Scheme I

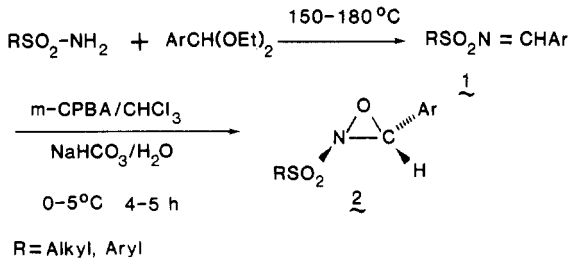


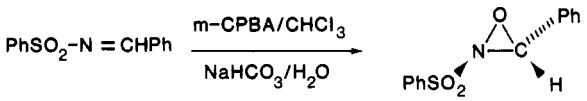
Table I. Preparation of 2-Sulfonyloxaziridines 2 by Using BTEAC

2			% yield[a]	
R	Ar	crystallization solvent	this procedure	old procedure[1]
Ph	Ph	EtOAc/ *n*-pentane	92	61
Ph	3-NO_2Ph	EtOH	83	
Ph	4-NO_2Ph	MeOH	80	43
Me	Ph	EtOAc/ *n*-pentane	85	64
$PhCH_2$	Ph	EtOAc/ *n*-pentane	90	50

[a] Isolated yields.

complete oxidation. Finally, the 2-sulfonyloxazridines prepared by using this modification were easier to purify. These results are summarized in Table I.

When the oxidation of *N*-benzylidine-2-benzenesulfonamide (3) was carried out by using a chiral phase-transfer catalyst, optically active 2-benzenesulfonyl-3-phenyloxazridine (4) was obtained. Thus oxidation of 3 with 0.1



molar equiv of (−)-benzylquinidinium chloride (QUIBEC) and (+)-benzylcinchoninium chloride (BCNC) gave (−)- and (+)-4, respectively. The asymmetric induction (% ee) of (−)- and (+)-4 was determined, using $Eu(hfc)_3$, to be 1.4–10.6% ee.

Attempts to effect the oxidation of 1 to 2 (R = Ph; Ar = *p*-NO_2Ph) by using PTC and more economical oxidizing agents such as alkaline H_2O_2, *t*-BuOOH, or NaOCl were unsuccessful. In each case only hydrolysis products were obtained.

Experimental Section

Melting points were determined on a Mel-Temp apparatus and are uncorrected. ^1H NMR spectra were measured on a Varian A-60A NMR spectrometer. Optical rotations were measured on a Perkin-Elmer 241 polarimeter. MCPBA was purchased from Aldrich, and solvents were used without additonal purification. (−)-QUIBEC and (+)-BCNC were purchased from Fluka.

General Procedure for Oxidation of Sulfonimines 1 to 2-Sulfonyloxaziridines 2. In a 500-mL three-necked Morton flask, equipped with a mechanical stirrer and dropping funnel, were placed 100-mL of saturated aqueous $NaHCO_3$, 10 g of the sulfonimine 1, and 0.11 molar equiv of benzyltriethylammonium chloride (BTEAC) in 75 mL of chloroform. The reaction mixture was cooled to 0–5 °C in an ice bath and stirred vigorously. A solution of 1.1 equiv of MCPBA (85% Aldrich) in 100 mL of chloroform was added dropwise over 30 min. After the mixture was stirred for an additional 15 min, the chloroform layer was separated and washed successively with 50 mL of water, 50 mL of 10% aqueous Na_2SO_3, water (2 × 50 mL), and finally 20 mL of saturated aqueous NaCl. After being dried over the anhydrous K_2CO_3, the solution was filtered and the solvent evaporated in vacuo below 40 °C. The crude oxaziridine was crystallized from the appropriate solvent (see below and Table I).

2-Benzenesulfonyl-3-(*m*-nitrophenyl)oxaziridine. The crude oxaziridine as obtained above was triturated under 50 mL of methanol for 3–5 min, filtered, washed with another 10 mL of methanol, and air-dried to give 8.75 g (83%) of a white powder, mp 108–110 °C. An analytical sample was crystalized from ethanol: mp 113–114 °C; IR (Nujol) 1528 and 1350 cm^{-1} (NO_2); NMR ($CDCl_3$) δ 5.62 (s, 1 H, oxaziridine 3-H), 7.6–8.3 (m, 9 H, Ar). Anal. Calcd for $C_{13}H_{10}N_2O_5S$: C, 50.98; H, 3.29. Found: C, 50.64; H, 3.31.

