in benzene in the presence of small amounts of pyridine to afford dithiosalicylyl chlorides, which were treated with Cl_2 in CCl_4 to give *o*-(chlorosulfenyl)benzoyl chlorides. A CCl_4 solution of an *o*-(chlorosulfenyl)benzoyl chloride was added to an aqueous ammonia (28%) solution with vigorous stirring. The products were purified by vacuum sublimation, followed by crystallization from methanol or methanol–water: 1,2-Benzisothiazolin-3-one (**1a**), mp 158–159 °C (lit.[12] mp 158 °C): 5-chloro-1,2-benzisothiazolin-3-one (**1b**), mp 265–267 °C (lit.[12] mp 265–266 °C); 6-chloro-1,2-benzisothiazolin-3-one (**1c**), mp 276–278 °C (lit.[12] mp 271–273 °C).

^{17}O-Enriched 1,2-Benzisothiazolin-3-one. Freshly crystallized (benzene) dithiosalicylyl chloride (700 mg) was dissolved in a THF (2 mL)–$H_2{}^{17}O$ (20.5 atom % of ^{17}O; purchased from Japan Radioisotope Association) (1 mL) solution, and the resultant homogeneous solution was stirred at room temperature for 2 days under a nitrogen atmosphere. The homogeneous reaction mixture was then completely evaporated to dryness in vacuo to afford a gray powder (600 mg); its IR spectrum agreed completely with that of an authentic dithiosalicylic acid.

The ^{17}O-enriched dithiosalicylic acid was converted to ^{17}O-enriched 1,2-benzisothiazolin-3-one by the procedure described above. Vacuum sublimation, followed by crystallization (methanol–water), gave colorless prisms with mp 159–160 °C. The ^{17}O atom % of this compound was determined by the mass spectrum to be 9.5%.

^{33}S-Enriched 1,2-Benzisothiazolin-3-one. ^{33}S-Enriched dithiosalicylic acid was prepared from 302 mg (2.2 mmol) of *o*-aminobenzoic acid by using 75 mg (2.3 mmol) of ^{33}S-enriched sulfur (17.5 atom % of ^{33}S; purchased from Japan Radioisotope Association) according to the reported procedure.[10] The ^{33}S-enriched dithiosalicylic acid was converted to ^{33}S-enriched 1,2-benzisothiazolin-3-one by the procedure described above. Vacuum sublimation, followed by crystallization (methanol–water), gave colorless prisms with mp 158–159 °C. The ^{33}S atom % of this compound was determined by the mass spectrum to be 7.6%.

ESR Measurements. ESR spectra were recorded on a JEOL JES-FE-2XG spectrometer equipped with an X-band microwave unit and 100-kHz field modulation. All solutions used for ESR experiments were carefully degassed by three freeze–pump–thaw cycles using a high vacuum system. Photolysis was carried out using a 1-kW xenon lamp. Hyperfine splitting constants and g values were determined by a comparison with Fremy's salt in K_2CO_2 aqueous solution (a_N, 13.09 G; g = 2.0057). Estimated accuracy: a_N and a_H, ±0.1 G; $a_{^{17}O}$ and $a_{^{33}S}$, ±0.2 G; g, ±0.0002.

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Registry No. **1a**, 2634-33-5; **1b**, 4337-43-3; **1c**, 70-10-0; **2a**, 114378-36-8; **2a**(O^{17}), 114378-39-1; **2a**(S^{33}), 114394-80-8; **2b**, 114378-37-9; **2c**, 114378-38-0.

Supplementary Material Available: Figures of ESR spectra of **2a** and ^{17}O-enriched **2a** radicals (2 pages). Ordering information is given on any current masthead page.

