5-*tert*-Butyl-8-methyl-12-methoxy[2.2]metacyclophane (11a): colorless oil; ^{1}H NMR ($CDCl_3$) δ 0.57 (3 H, s), 1.35 (9 H, s), 1.69–1.80 (1 H, m), 2.11–2.20 (1 H, m), 2.53–2.64 (2 H, m), 2.85–2.98 (3 H, m), 3.51–3.58 (1 H, m), 3.63 (1 H, d, J = 2.0 Hz), 3.81 (3 H, s), 6.58 (1 H, d, J = 8.3 Hz), 7.02–7.06 (3 H, m); MS m/e 308 (M^+). Anal. Calcd for $C_{22}H_{28}O$: C, 85.66; H, 9.15. Found: C, 85.59; H, 9.21.

5-*tert*-Butyl-8-methyl-12-methoxy-13-bromo[2.2]metacyclophane (12a): colorless prisms (hexane); mp 104–106 °C; ^{1}H NMR ($CDCl_3$) δ 0.62 (3 H, s), 1.33 (9 H, s), 1.80–3.47 (8 H, m), 3.57 (1 H, d, J = 2.0 Hz), 3.82 (3 H, s), 7.03 (1 H, d, J = 2.4 Hz), 7.04 (1 H, d, J = 2.4 Hz), 7.24 (1 H, d, J = 2.0 Hz); MS m/e 386 388 (M^+). Anal. Calcd for $C_{22}H_{27}BrO$: C, 68.22; H, 7.03. Found: C, 68.59; H, 7.21.

5-*tert*-Butyl-8-methoxy-12-hydroxy[2.2]metacyclophane (11c): colorless oil; IR (KBr) 3350 (OH) cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 1.35 (9 H, s), 1.72–3.48 (8 H, m), 3.05 (3 H, s), 3.90 (1 H, d, J = 2.0 Hz), 5.29 (1 H, s), 6.55 (1 H, d, J = 8.3 Hz), 6.91 (1 H, dd, J = 8.3, 2.0 Hz), 7.05 (1 H, d, J = 2.4 Hz), 7.07 (1 H, d, J = 2.4 Hz); MS m/e 310 (M^+). Anal. Calcd for $C_{21}H_{26}O_2$: C, 81.25; H, 8.44. Found: C, 81.20; H, 8.62.

5-*tert*-Butyl-8-methoxy-12-hydroxy-13-bromo[2.2]metacyclophane (12c): pale yellow oil; IR (KBr) 3450 (OH) cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 1.34 (9 H, s), 1.71–3.54 (8 H, m), 3.06 (3 H, s), 3.88 (1 H, d, J = 2.0 Hz), 5.39 (1 H, s), 7.03 (1 H, d, J = 2.4 Hz), 7.07 (1 H, d, J = 2.4 Hz), 7.14 (1 H, d, J = 2.4 Hz); MS m/e 388, 390 (M^+). Anal. Calcd for $C_{21}H_{25}O_2$: C, 64.79; H, 6.47. Found: C, 64.50; H, 6.62.

Registry No. **5a**, 144182-39-8; **5b**, 144182-48-9; **6a**, 144182-40-1; **7b**, 144182-41-2; **8a**, 144182-42-3; **9b**, 144182-43-4; **10b**, 144182-44-5; **11a**, 144182-45-6; **11b**, 118249-24-4; **11c**, 144182-49-0; **12a**, 144182-46-7; **12b**, 144182-47-8; **12c**, 144182-50-3.

Palladium-Catalyzed, Carbonylative, Intramolecular Coupling of Hydroxy Vinyl Triflates. Synthesis of Substituted α,β-Butenolides

Geoffrey T. Crisp* and Adam G. Meyer

Department of Organic Chemistry, University of Adelaide, G.P.O. Box 498, Adelaide, South Australia, Australia, 5001

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The α,β-butenolide substructure is found in a wide variety of natural products including many flavor components and insect pheromones.[1a] In addition, compounds incorporating functionalized α,β-butenolides, or their derivatives, have been shown to be biologically active and some display antitumor activity.[1b] Although approaches to the synthesis of α,β-butenolides have been diverse they can be classified as either elaboration of an existing five-membered ring or cyclization of an appropriate acyclic precursor.[1a,b] Our approach to the synthesis of α,β-butenolides relies on a palladium-catalyzed, carbonylative, intramolecular coupling of a hydroxy vinyl trifluoromethanesulfonate (triflate) to effect the desired ring closure. Palladium-catalyzed methodologies have been reported previously for the synthesis of α,β-butenolides and these have included (a) the hydroarylation of alkyl 4-hydroxy-2-alkynoates,[2] and (b) the carbonylative cyclization of hydroxy vinyl iodides.[3a,b] The advantages offered

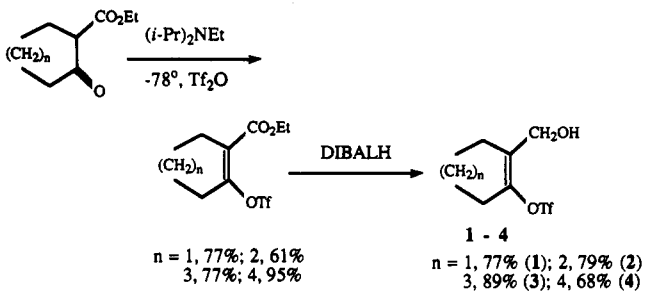


Figure 1.

