substituent. *anhydro*-3-Hydroxy-5-methylthiazolo[3,2-*c*]quinazolin-4-ium hydroxide (**2a**) reported[4] earlier as an air-sensitive material stable only in suspension in dry ether, can now be conveniently prepared and reacted in situ with dipolarophiles and its cycloaddition products characterized. The 2-phenyl analogue **2b** was readily isolated as air-stable, deep purple needles, but a strongly electron-withdrawing trifluoromethyl group in the 5-position made the quinazoline nucleus more susceptible to hydrolysis, and the corresponding mesoionic system **2c** could not be isolated (see below).

4(3*H*)-Quinazolinethiones **1** are convenient precurosrs to **2**. Direct thiation of 4(3*H*)-quinazolinone with P_4S_{10} in boiling pyridine[5] gave **1** (R = H) in good yield, but for **1** (R = CH_3) the conversion of anthranilonitrile into *o*-acetamidothiobenzamide and subsequent thermal cyclization above its melting point to 2-methyl-4(3*H*)-

(1) (a) Abstracted from the MS (R.L.S.) and Ph.D. (K.G.B.) theses, Rensselaer Polytechnic Institute. (b) Undergraduate Research Participant.

(2) For a recent review, see: Potts, K. T. In "1,3-dipolar Cycloaddition Chemistry"; Padwa, A., Ed.; Wiley: New York, 1984; Chapter 8.

(3) Potts, K. T.; Kanemasa, S. *J. Org. Chem.* **1979**, *44*, 3803, 3808 and references listed therein.

(4) Talukdar, P. B.; Sengupta, S. K.; Datta, A. K.; Roy, T. K. *Indian J. Chem., Sect. B* **1977**, *15B*, 41.

(5) Fry, D. J.; Kendall, J. D.; Morgan, A. J. *J. Chem. Soc.* **1960**, 5062.

(6) Bogert, M. T.; Breneman, H. C.; Hand, W. F. *J. Am. Chem. Soc.* **1903**, *25*, 372. See also: Armarego, W. L. F. In "Quinazolines"; Brown, D. J., Ed.; Interscience: New York, 1967; p 277.

(7) Ferry, M.; Robert, A.; Foucand, A. *Synthesis* **1976**, 261.

0022-3263/85/1950-1666$01.50/0