Solvolyses of 1-Adamantyl Triflate and Tresylate and 2-Adamantyl Tresylate: Y_{OTr} Scale and Relative Nucleofugalities of Various Leaving Groups Based on 1-Adamantyl Ethanolysis

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Introduction

The mY relationship (eq 1) has made a major contribution in the mechanistic studies of solvolytic reactions.[1]

$$\log (k/k_o)_{RX} = mY \tag{1}$$

In the pioneering work by Grunwald and Winstein the solvent ionizing power (Y) of a given solvent was determined from the first-order rate constant of *tert*-butyl chloride (RX) in that solvent (k) and that in 80% ethanol (k_o) at 25.0 °C, with m = 1.000 for *tert*-butyl chloride by definition.[2] The original Y values have been examined for various substrates and solvents. The finding that 1-adamantyl and 2-adamantyl systems are more suitable than the *tert*-butyl system to define the Y values led to the determination of Y_{Cl},[3] Y_{Br},[3] Y_I,[4] Y_{OTs},[5,6] Y_{OTf},[7,8] Y_{OClO3},[6,8] and Y_{Pic} (picrate)[6,8] values based on 1- or 2-adamantyl system. The Y_{OTf} values have also been determined based on the solvolysis of 7-norbornyl triflate.[9] Considering the variety of "standard" substrates proposed by different authors, it is advised to express the Y values in the form of Y_{RX} (RX; substrate) with m = 1.000 in eq 1 (eq 2).[10]

$$\log (k/k_o)_{RX} = Y_{RX} \tag{2}$$

Meanwhile, it has been found that the correlation between $Y_{2\text{-AdOTf}}$ and $Y_{2\text{-AdOTs}}$ values is poor and the points for aqueous acetone, carboxylic acids, and fluorinated alcohols considerably deviate from the aqueous ethanol–aqueous methanol line.[7-9] 2-AdOTf is more reactive in aqueous acetone and less reactive in carboxylic acids and fluorinated alcohols than expected from $Y_{2\text{-AdOTs}}$ values.[7-9]

The 2,2,2-trifluoroethanesulfonate (tresylate) anion was first reported by Crossland, Wells, and Shiner as a useful leaving group with nucleofugality lying between triflate and tosylate.[11a] Despite such characteristics, only a few tresylates have been subjected to solvolytic studies.[11,12] In the course of our study on the evaluation of stability of α-keto cations on the basis of the bridgehead reactivity in the solvolysis of various bicyclic and tricyclic compounds containing the oxo substituent on a vicinal carbon,[13] we required the Y_{OTr} values in order to examine the S_N1 character of the solvolysis. Consequently, we determined the $Y_{1\text{-AdOTr}}$ and $Y_{2\text{-AdOTr}}$ values and compared these values with $Y_{1\text{-AdOTs}}$,[6] $Y_{1\text{-AdOMs}}$, $Y_{2\text{-AdOTs}}$,[5] and $Y_{2\text{-AdOTf}}$[7,8] values. We also wished to obtain the conversion factors for the rate of ethanolysis at 25 °C of bridgehead substrates covering from chloride to triflate based on the 1-adamantyl system as a single system. Previously, the conversion factors have been determined by combining the reactivities of two[8] or

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Table I. Rates of Solvolysis of 1-AdOTr and 2-AdOTr and Y Values for Various Sulfonate Leaving Groups at 25.0 °C

	k_1, s^{-1}		$Y_{\text{1-AdX}}$, X			$Y_{\text{2-AdX}}$, X		
solv[a]	1-AdOTr	2-AdOTr	OTr	OTs[p]	OMs[t]	OTr	OTs[y]	OTf
100E	3.60×10^{-3} [d,f]	4.95×10^{-8} [e,j]	−2.063	−1.962	−2.224[e,o,u]	−1.798	−1.75	−1.756[aa]
80E	4.16×10^{-1} [d,q]	3.11×10^{-6} [e]	0.000	0.000	0.000	0.000	0.000	0.000
60E	6.2[d,h]	2.78×10^{-5} [e]	1.173	1.020[d,o,q]	1.132	0.951	0.92	0.948[cc]
50E		7.92×10^{-5} [e,k]		1.574[d,o,r]	1.649	1.406	1.29	1.35[dd]
MeOH	2.88×10^{-2} [d]	2.81×10^{-7} [e,l]	−1.160	−0.924	−1.171	−1.044	−0.92	−0.878[aa] −0.79[dd]
90A	5.24×10^{-3} [d]	5.50×10^{-8} [e,m]	−1.900	−1.986	−2.258[e,o,v]	−1.752		−0.64[dd]
80A	5.41×10^{-2} [d]	3.82×10^{-7} [e]	−0.886	−0.942	−0.949[e,o,w]	−0.911	−0.927[e,o,z]	0.04[dd]
100T	33[d,i]	1.32×10^{-4} [d]	1.899	2.157[d,o,s]	1.896[d,o,x]	1.628	1.80	1.227[aa,bb]
97T		1.705×10^{-4} [n]			1.924	1.739	1.83	1.355[aa,bb] 0.95[dd]
AcOH[b]	2.71×10^{-2} [e]	3.71×10^{-7} [e]	−1.186	−0.896	−0.817	−0.923	−0.61	−1.664[aa] −2.0[dd]
HCO_2H[c]		1.37×10^{-3} [e]				2.644	3.04	1.65[dd]