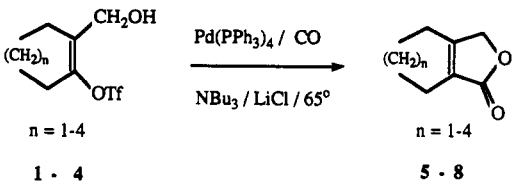


Figure 2.

by the use of vinyl triflates is their ease of formation from ketones using standard enolate chemistry and their ability to undergo palladium-catalyzed couplings readily.[4a,b] We wish to report that vinyl triflates can be used efficaciously for the synthesis of α,β-butenolides.

Results and Discussion

Cyclic vinyl triflates were readily prepared from the corresponding β-keto esters by a two-step process as indicated in Figure 1. Addition of *N,N*-diisopropylethylamine to the β-keto ester at low temperature, followed by the addition of triflic anhydride (Tf_2O) gave the corresponding ethoxycarbonyl-substituted vinyl triflate[5] in good yield for the ring sizes five through eight. The addition of 2 equiv of DIBALH to the ethoxycarbonyl-substituted vinyl triflates resulted in a clean reduction of the ester to the expected hydroxymethylene with no reduction of the triflate group. The same procedure was used on ethyl salicylate to give 2-[[(trifluoromethyl)sulfonyl]oxy]benzyl alcohol. The initial conditions used for the carbonylative coupling of the hydroxy vinyl triflates were similar to those reported for the reaction of hydroxy vinyl iodides.[3b] Thus addition of hydroxy vinyl triflate **2** to an acetonitrile solution of $Pd(PPh_3)_4$ (10 mol %), potassium carbonate and lithium chloride under 1 atmosphere of carbon monoxide gave the expected 4,5,6,7-tetrahydro-1(3*H*)-isobenzofuranone (**6**) in 43% yield. The observed yields for the carbonylative couplings of the other hydroxy vinyl triflates described in Figure 1 were also in the range of 40–50% under these conditions. Improved yields of products (75–95%) were obtained by performing the intramolecular cyclizations with tri-*n*-butylamine in place of potassium carbonate as described in Figure 2. The size of the ring appears to have negligible influence on the yield of the α,β-butenolide (entires 1–4, Table I). The hydroxyaryl triflate 2-[[(trifluoromethyl)sulfonyl]oxy]benzyl alcohol also underwent the intramolecular coupling in moderate yield (entry 5, Table I). The reaction mixtures changed from a initial yellow color through orange to black as the reaction proceeded. The black color is presumably caused by the precipitation of palladium and usually indicated that the reaction was complete. The course of the reaction was conveniently monitored by TLC analysis of the mix-

(1) Review: (a) Rao, Y. S. *Chem. Rev.* **1976**, *76*, 625. (b) Nagao, Y.; Dai, W.-M.; Ochiai, M.; Shiro, M. *J. Org. Chem.* **1989**, *54*, 5211 and references cited therein.

(2) Arcadi, A.; Bernocchi, E.; Burini, A.; Cacchi, S.; Marinelli, F.; Pietroni, B. *Tetrahedron* **1988**, *44*, 481.

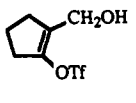
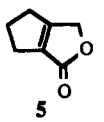
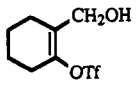
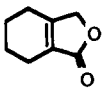
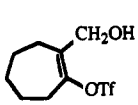
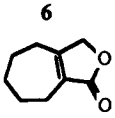
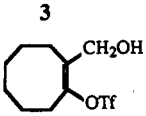
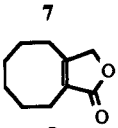
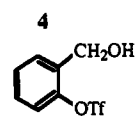
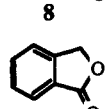
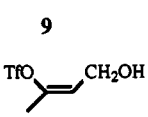
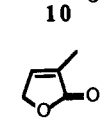
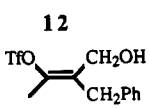
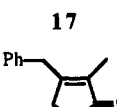
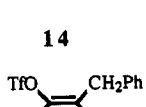
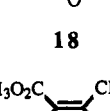
(3) (a) Mori, M.; Washioka, Y.; Urayama, T.; Yoshiura, K.; Chiba, K.; Ban, Y. *J. Org. Chem.* **1983**, *48*, 4058. (b) Cowell, A.; Stille, J. K. *J. Am. Chem. Soc.* **1980**, *102*, 4193.

(4) (a) Stille, J. K. *Angew. Chem., Int. Ed. Engl.* **1986**, *25*, 508. (b) Scott, W. J.; McMurray, J. E. *Acc. Chem. Res.* **1988**, *21*, 47.

(5) Saulnier, M. G.; Kadow, J. F.; Tun, M. M.; Langley, D. R.; Vyas, D. M. *J. Am. Chem. Soc.* **1989**, *111*, 8320.

0022-3263/92/1957-6972$03.00/0

Table I. Products from the Palladium-Catalyzed Carbonylation of Hydroxy Triflates

entry	hydroxy triflate	product	isolated yield, %
1	 1	 5	83
2	 2	 6	75
3	 3	 7	95
4	 4	 8	81
5	 9	 10	60
6	 12	 17	75
7	 14	 18	71
8	 16	 19	23

ture, and isolation of the product involved simple extraction followed by chromatography or distillation depending on the product (see Experimental Section).

