Hz, $-CH_3$); 1.99 (m, 1 H, H-4); 2.48 (m, 1 H, H-2); AB-part of ABX-system (δ_A 3.07, δ_B 3.12, J_{AB} = 9 Hz, J_{AX} = 5.5 Hz, J_{BX} = 6.8 Hz, 2 H, H-5); 4.04 (t, $J_{3,2} = J_{3,4}$ = 5.5 Hz, 1 H, H-3); AB-system (δ_A 4.31, δ_B 4.43, J_{AB} = 11 Hz, 2 h, OCH_2Ph), 7.19 (m, 15 H, phenyl-H), 7.47 (m, 5 H, phenyl-H), 9.74 (d, J = 1.9 Hz, CHO). ^{13}C NMR: δ 11.18 and 17.08 (2-CH_3 and 4-CH_3); 36.65 (C-4); 41.49 (C-2); 66.36 (C-5); 74.74 (-OCH_2-Ph); 83.21 (C-3); 126.90, 127.22, 127.64, 127.73, 128.10, 128.75 and 144.39 (20C, phenyl-C); 142.02 (C-1). Anal. Calcd for $C_{33}H_{34}O_3$: C, 82.64; H, 7.14. Found: C, 82.60; H, 7.31.

(4*R*,5*R*,6*S*)-Methyl 5-(Benzyloxy)-2,4,6-trimethyl-7-(trityloxy)-(*E*)-hept-2-enoate (18b). **18a** (8.40 g, 18.16 mmol) in THF (80 mL) was treated with (α-carbomethoxyethylidene)triphenylphosphorane (6.96 g, 20.0 mmol) for 24 h at 22 °C. After removal of the solvent the crude product was chromatographed (hexane/ethyl acetate, 10/1) to furnish **18b** (5.20 g, 52%) as a colorless oil, $[\alpha]^{20}_D$ +11.6° (c 2). IR (film): 3500, 3030, 3060, 2950, 1730, 1640, 1590, 1490, 1250, 1060, 910, 730, 700 cm^{-1}. ^1H NMR: δ 0.86 (d, J = 7.5 Hz, 3 H, 6-CH_3), 1.12 (d, J = 7.5 Hz, 3 H, 4-CH_3), 1.85 (s, 2 H, 2-CH_3), 1.94 (m, 1 H, H-6), 2.76 (m, 1 H, H-4); AB part of ABX system (δ_A 3.08, δ_B 3.14, J_{AB} = 9.2 Hz, J_{AX} = 8.0 Hz, J_{BX} = 6.0 Hz, 2 H, H-7), 3.61 (dd, J = 2.7 Hz, J = 8.5 Hz, 1 H, H-5), 3.74 (s, 3 H, OCH_3); AB system (δ_A 4.33, δ_B 4.44, J_{AB} = 11.0 Hz, 2 H, OCH_2Ph), 6.6 (dd, J = 10.7 Hz, J = 1.6 Hz, 1 H, H-3), 7.10 (m, 2 H, phenyl-H), 7.22 (m, 13 H, phenyl-H), 7.44 (m, 5 H, phenyl-H). ^{13}C NMR: δ 11.20 and 12.47 (6- and 2-CH_3), 16.66 (4-CH_3), 37.09 and 37.37 (C-4 and C-6), 51.59 (OCH_3), 66.17 (C-7), 74.99 (OCH_2Ph), 82.98 (C-5), 86.57 (4-CH_3), 126.85–128.51, 138.60 and 144.15 (20 phenyl-C, C-3 and C-2), 168.80 (C-1). Anal. Calcd for $C_{37}H_{40}O_4$: C, 80.99; H, 7.35. Found: C, 80.88; H, 7.59.