[a] E, A, and T denote ethanol, acetone, and 2,2,2–trifluoroethanol, respectively. The numbers mean volume % of the organic components in aqueous mixtures except for 97T, which means 97 weight % of T. All the solvents except for AcOH and HCO_2H are buffered with 0.025 M 2,6–lutidine. [b] Buffered with 0.025 M NaOAc. [c] Buffered with 0.025 M NaOCHO. [d] Conductimetric method. [e] Titrimetric method. [f] 1.91×10^{-3} s^{-1} (20.0 °C), 2.27×10^{-2} s^{-1} (40.1 °C); $\Delta H^{\ddagger}$ 21.9 kcal/mol; $\Delta S^{\ddagger}$ 3.7 eu. [g] Extrapolated from 1.42×10^{-1} s^{-1} (15.0 °C), 7.35×10^{-2} s^{-1} (10.0 °C), 4.34×10^{-2} s^{-1} (5.0 °C); $\Delta H^{\ddagger}$ 18.2 kcal/mol; $\Delta S^{\ddagger}$ 0.9 eu. [h] Extrapolated from 3.53×10^{-1} s^{-1} (1.6 °C), 9.57×10^{-2} s^{-1} (−7.3 °C), 3.02×10^{-2} s^{-1} (−15.2 °C); $\Delta H^{\ddagger}$ 20.0 kcal/mol; $\Delta S^{\ddagger}$ 12.4 eu. [i] Extrapolated from 2.97×10^{-1} s^{-1} (−20.9 °C), 1.58×10^{-1} s^{-1} (−25.1 °C), 3.32×10^{-2} s^{-1} (−37.7 °C), 2.93×10^{-2} s^{-1} (−37.8 °C); $\Delta H^{\ddagger}$ 14.9 kcal/mol; $\Delta S^{\ddagger}$ −1.5 eu. [j] Extrapolated from 5.91×10^{-5} s^{-1} (75.0 °C);, 2.25×10^{-6} s^{-1} (50.0 °C); $\Delta H^{\ddagger}$ 28.6 kcal/mol; $\Delta S^{\ddagger}$ 4.1 eu. [k] Reported $k_1 = 8.172 \times 10^{-5}$ s^{-1} (ref 11b). [l] Extrapolated from 2.81×10^{-4} s^{-1} (75.0 °C), 1.16×10^{-5} s^{-1} (50.0 °C); $\Delta H^{\ddagger}$ 27.9 kcal/mol; $\Delta S^{\ddagger}$ 5.1 eu. [m] Extrapolated from 4.08×10^{-5} s^{-1} (75.0 °C), 1.93×10^{-6} s^{-1} (50.0 °C); $\Delta H^{\ddagger}$ 26.7 kcal/mol; $\Delta S^{\ddagger}$ −2.2 eu. [n] Reference 11b. [o] This work. [p] Reference 6. [q] Obtained from 4.22×10^{-2} s^{-1} in 60E and 4.03×10^{-3} s^{-1} in 80E (ref 6b). [r] Obtained from 1.51×10^{-1} s^{-1} in 50E and 4.03×10^{-3} s^{-1} in 80E (ref 6b). [s] Obtained from 5.78×10^{-1} s^{-1} in 100T [extrapolated from 1.71×10^{-1} s^{-1} (12.6 °C) and 5.23×10^{-2} s^{-1} (1.5 °C); $\Delta H^{\ddagger}$ 16.0 kcal/mol; $\Delta S^{\ddagger}$ −5.8 eu] and 4.03×10^{-3} s^{-1} in 80E (ref 6b). [t] Reference 16. [u] Obtained from 2.49×10^{-5} s^{-1} in 100E and 4.17×10^{-3} s^{-1} in 80E (ref 16). [v] Obtained from 2.30×10^{-5} s^{-1} in 90A and 4.17×10^{-3} s^{-1} in 80 E (ref 16). [w] Obtained from 4.69×10^{-4} s^{-1} in 80A and 4.17×10^{-3} s^{-1} in 80E (ref 16). [x] Obtained from 3.28×10^{-1} s^{-1} in 100T [extrapolated from 9.96×10^{-2} s^{-1} (12.6 °C) and 3.13×10^{-2} s^{-1} (1.5 °C); $\Delta H^{\ddagger}$ 15.7 kcal/mol; $\Delta S^{\ddagger}$ −8.2 eu] and 4.17×10^{-3} s^{-1} in 80E (ref 16). [y] Reference 5. [z] Obtained from 2.84×10^{-9} s^{-1} in 80A [extrapolated from 5.70×10^{-5} s^{-1} (100.0 °C) and 3.37×10^{-6} s^{-1} (75.0 °C); $\Delta H^{\ddagger}$ 28.6 kcal/mol; $\Delta S^{\ddagger}$ −1.7 eu] and 2.4×10^{-8} s^{-1} in 80E (ref 5). [aa] Reference 7. [bb] At −20.0 °C. [cc] Estimated from $Y_{\text{2-AdOTf}} = 1.02Y_{\text{2-AdOTs}} + 0.01$; see ref 8. [dd] Reference 8.