2-Benzenesulfonyl-3-(*p*-nitrophenyl)oxaziridine. The crude oxaziridine as obtained above was triturated under 50 mL of methanol for 3–5 min, filtered, washed with another 10 mL of methanol, and air-dried to give 8.63 g (80%) of white fluffy crystals: mp 134–136 °C; IR (Nujol) 1525 and 1350 cm^{-1} (NO_2); NMR ($CDCl_3$) δ 5.78 (s, 1 H, oxaziridine 3-H), 7.55–8.33 (m, 9 H, Ar). Anal. Calcd for $C_{13}H_{10}N_2O_5S$: C, 50.98; H, 3.29. Found: C, 50.70; H, 3.00.

(+)- and (−)-2-Benzenesulfonyl-3-phenyloxaziridine (4). A solution of 2.45 g (0.01 moL) of *N*-benzylidinebenzenesulfonamide (3) and 0.0015 moL of (−)-QUIBEC or (+)-BCNC in 20 mL of chloroform and 30 mL of saturated aqueous Na_2CO_3 was treated as described above with 3.23 g (0.018 moL) of MCPBA in 15 mL of chloroform. After the workup, the residue was extracted with portions of ether (2 × 30 mL). The combined extracts were filtered, and the solvent was removed in vacuo to afford the crude optically active oxaziridine which was crystalized from ether/*n*-pentane.

(−)-4: first crop of crystals, 20%, mp 96–98 °C, $[\alpha]_D$ −0.56° (*c* 1.0, $CHCl_3$) (3.1% ee); second crop of crystals, 15%, mp 96–97 °C, $[\alpha]_D$ −2.63° (*c* 1.0, $CHCl_3$) (10.6% ee).

(+)-4: first crop of crystals, 23%, mp 96–98 °C, $[\alpha]_D$ +0.49° (*c* 1.0 $CHCl_3$) (1.4% ee); second crop of crystals, 15%, mp 96–98 °C, $[\alpha]_D$ +1.16° (*c* 1.0 $CHCl_3$) (10.2% ee).

Determination of Enantiomeric Compositions. The optical purity of (+)- and (−)-4 in $CDCl_3$ was determined by a series of 60-MHz ^1H NMR spectra obtained at increasing concentrations of the chiral shift reagent tris[3-[(heptafluoropropyl)hydroxymethlene]-*d*-camphorato]europium(III) derivative [$Eu(hfc)_3$]. When the shift difference of the oxaziridine 3-proton was approximately 9 Hz, the peak areas were determined by integration.

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Registry No. 2 (R = Ph; Ar = 3-NO_2Ph), 80997-73-5; **2** (R = Ph; Ar = 4-NO_2Ph), 78377-89-6; **2** (R = Me; Ar = Ph), 73844-99-2; **2** (R = $PhCH_2$; Ar = Ph), 73845-00-8; (−)-4, 80997-74-6; (+)-4, 80997-75-7.

Reductive Cyclization of 2-[(2-Propynyl)oxy]ethyl Bromides by a Cobalt Complex, Cobaloxime(I). A New Method for the Synthesis of α-Methylene-γ-butyrolactones

Masami Okabe, Masayoshi Abe, and Masaru Tada*

Department of Chemistry, School of Science and Engineering, Waseda University, Shinjuku, Tokyo 160, Japan

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The α-methylene-γ-butyrolactone structural unit is present in a wide variety of sesquiterpenes and other natural products[1] and has been suggested to be of central

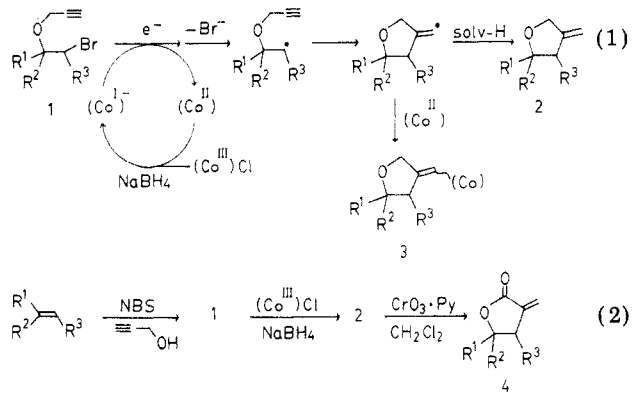
Table I. Isolated Yields[a] of 2-[(2-Propynyl)oxy]ethyl Bromides (1), 3-Methyleneoxolanes (2), and α-Methylene-γ-butyrolactones (4)

starting olefin	R^1	R^2	R^3	product yield, % 1	2	4
a	Ph	Ph	H	82	85	59
b	Ph	Me	H	82	73	60
c	Ph	H	H	80	78	33
d	H	$-(CH_2)_4-$		83	64	62
e	H	$-(CH_2)_3-$		70	48	61