Attention was then directed to the synthesis of acyclic hydroxy vinyl triflates by a route similar to that described in Figure 1. The generation of an enol or enolate from a β-keto ester can, potentially, give rise to *E* and *Z* isomers. When ethyl acetoacetate was reacted with *N,N*-diisopropylethylamine and Tf_2O (as described in Figure 1) then a 2.2:1 mixture of ethyl (*E*)- and (*Z*)-3-[[(trifluoromethyl)sulfonyl]oxy]-2-butenoate was obtained.[5] Since the intramolecular carbonylative coupling can only take place from hydroxy vinyl triflates with the *Z* configuration[3b] a method was sought which would deliver the required triflate with good stereospecificity. The addition of ethyl acetoacetate to a THF solution of potassium bis(trimethylsilyl)amide (KHMDS) at −78 °C followed by the addition of 1,1,1-trifluoro-*N*-phenyl-*N*-[(trifluoromethyl)sulfonyl]methanesulfonimide (Tf_2NPh) gave the required ethyl (*Z*)-3-[[(trifluoromethyl)sulfonyl]oxy]-2-butenoate (11) in 76% yield as the only isolated product (Figure 3). Reduction of 11 with DIBALH gave the corresponding acyclic hydroxy vinyl triflate 12 in 72% yield. Carbonylative coupling of 12 gave the α,β-butenolide 17 in 75% yield (entry 6, Table I).

Interestingly, when ethyl 2-benzylacetoacetate was treated under the conditions described in Figure 1 only

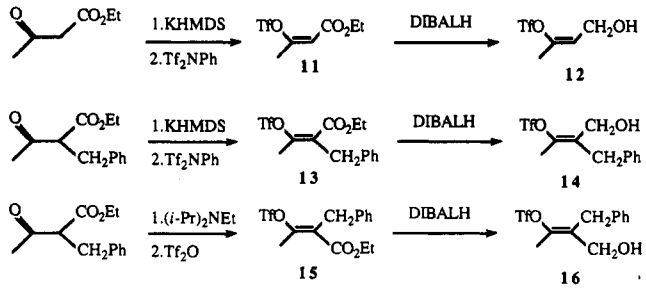


Figure 3.

the (*E*)-vinyl triflate 15 was isolated (Figure 3). Reduction of 15 with DIBALH delivered the expected (*E*)-hydroxy vinyl triflate 16. Carbonylative coupling of 16, with the addition of methanol to the carbonylative coupling mixture, gave the methyl ester 19 in low yield (23%) (entry 8, Table I). Treatment of ethyl 2-benzylacetoacetate with KHMDS followed by Tf_2NPh gave a 3:1 mixture of the (*E*)- and (*Z*)-vinyl triflates from which a low yield (12%) of the required (*Z*)-vinyl triflate 13 was isolated. Compound 13 could be reduced with DIBALH to the (*Z*)-hydroxy vinyl triflate 14 in moderate yield (64%) (Figure 3). Carbonylative coupling of 14 gave the α,β-butenolide 18 in 71% yield (entry 7, Table I).

In summary, hydroxy vinyl triflates can be generated readily from β-keto esters and can be converted to α,β-butenolides in good yield via a palladium-catalyzed, carbonylative coupling.

Experimental Section

Solvents were purified by standard procedures with all reactions conducted under nitrogen unless otherwise stated. All organic extracts were dried over magnesium sulfate. TLC analysis of reaction mixtures were performed on aluminum-backed plates of Kieselgel 60_{F254} silica and were visualized with an ethanol solution of 5% phosphomolybdic acid; column chromatography was carried out on Merck silica gel 60_{PF254}. ^1H and ^{13}C NMR spectra were recorded on a Bruker ACP 300 spectrometer in $CDCl_3$ unless otherwise stated.

The following compounds were prepared by literature procedures: ethyl 2-[[(trifluoromethyl)sulfonyl]oxy]-1-cyclopentene-1-carboxylate;[6] 1-(hydroxymethyl)-2-[[(trifluoromethyl)-sulfonyl]oxy]-1-cyclopentene (1);[5] ethyl 2[[(trifluoromethyl)-sulfonyl]oxy]benzoate;[7] 2-[[(trifluoromethyl)sulfonyl]oxy]benzyl alcohol;[8] ethyl 2-[[(trifluoromethyl)sulfonyl]oxy]-1-cyclohexene-1-carboxylate;[9] ethyl 1-oxo-2-cycloheptanecarboxylate;[10] ethyl 1-oxo-2-cycooctanecarboxylate;[10] tetrakis(triphenylphosphine) palladium(0), $Pd(PPh_3)_4$.[11]

Ethyl 2-[[(Trifluoromethyl)sulfonyl]oxy]-1-cycloheptene-1-carboxylate. Ethyl 1-oxo-2-cycloheptanecarboxylate (8.0 g, 44 mmol) was dissolved in dry dichloromethane (100 mL) and cooled to −78 °C. *N,N*-Diisopropylethylamine (38 mL) was added and the mixture allowed to stir for 10 min. Tf_2O (8.8 mL, 52.4 mmol) was added dropwise followed by slow warming to room temperature overnight. The mixture was washed with water (150 mL) and 10% citric acid solution (2 × 150 mL) and dried and the solvent removed under reduced pressure. The resultant red-brown oil was distilled (69–70 °C/0.06 mm) to yield a light yellow oil (10.6 g, 77%): IR (neat) 2930, 1725, 1655, 1210, 1005 cm^{-1}; ^1H NMR 1.32 (t, 3 H, J = 7.0 Hz, CH_3), 1.66–1.78 (m, 6 H, CH_2), 2.55 (m, 4 H, $CH_2C{=}C$), 4.26 (q, 2 H, J = 7.1 Hz, OCH_2);