more[14] systems because of too wide range of nucleofugalities (OTf/Cl = ca. 10^{12}).

Results and Discussion

Synthesis. 1-Adamantyl triflate was prepared from 1-adamantyl bromide and silver triflate as described previously.[15] 1-Adamantyl tresylate was synthesized by treating 1-adamantyl bromide with silver tresylate in hexane at room temperature. This compound was stable in a hexane solution containing a small amount of 2,6-lutidine as a stabilizer and safely recrystallized from hexane. 2-Adamantyl tresylate has been described in the literature.[11b]

$Y_{\text{1-AdOTr}}$ and $Y_{\text{2-AdOTr}}$ Values. The rates of solvolysis of 1-AdOTr and 2-AdOTr at 25.0 °C were determined by titrimetric or conductimetric method in EtOH, MeOH, AcOH, TFE, aqueous ethanol, and aqueous acetone. The rate data are summarized in Table I, together with $Y_{\text{1-AdX}}$ (X = OTr, OTs, OMs) and $Y_{\text{2-AdX}}$ (X = OTr, OTs, OTf) values. Most of the $Y_{\text{1-AdOTs}}$,[6] $Y_{\text{1-AdOMs}}$,[16] $Y_{\text{2-AdOTs}}$[5] values and all of the $Y_{\text{2-AdOTf}}$ values[7,8] were taken from the literature or calculated by our hands using reported data.

First, a plot of $Y_{\text{2-AdOTr}}$ vs $Y_{\text{1-AdOTr}}$ shows a linear correlation with a slope 0.868 (r 0.998). This nicely linear correlation reinforces the previous conclusion from a plot of $Y_{\text{2-AdOTs}}$ vs $Y_{\text{1-AdOTs}}$ (slope 0.863; r 0.997) that the 2-adamantyl system undergoes limiting solvolysis.[5] Secondly, three correlations for $Y_{\text{1-AdOTr}}$ vs $Y_{\text{1-AdOTs}}$ (slope 0.986; r 0.993), $Y_{\text{1-AdOTr}}$ vs $Y_{\text{1-AdOMs}}$ (slope 0.952; r 0.991), and $Y_{\text{2-AdOTr}}$ vs $Y_{\text{2-AdOTs}}$ (Figure 1; slope 0.968; r 0.995) are all nicely linear. In contrast, a plot of $Y_{\text{2-AdOTr}}$ vs $Y_{\text{2-AdOTf}}$ shows marked deviations from the methanol–ethanol–aqueous ethanol line for acetic acid, formic acid, trifluoroethanol, and aqueous acetone (Figure 2). It is notable that mere insertion of a methylene between the sulfur and the trifluoromethyl group in the triflate completely eliminates the anomalous behavior of the triflate with respect to the response to solvent ionizing power.