[a] The numbers in the table are yields of each step.

importance for the biological activities of those compounds.[2] Several synthetic procedures have been developed for the lactones;[3] most of them involve the introduction of a methylene group at the α-position of butyrolactones or the lactonization of α-methylene carboxylic acid derivatives. In this paper we report a new method for the synthesis of α-methylene-γ-butyrolactones which involves the reductive cyclization of 2-[(2-propynyl)oxy]-ethyl bromides and the oxidation of the resultant 3-methyleneoxolanes.

We have reported that the reaction of bis(dimethylglyoximato)(pyridine)cobalt(I) [hereafter cobaloxime(I) in the text and $(Co^I)^-$ in the equations] with 2-allyloxyethyl bromides gives 3-(cobaloximatomethyl)oxolanes via 2-(allyloxy)ethyl radicals generated by a single-electron-transfer process.[4] In a similar manner, the reaction of cobaloxime(I) with 2-[(2-propynyl)oxy]ethyl bromides (1) gives 3-methyleneoxolanes (2) and 3-(cobaloximatomethylene)oxolanes (3) (eq 1). Cobaloxime(I) is prepared



(1)

(2)

in situ via the reduction of chlorocobaloxime(III)[5] by sodium borohydride, and cobaloxime(I) thus formed is oxidized by the bromide 1 to cobaloxime(II). Since sodium borohydride easily reduces cobaloxime(II) to cobaloxime(I), the cobaloxime can be recycled in the reaction system. Formation of the 3-(cobaloximatomethylene)oxolane (3) is made negligible by the use of a catalytic amount of chlorocobaloxime(III), resulting in a low concentration of the cobaloxime(II) intermediate which couples with the (3-oxolanyl)methylene radical (see eq 1). 2-[(2-Propynyl)oxy]ethyl bromides (1) were easily prepared by treatment of the corresponding olefins in 2-propynol with *N*-bromosuccinimide (eq 2 and Table I). 3-Methyleneoxolanes (2) obtained by the reductive cyclization (Table I) were oxidized to α-methylene-γ-butyrolactones (4) by excess chromium trioxide–pyridine complex in dichloromethane[6] (eq 2 and Table I).

9-Methylene-7-oxabicyclo[4.3.0]nonane (**2d**) and 4-methylene-2-oxabicyclo[3.3.0]octane (**2e**) are cis-fused since their oxidation products, **4d** and **4e**, are identical with the cis lactones.[7,8] Byproducts from the oxidation of **2a** and **2b** are benzophenone and acetophenone, respectively, and the low yield of the lactone **4c** can be accounted for by the existence of a benzylic hydrogen in **2c**. In addition, the low yields in the last oxidation step result mainly from the difficulty in the workup due to the formation of a large quantity of the insoluble chromium complex, but a large excess of the oxidation reagent is necessary for the complete consumption of the oxolanes. The yields listed in the Table I have not been optimized.

Other oxidation reagents such as selenium dioxide/ethanol, chromium trioxide/acetic acid, and *tert*-butyl chromate/acetic anhydride/carbon tetrachloride gave complex mixtures and unsatisfactory results. Cobaloxime(I) is not reactive to a wide variety of functional groups except strong electrophiles and electron acceptors such as tosylate, halide, unsaturated carbonyl, and unsaturated nitrile. The method described in this paper is characterized by the introduction of the carbonyl group at the last stage, and this is the new aspect in the synthesis of α-methylene-γ-butyrolactones. The present method does not require vigorous conditions, e.g., strong base, and should be a useful tool for the synthesis of 3-methyleneoxolanes and α-methylene-γ-butyrolactones.