(6) Lipschutz, B. H.; Reuter, D. C.; Ellsworth, E. L. *J. Org. Chem.* **1989**, *54*, 4975.
(7) Beyl, V.; Niederprum, H.; Voss, P. *Justus Liebig Ann. Chem.* **1970**, *731*, 58.
(8) Echavarren, A. M.; Stille, J. K. *J. Am. Chem. Soc.* **1988**, *110*, 1557.
(9) Hatanaka, Y.; Ebina, Y.; Hiyama, T. *J. Am. Chem. Soc.* **1991**, *113*, 7075.
(10) Krapcho, A. P.; Diamanti, J.; Cayen, C.; Bingham, R. *Org. Synth.* **1967**, *47*, 20.
(11) Coulson, D. R. *Inorg. Synth.* **1972**, *13*, 121.

^{13}C NMR 13.9, 23.8, 25.3, 28.1, 30.6, 33.7, 61.6, 118.4 (q, J = 324.5 Hz), 128.3, 154.5, 165.8; MS m/z 316 (M^+), 271, 167, 138 (100); HRMS calcd for $C_{11}H_{15}F_3O_5S$ 316.0592, found 316.0601. Anal. Calcd for $C_{11}H_{15}F_3O_5S$: C,41.77; H,4.78. Found: C,41.43; H,4.95.

1-(Hydroxymethyl)-2-[[(trifluoromethyl)sulfonyl]oxy]-1-cycloheptene (3). To a THF (50 mL) solution of ethyl 2-[[(trifluoromethyl)sulfonyl]oxy]-1-cycloheptene-1-carboxylate (2.5 g, 7.9 mmol) at −78 °C was added dropwise DIBALH (3.1 mL, 17.3 mmol). The solution was warmed slowly to room temperature over 2 h and the solvent removed under reduced pressure. The residue was dissolved in dichloromethane (100 mL), washed with water (2 × 100 mL), and dried and the solvent removed under reduced pressure. The residue was purified by flash chromatography (hexanes/ethyl acetate; 4:1) to give the title compound as a yellow oil (1.92 g, 89%). A small sample was distilled by Kugelrohr (85–90 °C/0.03 mm) to give a colorless oil: IR (neat) 3350, 2930, 1690, 1415, 1215, 1140 cm^{-1}; ^1H NMR 1.63–1.76 (m, 6 H, CH_2), 2.36 (m, 2 H, $CH_2C{=}C$), 2.53 (m, 2 H, $CH_2C{=}C$), 4.17 (m, 2 H, CH_2OH); ^{13}C NMR 24.4, 25.6, 28.4, 30.5, 32.8, 61.2, 118.3 (q, J = 317 Hz), 134.9, 147.5; MS m/z 274 (M^+), 256, 141, 123, 95 (100); HRMS calcd for $C_9H_{13}F_3O_4S$ 274.0487, found 274.0496. Anal. Calcd for $C_9H_{13}F_3O_4S$: C,39.42; H,4.78. Found: C,39.40; H,5.03.

1-(Hydroxymethyl)-2-[[(trifluoromethyl)sulfonyl]oxy]-1-cyclohexene (2). This compound was prepared in an analogous manner to that described for **3**, yielding a colorless oil (0.86 g, 79%). A sample was distilled by Kugelrohr (60–70 °C/0.02 mm): IR (neat) 3370, 2940, 1735, 1660, 1415, 1215, 1140 cm^{-1}; ^1H NMR 1.62–1.81 (m, 4 H, CH_2), 2.34 (m, 4 H, $CH_2C{=}C$), 4.20 (m, 2 H, OCH_2); ^{13}C NMR 21.3, 22.8, 26.1, 27.5, 59.4, 118.2 (q, J = 317 Hz), 129.8, 143.9; MS m/z 260 (M^+), 243 (100); HRMS calcd for $C_8H_{11}F_3O_4S$ 260.0330, found 260.0332. Anal. Calcd for $C_8H_{11}F_3O_4S$: C,36.92; H,4.26. Found: C,36.85; H, 4.33.

Ethyl 2-[[(Trifluoromethyl)sulfonyl]oxy]-1-cyclooctene-1-carboxylate. To ethyl 1-oxo-2-cyclooctanecarboxylate (5.0 g, 25.2 mmol) in dichloromethane (70 mL) at −78 °C was added *N,N*-diisopropylethylamine (22.0 mL, 126.1 mmol). The reaction was stirred for 10 min, followed by the addition of Tf_2O (5.1 mL, 30.3 mmol) and warming to room temperature overnight. GLC analysis of the mixture indicated that starting material was still present, so an additional 2 equiv of Tf_2O (8.0 mL) and *N,N*-diisopropylethylamine (10 mL) were added, and the mixture was stirred for an additional 48 h. At this point all the starting material was consumed, the mixture was washed with water (100 mL) and a 10% citric acid solution (2 × 100 mL) and dried and the solvent removed under reduced pressure. The resultant red/black oil was distilled (70–71 °C/0.03 mm) to give a light yellow oil (7.89 g, 95%): IR (neat) 2930, 1730, 1580, 1425, 1215, 1135, 950 cm^{-1}; ^1H NMR 1.33 (t, 3 H, J = 7.1 Hz, CH_3), 1.57 (m, 4 H, CH_2), 1.76 (m, 4 H, CH_2), 2.50 (m, 4 H, $CH_2C{=}C$), 4.28 (q, 2 H, J = 6.9 Hz, OCH_2); ^{13}C NMR 13.8, 25.4, 26.0, 27.8, 28.3, 29.4, 30.9, 61.5, 118.3 (q, J = 317 Hz), 125.5, 151.5, 152.1; MS m/z 331 ($M + 1$)$^+$, 285, 151 (100); HRMS calcd for $C_{12}H_{18}F_3O_5S$ ($M + 1$) 331.0827, found 331.0832. Anal. Calcd for $C_{12}H_{17}F_3O_5S$: C,43.63; H,5.19. Found: C,43.69; H,5.28.