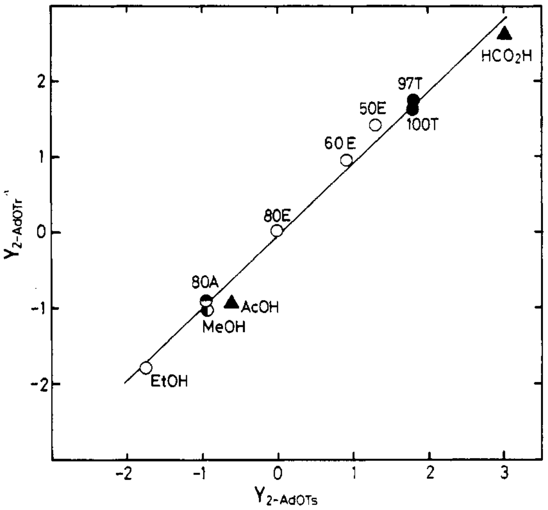

Figure 1. A plot of $Y_{\text{2-AdOTr}}$ vs $Y_{\text{2-AdOTs}}$ (slope, 0.968; r 0.995). For the rate data, see Table I and references cited therein.

Conversion Factors for Various Leaving Groups Based on 1-Adamantyl Ethanolysis. 1-Adamantyl triflate is so reactive as to abstract hydride from hexane, presumably catalyzed by a trace of triflic acid.[15] The hexane solution can be stored if a small amount of 2,6-di-*tert*-butyl-4-methylpyridine is added as a stabilizer. Despite such high reactivity, the rate of ethanolysis at 25.0 °C was determined by extrapolation from the conductimetric data at lower temperatures. The results are given in Table II.

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Table II. Rates and Relative Rates for Ethanolysis of Some Common 1-Adamantyl Substrates at 25.0 °C

	1-AdX, X						
	Cl	Br	I	OMs	OTs	OTr	OTf
k_1, s^{-1}	2.5×10^{-11} [a,b]	1×10^{-9} [a,b]	3.7×10^{-9} [b,c]	2.49×10^{-5} [d,e]	4.40×10^{-5} [f]	3.60×10^{-3} [d,g]	35.1 [d,h]
rel rate	1.0	40	1.5×10^2	1.0×10^6	1.8×10^6	1.4×10^8	1.4×10^{12}
					1.0	82	8.0×10^5

[a] Reference 3. [b] Estimated from mY relationship. [c] Reference 4. [d] This work. [e] Determined titrimetrically. [f] Reference 6b. [g] Determined conductimetrically. [h] Extrapolated from 1.41×10^{-1} s^{-1} (−19.6 °C), 6.92×10^{-2} s^{-1} (−25.0 °C), 3.36×10^{-2} s^{-1} (−29.2 °C), and 1.76×10^{-2} s^{-1} (−33.4 °C); $\Delta H^\ddagger$ 17.9 kcal/mol; $\Delta S^\ddagger$ 8.5 eu.