Experimental Section

Syntheses of 2-[(2-Propynyl)oxy]ethyl Bromides (1). Typical Procedure. To a cooled solution (below −30 °C) of *N*-bromosuccinimide (4.30 g, 24 mmol) in 20 mL of 2-propynol was added dropwise a solution of 2-phenylpropene (2.36 g, 20 mmol) in 10 mL of dichloromethane (methanol free) over a period of 1 h. The reaction mixture was stirred for 2 h below −20 °C and overnight at room temperature (ca. 15 °C). After addition of 25 mL of 1 N aqueous NaOH, the mixture was extracted with dichloromethane (3 × 20 mL). The extract was washed with 1 N aqueous NaOH (10 mL) and dried over sodium sulfate. Evaporation of the solvent and recrystallization of the residue from methanol gave bromide **1b**: 4.17 g (82%); mp 62–64 °C; IR (CCl_4) 3310, 2149, 1071, 700 cm^{-1}; ^1H NMR (CCl_4) δ 1.82 (s, 3 H), 2.31 (t, 1 H, J = 3 Hz), 3.57 (d, 1 H, J = 11 Hz), 3.71 (d, 1 H, J = 11 Hz), 4.02 (d, 2 H, J = 3 Hz), 7.50–7.80 (m, 5 H). Anal. Calcd for $C_{12}H_{13}BrO$: C, 56.94; H, 5.18. Found: C, 56.63; H, 5.13.

The same procedure gave bromide **1a**, and distillation instead of recrystallization at the last stage gave bromides **1c–e** in the yields listed in Table I.

1a: mp 97–98 °C; IR (CCl_4) 3310, 2149, 1070, 697 cm^{-1}; ^1H NMR (CCl_4) δ 2.24 (t, 1 H, J = 3 Hz), 3.92 (d, 2 H, J = 3 Hz), 4.13 (s, 2 H), 7.29–7.56 (m, 10 H). Anal. Calcd for $C_{17}H_{15}BrO$: C, 64.78; H, 4.80. Found: C, 64.69; H, 4.73.

1c: bp 72–73 °C (0.15 mm); IR (CCl_4) 3310, 2148, 1093, 699 cm^{-1}; ^1H NMR (CCl_4) δ 2.35 (t, 1 H, J = 3 Hz), 3.54 (t, 2 H, J = 7 Hz), 3.99 (dd, 1 H, J = 3, 16 Hz), 4.26 (dd, 1 H, J = 3, 16 Hz), 4.82 (t, 1 H, J = 7 Hz), 7.52 (s, 5 H). Anal. Calcd for $C_{11}H_{11}BrO$: C, 55.25; H, 4.64. Found: C, 55.37; H, 4.51.

1d: bp 91–96 °C (8.0 mm); IR (CCl_4) 3310, 2145, 1092 cm^{-1}; ^1H NMR (CCl_4) δ 1.15–2.40 (m, 8 H), 2.25 (t, 1 H, J = 3 Hz), 3.49 (dt, 1 H, J = 4, 7 Hz), 3.93 (dt, 1 H, J = 4, 7 Hz), 4.14 (d, 2 H, J = 3 Hz); mass spectrum, m/e 216.0144, 218.0090 (M^+) (calcd for $C_9H_{13}{}^{79}BrO$, 216.0149; $C_9H_{13}{}^{81}BrO$, 218.0129).

1e: bp 104 °C (23.0 mm); IR (CCl_4) 3315, 2146, 1081 cm^{-1}; ^1H NMR (CCl_4) δ 1.60–2.46 (m, 6 H), 2.37 (t, 1 H, J = 3 Hz), 4.20 (d, 2 H, J = 3 Hz), 4.23–4.41 (m, 2 H). Anal. Calcd for $C_8H_{11}BrO$:

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C, 47.31; H, 5.46. Found: C, 47.36; H, 5.31.

Syntheses of 3-Methyleneoxolanes (2). Typical Procedure. To a solution of bromide **1b** (2.53 g, 10 mmol) in 50 mL of ethanol were added 1.0 mL of 10 N aqueous NaOH and sodium borohydride (380 mg, 10 mmol). The solution was warmed to 50 °C under a nitrogen atmosphere, and powdered chlorocobaloxime(III)[5] (240 mg, 0.6 mmol) was added in portions over a period of 1 h. The temperature of the reaction mixture was kept between 50 and 60 °C. After the completion of the addition, the reaction mixture was further stirred for 30 min at the same temperature. Most of the ethanol was removed under reduced pressure, and after the addition of 50 mL of saturated aqueous NaCl, the mixture was extracted with pentane–ether (4:1) several times. The extracts were washed with saturated aqueous NaCl and dried over sodium sulfate. After the evaporation of the solvents, the residue was distilled under reduced pressure to give oxolane **2b**: 1.27 g (73%); bp 62–63 °C (0.5 mm); IR (CCl_4) 1671, 1044, 884, 700 cm^{-1}; ^1H NMR (CCl_4) δ 1.48 (s, 3 H), 2.70 (diffused d, 1 H, J = 16 Hz), 2.91 (diffused d, 1 H, J = 16 Hz), 4.42 (diffused t, 2 H, J = 15 Hz), 4.87 (t, 1 H, J = 2 Hz), 4.97 (t, 1 H, J = 2 Hz), 7.20–7.50 (m, 5 H); mass spectrum, m/e 174.1041 (M^+) (Calcd for $C_{12}H_{14}O$ 174.1043).