1-(Hydroxymethyl)-2-[[(trifluoromethyl)sulfonyl]oxy]-1-cyclooctene (4). This compound was prepared in an analogous manner to that described for **3**, yielding a yellow oil (2.09 g, 68%). A sample was distilled by Kugelrohr (105–110 °C/0.02 mm); IR (neat) 3365, 2930, 1690, 1410, 1220, 1140, 920 cm^{-1}; ^1H NMR 1.53–1.70 (m, 8 H, CH_2), 2.37 (m, 2 H, $CH_2C{=}C$), 2.50 (m, 2 H, $CH_2C{=}C$), 4.21 (m, 2 H, OCH_2); ^{13}C NMR 25.8, 26.0, 27.8, 28.0, 29.1, 29.8, 59.5, 118.4 (q, J = 324.5 Hz), 132.1, 145.3; MS m/z 288 (M^+), 155, 95, 67 (100); HRMS calcd for $C_{10}H_{15}F_3O_4S$ 288.0643, found 288.0634. Anal. Calcd for $C_{10}H_{15}F_3O_4S$: C,41.66; H,5.24. Found: C,41.76; H, 5.44.

3,4,5,6-Tetrahydro-1*H*-cyclopenta[*c*]furan-1-one (5).[12] Carbon monoxide was bubbled through a solution of **1** (0.30 g, 1.22 mmol), $Pd(PPh_3)_4$, 0.122 mmol), tri-*n*-butylamine (0.58 mL, 2.44 mmol), and lithium chloride (0.052 g, 1.22 mmol) in acetonitrile (40 mL) for 20 min. The mixture was heated at 65 °C under 1 atmosphere of carbon monoxide (balloon placed over the reflux condenser) for 12 h. Diethyl ether (20 mL) was added to the cooled solution, the mixture filtered through a pad of Celite, and the pad rinsed with diethyl ether (2 × 10 mL). The solvent was removed under reduced pressure, and the residue was dissolved in dichloromethane and purified by flash chromatography (hexanes/ethyl acetate, 7:3) to give the title product as reddish crystals. Recrystallization from hexane/benzene gave oblong, translucent crystals (83%): mp 48–49 °C [lit.[12] mp 48–49 °C]; IR (CH_2Cl_2) 2925, 1750, 1660, 1380, 1040 cm^{-1}; ^1H NMR 2.43–2.54 (m, 4 H, CH_2), 2.62–2.69 (m, 2 H, $CH_2C{=}C$), 4.79 (m, 2 H, OCH_2); ^{13}C NMR 24.8, 28.7, 29.1, 69.2, 137.2, 170.0, 174.2; Ms m/z 125 ($M + 1$)$^+$, 124, 95 (100).

Tetrahydro-1(3*H*)-isobenzofuranone (6).[13] This compound was prepared in an analogous manner to that described for **5** using the hydroxy vinyl triflate **2**. Flash chromatography (hexanes/ethyl acetate, 9:1) gave the title product as a red/brown solid. Recrystallization from chloroform/hexanes gave oblong, translucent crystals (75%): mp 53–54 °C [lit.[13] mp 53–54 °C]; IR (CH_2Cl_2) 1750, 1690 cm^{-1}; ^1H NMR 1.67 (m, 4 H, CH_2), 2.10–2.14 (m, 2 H, $CH_2C{=}C$), 2.24 (m, 2 H, $CH_2C{=}C$), 4.60 (s, 2 H, OCH_2); ^{13}C NMR 19.8, 21.3, 21.5, 23.5, 72.0, 126.2, 161.0, 174.3; MS m/z 139 ($M + 1$)$^+$, 138, 109 (100).

3,4,5,6,7,8-Hexahydro-1*H*-cyclohepta[*c*]furan-1-one (7).[14] This compound was prepared in an analogous manner to that described for **5** using hydroxy vinyl triflate **3**. Flash chromatography (hexanes/ethyl acetate, 9:1) gave the titled product as a colorless oil (95%): IR (neat) 2925, 1755, 1675, 1450, 1030, 890 cm^{-1}; ^1H NMR 1.59–1.86 (m, 6 H, CH_2), 2.41 (m, 4 H, $CH_2C{=}C$), 4.60 (s, 2 H, OCH_2); ^{13}C NMR 25.0, 26.8, 26.9, 28.5, 30.6, 71.6, 128.8, 146.0, 162.5; MS m/z 152 (M^+), 123, 86, 84, 49 (100); HRMS calcd for $C_9H_{12}O_2$ 152.0837, found 152.0832.