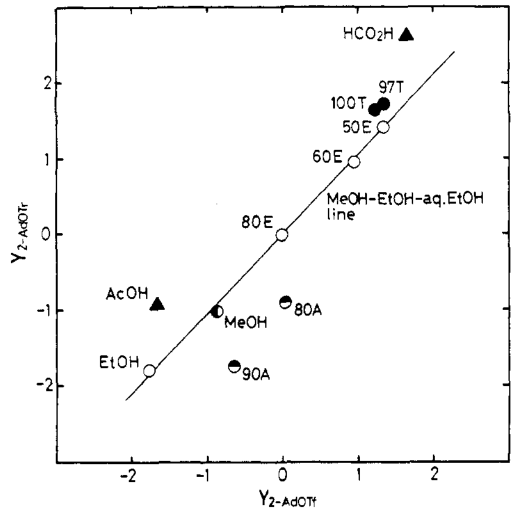

Figure 2. A plot of $Y_{\text{2-AdOTr}}$ vs $Y_{\text{2-AdOTf}}$. The slope for the MeOH–EtOH–aqueous EtOH line is 1.04 with correlation coefficient 0.999. For the rate data, see Table I and references cited therein.

The rates of ethanolysis at 25.0 °C of various 1-adamantyl substrates have been reported in the literature. In Table II are summarized the reported data for 1-adamantyl chloride, bromide, iodide, and tosylate, along with the present data for the mesylate, tresylate, and triflate. Although the rates of ethanolysis for 1-adamantyl chloride,[3] bromide,[3] and iodide[4] are estimated values from $mY_{t\text{-BuCl}}$ relations, the relative rates in Table II are the first case which covers a reactivity range of 10^{12} based on a single system solvolyzing via a typical S_N1 mechanism. It should be pointed out, however, that the relative rates of Table II should be used only for typical S_N1 ethanolysis at 25 °C, such as for bridgehead substrates. For example, a much lower OTf/OTr ratio of 4×10^2 as compared to 9.8×10^3 of the present work has been estimated.[11a] The conversion factors in the solvents other than ethanol for the leaving groups herein shown, except for tresylate, have been compiled by Bentley.[8,17]

Conclusion. The rates of solvolysis of 1- and 2-adamantyl tresylates at 25 °C were determined in ethanol, aqueous ethanol, methanol aqueous acetone, TFE, acetic acid, and formic acid. The $Y_{\text{1-AdOTr}}$ and $Y_{\text{2-AdOTr}}$ values linearly correlate with $Y_{\text{1-AdOTs}}$, $Y_{\text{1-AdOMs}}$, and $Y_{\text{2-AdOTs}}$, but deviations exist in a plot with $Y_{\text{2-AdOTf}}$. Thus, mere insertion of a methylene between the sulfur and the trifluoromethyl group in the triflate completely eliminates the anomalous behavior of the triflate with respect to the response to solvent ionizing power.

The rate of ethanolysis of 1-adamantyl triflate at 25 °C was determined and compared with the rates in ethanol of 1-adamantyl chloride, bromide, iodide, mesylate, tosylate, and tresylate. The results cover the conversion factors over a reactivity range of 10^{12} for different leaving groups attached to a bridgehead position.

Experimental Section

General Comments. Melting and boiling points are uncorrected. IR spectra were recorded on a Hitachi 215 spectrophotometer. ^{1}H NMR (60 MHz) spectra were recorded on a Hitachi R-24 spectrometer with TMS as internal standard. ^{13}C NMR (22.5 MHz) spectra were obtained on a JEOL FX90A spectrometer with the δ values being calculated on the basis of $\delta = 76.95$ for $CDCl_3$. Ethanol and methanol were refluxed over the corresponding magnesium alkoxide and distilled. Acetone and trifluoroethanol were stored over 4- and 5-Å sieves, respectively, and distilled. Acetic acid was refluxed with 3% acetic anhydride and distilled. Formic acid was dried over boric anhydride and distilled, bp 46.5–47 °C (55 mmHg). The other solvents used for syntheses were dried by standard methods as required. 2,2,2-Trifluoroethanesulfonyl chloride (tresyl chloride),[11a] 2-adamantyl tresylate,[11b] 1-adamantyl mesylate,[18] and 1-adamantyl triflate[15] were prepared by the literature methods. Aqueous ethanol and aqueous acetone of various volume percentages were prepared by mixing weighed components by using densities 0.78504, 0.78440, and 0.99705 at 25.0 °C[19] for ethanol, acetone, and water, respectively.