The same procedure gave oxolanes **2c–e**, and chromatography on silica gel instead of distillation gave **2a** in the yield listed in Table I.

2a: mp 51–51.5 °C; IR (CCl_4) 1670, 1046, 883, 698 cm^{-1}; ^1H NMR (CCl_4) δ 3.10–3.20 (m, 2 H), 4.27–4.36 (m, 2 H), 4.72–4.80 (m, 1 H), 4.85–4.96 (m, 1 H), 7.00–7.40 (m, 10 H). Anal. Calcd for $C_{17}H_{16}O$: C, 86.40; H, 6.83. Found: C, 86.21; H, 6.80.

2c: mp 94 °C (7.0 mm); IR (CCl_4) 1670, 1054, 883, 695 cm^{-1}; ^1H NMR (CCl_4) δ 2.24 (diffused dd, 1 H, J = 7, 16 Hz), 2.85 (diffused dd, 1 H, J = 6, 16 Hz), 4.23 (diffused d, 1 H, J = 13 Hz), 4.42 (diffused d, 1 H, J = 13 Hz), 4.71–5.00 (m, 3 H), 7.23 (m, 5 H); mass spectrum, m/e 160 (M^+). Hydrogenolysis of **2c** over Pd/C in ethanol gave 2-methyl-4-phenylbutanol which was identified by comparison with an authentic sample.[9]

2d: bp 95–100 °C (85 mm); IR (CCl_4) 1669, 1032, 885 cm^{-1}; ^1H NMR (CCl_4) δ 1.20–2.00 (m, 8 H), 2.49 (br s, 1 H), 3.85–4.01 (m, 1 H), 4.25 (diffused d, 1 H, J = 14 Hz), 4.46 (diffused d, 1 H, J = 14 Hz), 4.86–5.01 (m, 2 H); mass spectrum, m/e 138.1049 (M^+) (calcd for $C_9H_{14}O$ 138.1045).

2e: bp 90–95 °C (101 mm); IR (CCl_4) 1670, 1060, 887 cm^{-1}; ^1H NMR (CCl_4) δ 1.47–2.03 (m, 6 H), 3.02 (br s, 1 H), 4.17 (diffused d, 1 H, J = 14 Hz), 4.34 (diffused d, 1 H, J = 14 Hz), 4.46–4.62 (m, 1 H), 4.93–5.00 (m, 2 H); mass spectrum, m/e 124.0881 (M^+) (calcd for $C_8H_{12}O$ 124.0887).

Syntheses of α-Methylene-γ-butyrolactones (4). Typical Procedure. Chromium trioxide (12.0 g, 120 mmol) was added to a mixture of pyridine (12 mL) and dichloromethane (methanol free, 120 mL),[6] and the resulting solution was stirred for 20 min. To the mixture was added 5 mL of a dichloromethane solution of 3-methyleneoxolane **2b** (1.04 g, 6 mmol), and the reaction mixture was refluxed for 1 h. The solution part of the mixture was separated by decantation, and the residue was washed with dichloromethane. The dichloromethane solution was washed with saturated aqueous $NaHCO_3$. The solid residue of the reaction mixture was dissolved in a large amount (ca. 300 mL) of saturated aqueous $NaHCO_3$ and extracted with dichloromethane. The combined dichloromethane extracts were washed with 2 N aqueous HCl, passed through a short column of silica gel (1 cm i.d. × 10 cm) to remove the chromium compound, and condensed under reduced pressure. Distillation of the condensate gave γ-methyl-α-methylene-γ-phenyl-γ-butyrolactone (**4b**):[10] 6.77 g (60%); bp 94–97 °C (0.25 mm); IR (CCl_4) 1779, 1674, 702 cm^{-1}; ^1H NMR (CCl_4) δ 1.68 (s, 3 H), 3.05 (t, 2 H, J = 3 Hz), 5.46 (t, 1 H, J = 3 Hz), 6.06 (t, 1 H, J = 3 Hz), 7.10–7.35 (m, 5 H).