1,3,4,5,6,7,8,9-Octahydrocycloocta[*c*]furan-1-one (8).[15] This compound was prepared in an analogous manner to that described for **5** using hydroxy vinyl triflate **4**. Flash chromatography (hexanes/ethyl acetate, 9:1) gave the titled product as a colorless oil (81%): IR (neat) 2930, 1745, 1670, 1455, 1020 cm^{-1}; ^1H NMR 1.47–1.60 (m, 4 H, CH_2), 1.68 (m, 2 H, CH_2), 1.84 (m, 2 H, CH_2), 2.49 (m, 4 H, $CH_2C{=}C$), 4.63 (s, 2 H, OCH_2); ^{13}C NMR 22.9, 26.1, 26.7, 26.8, 27.3, 27.7, 72.3, 127.6, 150.0, 162.3; MS m/z 166 (M^+), 137(100); HRMS calcd for $C_{10}H_{14}O_2$ 166.0994, found 166.0998.

1(3*H*)-Isobenzofuranone (10).[16] This compound was prepared in an analogous manner to that described for **5** using 2-[[(trifluoromethyl)sulfonyl]oxy]benzyl alcohol (**9**). Flash chromatography (hexanes/ethyl acetate, 19:1) gave the titled product (60%): IR (CH_2Cl_2) 1740, 1040, 995 cm^{-1}; ^1H NMR 5.34 (s, 2 H, OCH_2), 7.30–8.00 (m, 4 H); ^{13}C NMR 69.7, 125.8, 128.7, 129.1, 129.4, 130.0, 134.0, 160.1; MS m/z 134 (M^+), 105 (100); HRMS calcd for $C_8H_6O_2$ 134.0368, found 134.0377.

Ethyl (*Z*)-3-[[(Trifluoromethyl)sulfonyl]oxy]-2-butenoate (11).[5] A solution of ethyl acetoacetate (0.60 g, 4.61 mmol) in THF (10 mL) was added to KHMDS (11.1 mL, 5.53 mmol, 0.5 M in toluene) at −78 °C. While at −78 °C Tf_2NPh (1.98 g, 5.53 mmol) was added, and the mixture was allowed to warm to room temperature overnight. The mixture was washed with water (50 mL) and a 10% citric acid solution (2 × 50 mL) and dried and the solvent removed under reduced pressure. The residue was purified by flash chromatography (hexanes/ethyl acetate, 19:1) and gave the titled compound as a clear, light yellow oil (0.92 g, 76%): IR (neat) 2990, 1735, 1690, 1430, 1200, 1140, 930 cm^{-1}; ^1H NMR 1.30 (t, 3 H, J = 7.1 Hz, CH_2CH_3), 2.18 (s, 3 H, CH_3), 4.25 (q, 2 H, J = 7.0 Hz, OCH_2), 5.77 (m, 1 H, C=CH); ^{13}C NMR 13.8, 20.7, 61.1, 112.7, 118.2 (q, J = 317 Hz), 155.1, 162.2. MS m/z 262 (M^+), 234, 217, 153, 87, 69 (100); HRMS calcd for $C_7H_9F_3O_5S$ 262.0123, found 262.0112.

(*Z*)-3-[[(Trifluoromethyl)sulfonyl]oxy]-2-buten-1-ol (12). This compound was prepared in an analogous manner to that described for **3**. Flash chromatography (hexanes/ethyl acetate, 20:3) gave the titled product as a colorless oil (72%). A small sample was distilled by Kugelrohr (50–55 °C/0.03 mm): IR (neat) 3360, 2930, 1705, 1420, 1215, 1150, 1020, 955 cm^{-1}; ^1H NMR 2.10 (s, 3 H, CH_3), 4.27 (brs, 2 H, OCH_2), 5.55 (m, 1 H, C=CH); ^{13}C NMR 19.5, 56.5, 118.3 (q, J = 324.5 Hz), 120.9, 146.1; MS m/z

(12) Perotti, E.; Palladino, N.; Greco, M.; De Maldie, M. *Ann. Chim. (Rome)* **1966**, *56*, 1358.

(13) Butina, D.; Sondheimer, F. *Synthesis* **1980**, 543.
(14) Proctor, G. R. *J. Chem. Soc.* **1964**, 4274.
(15) Karim, M. R.; Sampson, P. *Tetrahedron Lett.* **1988**, *29*, 6897.
(16) Gardner, J. H.; Naylor, C. A. *Org. Synth.* **1950**, *2*, 526.

220 (M^+), 202, 121, 95, 87, 71, 69 (100); HRMS calcd for $C_5H_7F_3O_4S$ 219.9897, found 220.0023. Anal. Calcd for $C_5H_7F_3O_4S$: C,27.28; H,3.15. Found: C,26.95; H,3.34.