Silver Tresylate. To a stirred suspension of silver oxide (2.44 g, 10.5 mmol) in 20 mL of acetonitrile containing 0.18 g of added water was added tresyl chloride (1.83 g, 10.0 mmol) over 10 min with cooling in an ice bath. The ice bath was removed and then the mixture allowed to warm to room temperature. The solution containing precipitated silver chloride and small amounts of unreacted silver oxide was filtered with no. 5C filter paper. Evaporation of the solvent at a reduced pressure afforded a white solid (2.58 g), which was redissolved in ca. 3 mL of acetonitrile. Addition of 30 mL of ether at 0 °C gave a colorless oil, which was separated and stirred with 20 mL of ether to afford a white solid. The ether layer was removed and the precipitated silver tresylate washed with ether (15 mL × 2) and dried at 75–80 °C (5 mmHg) for 2 h: yield, 2.15 g (79%); ^{1}H NMR (CD_3CN) δ 3.50 (q, $J = 10.3$ Hz); IR (KBr) 3025 w, 2975 w, 1421 w, 1411 w, 1332 s, 1225 s, 1142 s, 1075 m, 1058 s, 889 w, 859 w, 799 w, 679 m cm^{-1}.

1-Adamantyl Tresylate. To silver tresylate (1.15 g, 4.23 mmol) placed in a dry flask was added a solution of 1-adamantyl bromide (0.73 g, 3.4 mmol) in 34 mL of dry hexane, and the suspension was stirred under nitrogen for 2 h. A portion of the supernatant solution was taken with a syringe and the hexane evaporated to give essentially pure 1-adamantyl tresylate as a highly hygroscopic solid. When the supernatant solution was stored in a freezer at −15 °C with added 2,6-lutidine (18 mg) as a stabilizer, 1-adamantyl tresylate crystallized as white needles. With chilling in an ice-salt bath, the mother liquor was removed with a syringe, and the crystals were washed with a small portion of dry pentane and dried in vacuo: mp 53–56 °C; ^{13}C NMR ($CDCl_3$) δ 31.5 (d), 35.1 (t), 42.6 (t), 54.7 (q, $J = 32$ Hz), 95.7 (s), 121.0 (q, $J = 278$ Hz); ^{1}H NMR (CCl_4) δ 1.67 (br s, 6 H), 2.23 (br s, 9 H), 3.72 (q, 2 H, $J = 8.3$ Hz).

Kinetic Methods. The solvolyses in ethanol, methanol, aqueous ethanol, aqueous acetone, and trifluoroethanol were conducted in the presence of 0.025 M 2,6-lutidine by the titrimetric or conductimetric method. In the titrimetric method liberated acids were titrated with 0.01 M KOH–ethanol by using bromcresol green–methyl red mixed indicator after an aliquot (1.000 or 2.000 mL) had been quenched in 10 mL acetone. Generally, the initial

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concentrations of the substrates were 0.010 or 0.020 M. In the conductimetric method 10–20 μL of a 10% solution of a substrate in dioxane, THF, or hexane, all containing 0.025 M 2,6-lutidine, was injected into a thermally equilibrated and magnetically stirred solvent (20 mL) placed in a conductivity cell (cell constant 0.1005). The temperature of the thermostat (kerosene) was maintained within ±0.05 °C during the measurement. The conductivity changes followed a good first-order kinetics. The acetolysis and formolysis were conducted in the presence of 0.0250 M sodium acetate or sodium formate, respectively, and the rates followed by titrating the unreacted base with 0.01 M $HClO_4$–acetic acid by using crystal violet as an indicator. For quenching of an aliquot, carbon tetrachloride in acetolysis and acetic acid in formolysis were used. For titrimetric runs at 25.0 °C, a pipet-out method was used, whereas for those at 50.0, 75.0, and 100.0 °C, an ampule technique was employed.