The same procedure gave α-methylene-γ-butyrolactones **4d** and **4e**, and recrystallization instead of distillation at the last stage gave lactones **4a** (methanol) and **4c** (hexane) in the yields listed in Table I. All α-methylene-γ-butyrolactones obtained in this work are identical with the reported ones in boiling and melting points and in spectroscopic properties.

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4a:[11] mp 101–103 °C; IR (CCl_4) 1777, 1672, 698 cm^{-1}; ^1H NMR (CCl_4) δ 3.64 (t, 2 H, J = 3 Hz), 5.66 (t, 1 H, J = 3 Hz), 6.28 (t, 1 H, J = 3 Hz), 7.22–7.67 (m, 10 H).

4c:[10] mp 52–53.5 °C; IR (CCl_4) 1800, 1674, 700 cm^{-1}; ^1H NMR (CCl_4) δ 2.65–2.96 (m, 1 H), 3.22–3.53 (m, 1 H), 5.44 (t, 1 H, J = 8 Hz), 5.61 (t, 1 H, J = 3 Hz), 6.22 (t, 1 H, J = 3 Hz), 7.27–7.43 (m, 5 H).

4d:[7] bp 95–99 °C (4.0 mm); IR (CCl_4) 1778, 1672 cm^{-1}; ^1H NMR (CCl_4) δ 1.25–2.10 (m, 8 H), 2.86–3.09 (m, 1 H), 4.44 (q, 1 H, J = 6 Hz), 5.42 (d, 1 H, J = 3 Hz), 6.07 (d, 1 H, J = 3 Hz).

4e:[8] bp 135–139 °C (31 mm); IR (CCl_4) 1770, 1669 cm^{-1}; ^1H NMR (CCl_4) δ 1.56–2.18 (m, 6 H), 3.25–3.49 (m, 1 H), 4.82–4.99 (m, 1 H), 5.54 (d, 1 H, J = 3 Hz), 6.12 (d, 1 H, J = 3 Hz).

Registry No. 1a, 81011-48-5; **1b**, 80997-76-8; **1c**, 80997-77-9; **1d**, 71960-57-1; **1e**, 80997-78-0; **2a**, 77862-49-8; **2b**, 81011-49-6; **2c**, 80997-79-1; **2d**, 75681-59-3; **2e**, 80997-80-4; **4a**, 29043-99-0; **4b**, 29043-98-9; **4c**, 26613-71-8; **4d**, 16822-06-3; **4e**, 61747-55-5; cobaloxime (I), 36451-60-2; 2-propynol, 107-19-7; 2-phenylpropene, 98-83-9; chlorocobaloxime (III), 59692-12-5; 2-methyl-4-phenylbutanol, 3023-61-8; 1,1'-ethylidenebis[benzene], 530-48-3; ethenylbenzene, 100-42-5; cyclohexene, 110-83-8; cyclopentene, 142-29-0.

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Unusual Cyclization of Amidine Salts in the Formation of Quinazolones

Niteen A. Vaidya and C. DeWitt Blanton, Jr.*

Department of Medicinal Chemistry, School of Pharmacy, University of Georgia, Athens, Georgia 30602

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When an aromatic amine, **1**, reacts with a benzoxazinone, **2** (i.e., acylanthranil), to give a quinazolone, **5**, it can do so by two pathways (Scheme I).[1] Pathway A involves formation of an intermediate *o*-(acylamido)benzamide, **3**, which cyclizes at temperatures above 200 °C. Pathway B involves the formation of an amidine salt **4** which undergoes facile cyclization to yield the quinazolone even at room temperature.[1d] In the examples presented by Errede and co-workers,[1] the oxazine (**2**) had no substituents at the 5- or 8-position, and cyclization of the intermediate amidine salt (**4**) presented no complications. However, while preparing various substituted quinazolone derivatives, we have observed that certain substituents can alter the course of amidine salt cyclodehydration.

In our study, 2-acetamido-3-(carbomethoxy)-5,6-dimethylbenzoic acid (**6**)[2] was converted to the acylanthranil **7** by refluxing with phosphorus oxychloride in toluene[3] (Scheme II). The acylanthranil was treated with aniline derivatives **8** in anticipation of the preparation of the substituted quinazolone derivatives **9**. However, acidic substances were isolated and subsequently assigned structure **10**.

Although the benzoic acid **6** was recovered unchanged after heating with the aromatic amines **8**, addition of trace amounts of acetic acid led to the formation of *o*-acetamidobenzamido acids **11** (Scheme II). Acids **11b** and **11c**

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