Ethyl (*Z*)-2-Benzyl-3-[[(trifluoromethyl)sulfonyl]oxy]-2-butenoate (13).[17] This compound was prepared in an analogous manner to that described for 11. Flash chromatography (hexanes/ethyl acetate, 19:1) gave the titled product as a pale yellow oil (12%) in addition to the *E* isomer: IR (neat) 2985, 1725, 1665, 1605, 1500, 1420, 1215, 1060, 955 cm^{-1}; ^1H NMR 1.21 (t, 3 H, J = 7.2 Hz, CH_2CH_3), 2.20 (s, 3 H, CH_3), 3.74 (s, 2 H, CH_2Ph), 4.20 (q, 2 H, J = 7.2 Hz, OCH_2), 7.27 (m, 5 H, Ph); ^{13}C NMR 13.7, 17.8, 34.9, 61.7, 118.3 (q, J = 324.5 Hz), 126.8, 128.0, 128.4, 128.6, 136.7, 149.1, 164.8; MS m/z 307 $(M - OEt)^+$, 219, 178, 173, 147, 131, 104 (100); HRMS calcd for $C_{12}H_{10}F_3O_4S$ (M – OEt) 307.0252, found 307.0241.

(*Z*)-2-Benzyl-3-[[(trifluoromethyl)sulfonyl]oxy]-2-buten-1-ol (14). This compound was prepared in an analogous manner to that described for 3. Flash chromatography (hexanes/ethyl acetate, 19:1) gave the title product as a colorless oil (81%). A small sample was distilled by Kugelrohr (105–110 °C/0.04 mm): IR (neat) 3385, 1690, 1605, 1500, 1410, 1210, 1015 cm^{-1}; ^1H NMR 2.21 (s, 3 H, CH_3), 3.62 (s, 2 H, CH_2Ph), 4.18 (m, 2 H, OCH_2), 7.26 (m, 5 H, Ph); ^{13}C NMR 16.8, 34.1, 58.4, 118.3 (q, J = 317 Hz), 126.7, 128.7, 131.1, 137.3, 142.9; MS m/z 310 (M^+), 219, 205, 177, 159, 142, 117, 91 (100); HRMS calcd for $C_{12}H_{13}F_3O_4S$ 310.0487, found 310.0502. Anal. Calcd for $C_{12}H_{13}F_3O_4S$: C,46.45; H,4.22. Found: C,46.31; H, 4.57.

Ethyl (*E*)-2-Benzyl-3-[[(trifluoromethyl)sulfonyl]oxy]-2-butenoate (15).[17] This compound was prepared in an analogous manner to that described for ethyl 2-[[(trifluoromethyl)-sulfonyl]oxy]-1-cycoheptane-1-carboxylate. Flash chromatography (hexanes/ethyl acetate, 19:1) gave the title product as a pale yellow oil (64%): ^1H NMR 1.15 (t, 3 H, J = 7.2 Hz, CH_2CH_3), 2.47 (s, 3 H, CH_3), 3.81 (s, 2 H, CH_2Ph), 4.13 (q, 2 H, J = 7.2 Hz, OCH_2), 7.24 (m, 5 H, Ph); ^{13}C NMR 13.8, 18.9, 33.7, 61.5, 118.2 (q, J = 317 Hz), 126.3, 126.7, 128.0, 128.5, 137.2, 153.7, 165.8. All other spectral and analytical data were identical to 13.

(*E*)-2-Benzyl-3-[[(trifluoromethyl)sulfonyl]oxy]-2-buten-1-ol (16). This compound was prepared in an analogous manner to that described for 3. Flash chromatography (hexanes/ethyl acetate, 19:1) gave the title product as a colorless oil (50%): ^1H NMR 2.21 (s, 3 H, CH_3), 3.68 (s, 2 H, CH_2Ph), 4.08 (m, 2 H, OCH_2), 7.31 (m, 5 H, Ph); ^{13}C NMR 16.6, 34.0, 60.0, 118.3 (q, J = 324.5 Hz), 126.8, 128.7, 128.9, 130.5, 137.3, 144.2. All other spectral and analytical data were identical to 14.

3-Methyl-2(5*H*)-furanone (17).[18] This compound was prepared in an analogous manner to that described for 5 using the hydroxy vinyl triflate 12. Upon workup this compound was not subjected to flash chromatography but distilled (55–60 °C/2 mm) [lit.[18] 82 °C/7 mm] to give the title product as a colorless oil (75%): IR (neat) 2960, 1750, 1655, 1260, 1090, 800 cm^{-1}; ^1H NMR 1.89 (m, 3 H, CH_3), 4.74 (m, 2 H, OCH_2), 7.09 (m, 1 H, CH=C); ^{13}C NMR 10.7, 70.0, 129.9, 144.9, 174.8; MS m/z 99 $(M + 1)^+$, 98, 69, 57 (100); HRMS calcd for $C_5H_6O_2$ 98.0368, found 98.0370.

3-Methyl-4-benzyl-2(5*H*)-furanone (18). This compound was prepared in an analogous manner to that described for 5 using the hydroxy vinyl triflate 14. Upon workup this compound was not subjected to flash chromatography but distilled by Kugelrohr (150–160 °C/0.04 mm) to give the title product as a pale yellow oil (71%): IR (neat) 2925, 1745, 1680, 1600, 1500, 1455, 1335, 1080, 1030, 755, 705 cm^{-1}; ^1H NMR 1.93 (s, 3 H, CH_3), 3.74 (s, 2 H, CH_2Ph), 4.56 (s, 2 H, OCH_2), 7.13–7.37 (m, 5 H, Ph); ^{13}C NMR 8.5, 33.3, 71.2, 127.1, 128.3, 128.9, 131.8, 136.1, 158.4, 175.2; MS m/z 188 (M^+), 142, 110, 91 (100); HRMS calcd for $C_{12}H_{12}O_2$ 188.0837, found 188.0847. Anal. Calcd for $C_{12}H_{12}O_2$: C,76.57; H,6.43. Found: C,76.92; H, 6.45.