Metachromins A and B, Novel Antineoplastic Sesquiterpenoids from the Okinawan Sponge *Hippospongia* cf. *metachromia*

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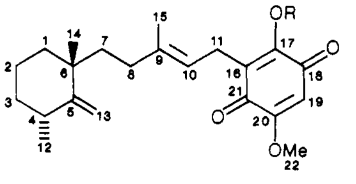
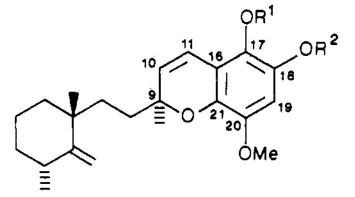
Many terpenoid quinones and phenols from marine sponges have exhibited interesting biological activities.[2] During our studies on bioactive metabolites from marine organisms,[3] we isolated a novel antineoplastic sesquiterpenoid quinone (**1**) and a chromenol (**2**), named metachromins A and B, respectively, from the Okinawan sponge *Hippospongia* cf. *metachromia*.[4] In this paper we describe the isolation and structure elucidation of **1** and **2**.

The purple-colored sponge *Hippospongia* cf. *metachromia* was collected at Okinawa Island and kept frozen until required. The methanolic extracts were partitioned between ethyl acetate and water. The ethyl acetate soluble fraction exhibiting antineoplastic activity was subjected to chromatography on Sephadex LH-20 (methanol/chloroform, 1:1) followed by a silica gel column (hexane/ethyl acetate, 4:1) to afford metachromins A (**1**, 0.42% yield, wet weight) and B (**2**, 0.024% yield) together with a known quinone compound, isospongiaquinone[5] (0.18% yield).

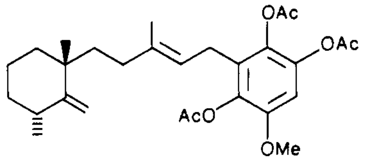
Metachromin A (**1**) was obtained as orange crystals from hexane, mp 80–82 °C. The molecular formula of **1** was determined as $C_{22}H_{30}O_4$ by HREIMS (*m/z* 358.2154, Δ +1.0 mmu). The UV (MeOH, 286 and 435 nm; MeOH + KOH, 220, 289, and 520 nm) and IR (3340, 1630, and 1590 cm^{-1}) absorptions suggested the presence of a hydroxy quinone moiety.[5,6] This was supported by formation of an acetate (**3**) on acetylation with acetic anhydride and pyridine and a leuco-triacetate (**4**) on reaction with zinc dust and acetic anhydride in the presence of pyridine. Treatment of **1** with diazomethane afforded a methyl ether (**5**).



1, R = H
3, R = Ac
5, R = Me



2, R¹ = H; R² = Me
9, R¹ = R² = Me
10, R¹ = Ac; R² = Me
11, R¹ = Me; R² = H



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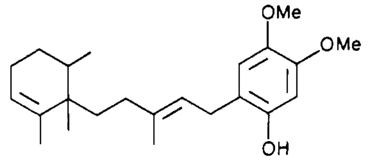
Comparison of the ^{1}H and ^{13}C NMR data of **1** with those of isospongiaquinone[5] or ilimaquinone[6] indicated that **1** possessed a 2-hydroxy-5-methoxybenzoquinone group. The ^{1}H NMR chemical shift for H-19 (δ 6.72) of the leuco-triacetate **4** implied that the substitution pattern of the benzoquinone group of **1** was the same as that of ilimaquinone.[6a] The ^{1}H and ^{13}C NMR spectra revealed that the remaining $C_{15}H_{25}$ part contained one tertiary and one secondary methyl groups and two olefins: an exomethylene and a trisubstituted double bond bearing a methyl group (δ_C 16.40 q; *E* configuration), from which the $C_{15}H_{25}$ part appeared to be a sesquiterpene having a structure similar to the sesquiterpene phenol **6** obtained from the sponge *Smenospongia echina*[7] or diterpenes such as agelasidine B or C[8] or ageline A[9,10] (**7**). The EIMS of **1** gave an intense



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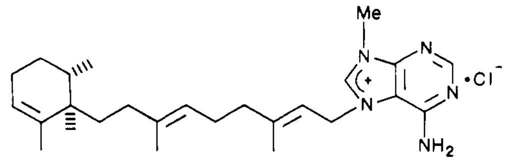

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