Methyl (*E*)-2-Methyl-3-benzyl-2-buten-1-ol (19). Carbon monoxide was bubbled through a solution of 16 (0.15 g, 0.48 mmol), $Pd(PPh_3)_4$ (0.056 g, 0.048 mmol), tri-*n*-butylamine (0.23 mL, 0.96 mmol), lithium chloride (0.021 g, 0.48 mmol), and methanol (0.1 mL, 2.42 mmol) in acetonitrile (20 mL) for 20 min. The mixture was heated to 65 °C under 1 atmosphere of carbon monoxide. Workup as described for 5 gave the titled compound as a yellow oil (0.025 g, 23%): IR (neat) 3410, 2950, 1715, 1655, 1600, 1495, 1435, 1235, 1165, 1010, 740, 700 cm^{-1}; ^1H NMR 1.99 (s, 3 H, CH_3), 3.77 (s, 3 H, OCH_3), 3.80 (s, 2 H, CH_2Ph), 4.14 (s, 2 H, OCH_2), 7.17–7.31 (m, 5 H, Ph); ^{13}C NMR 15.4, 37.4, 51.8, 61.3, 126.3, 127.1, 128.6, 128.9, 139.0, 143.9, 170.2; MS m/z 202 $(M - H_2O)^+$, 186, 159, 143 (100); HRMS calcd for $C_{13}H_{14}O_2$ (M – H_2O) 202.0994, found 202.0977. Anal. Calcd for $C_{13}H_{16}O_3$: C,70.89; H,7.32. Found: C,70.62; H, 7.52.

Registry No. 1, 122948-55-4; 2, 144242-01-3; 3, 144242-02-4; 4, 144242-03-5; 5, 14668-64-5; 6, 66309-76-0; 7, 935-90-0; 8, 99172-53-9; 9, 112533-09-2; 10, 87-41-2; 11, 122135-84-6; 12, 144242-04-6; 13, 143564-88-9; 14, 144242-05-7; 15, 134405-93-9; 16, 144242-06-8; 17, 22122-36-7; 18, 144242-07-9; 19, 144242-08-0; ethyl 2-[[(trifluoromethyl)sulfonyl]oxy]-1-cyclopentene-1-carboxylate, 122539-74-6; ethyl 2-[[(trifluoromethyl)sulfonyl]-oxy]-1-cyclohexene-1-carboxylate, 122135-83-5; ethyl 2-[[(trifluoromethyl)sulfonyl]oxy]-1-cycloheptene-1-carboxylate, 144242-09-1; ethyl 2-[[(trifluoromethyl)sulfonyl]oxy]-1-cyclooctene-1-carboxylate, 144242-10-4; ethyl 1-oxo-2-cyclopentanecarboxylate, 611-10-9; ethyl 1-oxo-2-cyclohexanecarboxylate, 1655-07-8; ethyl 1-oxo-2-cycloheptanecarboxylate, 774-05-0; ethyl 1-oxo-2-cyclooctanecarboxylate, 4017-56-5; ethyl acetoacetate, 141-97-9; ethyl α-benzylacetoacetate, 620-79-1.

(17) Finkelstein, J. A.; Weinstock, J.; Keenan, R. M. Eur. Pat. App. EP 90-306203, 1990.
(18) Houff, W. H.; Sell, H. M. *J. Am. Chem. Soc.* **1952**, *74*, 3183.

Novel Synthetic Route to Benzopolyazamacrocycles. Synthesis of 16-Membered Tetrabenzotetraazamacrocyles via Bisquinazolinone Annelation and Reductive Ring Enlargement[1]

Shoji Eguchi,* Yuji Matsushita, and Hisato Takeuchi

Institute of Applied Organic Chemistry, Faculty of Engineering, Nagoya University, Furo-cho, Chikusa-ku, Nagoya 464-01, Japan

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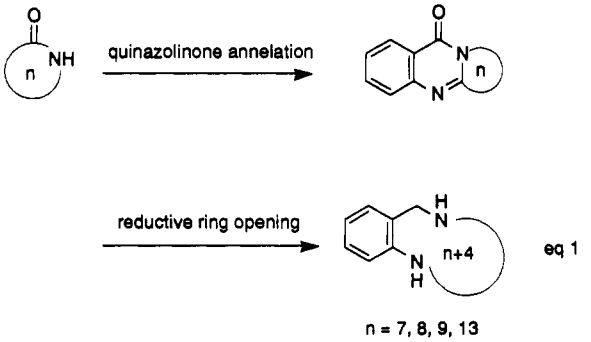
Recently we reported a new synthesis of benzoannelated macrocyclic 1,4-diamines via quinazolinone annelation of lactams, followed by reductive ring enlargement (eq 1).[2,3]



Polyazamacrocycles have drawn continued interest because of their utility as ligands as well as their ability to mimic enzyme functions.[4,5] As an application of our metho-

(1) Synthesis of Novel Carbo- and Heteropolycycles. 22. For part 21, see: Eguchi, S.; Yamashita, K.; Matsushita, Y. *Synlett.* **1992**, 295.
(2) Takeuchi, H.; Matsushita, Y.; Eguchi, S. *J. Org. Chem.* **1991**, *56*, 1535.
(3) For a recent review on ring enlargement, see: Hesse, M. *Ring Enlargement in Organic Chemistry*; VCH: Weinheim, 1991.

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