(2*S*,3*R*,4*R*,5*R*,6*S*)- and (2*R*,3*S*,4*R*,5*R*,6*S*)-Methyl 5-(Benzyloxy)-2,3-dihydroxy-2,4,6-trimethyl-7-(trityloxy)-heptanoate (17b and 19). **18b** (5.00 g, 9.13 mmol) was added dropwise to *N*-methylmorpholine *N*-oxide hydrate (2.08 g, 13.54 mmol) and osmium tetraoxide (0.83 mL of a 1% solution in *tert*-butyl alcohol) dissolved in a mixture of water (5 mL) and acetone (2.1 mL). After 18 h at 22 °C, a suspension of sodium hydrogen sulfite (0.5 g), magnesium silicate (4 g), and water (50 mL) was added, and the mixture was stirred for another 10 min, filtrated, neutralized with diluted sulfuric acid, and concentrated under reduced pressure. The residue was acidified to pH 2 and extracted with ethyl acetate. The organic phase was dried ($MgSO_4$) and evaporated to give a yellow oil (4.60 g), which was purified by preparative HPLC (nucleosil N, 5 M, hexane/2-propanol, 98/2, flow 40 mL/min, 40 bar) to give **17b** (2.50 g, 50%) and **19** (1.25 g, 25%) as viscous colorless oils. **17b**: $[\alpha]^{20}_D$ +6.8° (c 1). IR (film): 3500, 3100, 3060, 3030, 2950, 1730, 1590, 1490, 1450, 1260, 1060, 950, 700, 630 cm^{-1}: ^1H NMR: δ 1.04 (d, J = 7.0 Hz, 6 H, 4- and 6-CH_3), 1.32 (s 3 H, 2-CH_3), 2.08 (m, 1 H, H-6), 2.19 (m, 1 H, H-4), 2.82 (d, J = 7.0 Hz, 1 H, 3-OH), 3.13 (d, J = 6.0 Hz, 2 H, H-7), 3.54 (s, 1 H, 2-OH), 3.66 (dd, J = 6.0 Hz, J = 4.5 Hz, 1 H, H-5), 3.74 (s, 3 H, OCH_3), 3.92 (d, J = 7.5 Hz, 1 H, H-3); AB system (δ_A 4.38, δ_B 4.43, J_{AB} = 10.0 Hz, 2 H, -OCH_2 = Ph), 7.19 (m, 15 H, phenyl-H), 7.45 (m, 5 H, phenyl-H). ^{13}C NMR: δ 8.37 and 12.12 (4-CH_3 and 6-CH_3), 21.97 (2-CH_3), 35.72 and 36.34 (C-4 and C-6), 52.61 (1-OCH_3), 66.25 (C-7), 73.95 and 75.81 (C-5 and 5-OCH_2-), 77.39 (C-2), 83.80 (C-5), 86.21 (C-5), 126.61, 127.12, 127.30, 127.42, 127.91, 128.39, 138.05 and 143.88 (20 phenyl-C), 176.58 (C-1). Anal. Calcd for $C_{37}H_{42}O_6$: C, 76.26; H, 7.26. Found: C, 76.77; H, 7.39.

19: $[\alpha]^{20}_D$ −15.6° (c 5). ^1H NMR: δ 0.95 (d, J = 7.2 Hz, 3 H, CH_3), 1.01 (d, J = 7.2 Hz, 3 H, CH_3), 1.20 (s, 3 H, CH_3, 1.95 (m, 1 H, H-6), 2.08 (m, 1 H, H-4); AB part of ABX system (δ_A 2.96, δ_B 3.05, J_{AB} = 9.5 Hz, J_{AX} = J_{BX} = 5.7 Hz, 2 H, H-7), 3.40 (s, 1 H, 2-OH), 3.64 (s, 3 H, OCH_3), 3.68 (dd, J = 2.8 Hz, J = 6.8 Hz, 1 H, H-5), 3.97 (d, J = 7.5 Hz, 1 H, 3-OH), 4.23 (dd, J = 5.0 Hz, J = 2.3 Hz, 1 H, H-3); AB system (δ_A 4.34, δ_B 4.44, J_{AB} = 11.5 Hz, 2 H, -OCH_2Ph), 7.13 (m, 15 H, phenyl-H), 7.36 (m, 5 H, phenyl-H). ^{13}C NMR: δ 13.42 and 13.98 (4- and 6-CH_3), 21.86 (2-CH_3), 35.58 and 37.12 (C-4 and C-6), 52.78 (OCH_3), 66.87, 72.38, 79.35, and 81.13 (C-7, C-3, C-2, and -OC_2Ph), 86.53 (C-5), 126.87, 127.31, 127.42, 127.66, 128.29, 128.70, 138.29, and 144.09 20 Ar C), 176.85 (C-1).

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Registry No. **1a**, 108817-24-9; **1b**, 108817-25-0; **1c**, 108817-26-1; 1 (R^1 = R^2 = Ac), 108817-27-2; **2a**, 108867-45-4; **2b**, 108867-46-5; **2c**, 108867-47-6; **3**, 108867-50-1; **4a**, 88424-95-7; **4b**, 108817-20-5; **4c**, 108817-21-6; **4d**, 100791-35-3; **1e**, 108817-23-8; **5a**, 88424-94-6; **5b**, 108867-40-9; **5c**, 108867-41-0; **5d**, 100895-85-0; **5e**, 108867-44-3; **6**, 108817-22-7; *ent*-**6**, 108867-53-4; **7**, 108867-43-2; **8**, 94942-09-3; **9**, 86654-54-8; **10**, 108817-28-3; **11**, 108867-48-7; **12**, 108817-29-4; **13**, 108867-49-8; **14**, 108867-51-2; **15**, 108867-52-3; **17b**, 108817-32-9; **18a**, 108817-30-7; **18b**, 108817-31-8; **19**, 108834-53-3; $Ph_3P{=}C(Me)CO_2Me$, 2605-68-7; erythronolide A, 26754-37-0; erythronolide B, 3225-82-9.

Regioselectivity of Addition of Thiols and Amines to Conjugated Allenic Ketones and Esters

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Regioselectivity of nucleophilic addition to conjugated allenic ketones depends strongly on the nucleophile: anionic nucleophiles, e.g., triethylamine salts of benzenethiols, gave the β-substituted β,γ-unsaturated ketones with high selectivity. In contrast, neutral nucleophile molecules, e.g., benzenethiols or aniline, afforded the β-substituted α,β-unsaturated ketones. The reactions to allenecarboxylic esters indicated the same regiochemical tendency, but lower selectivities were observed in the reactions with benzenethiol.

Nucleophilic addition reactions to conjugated allenic carbonyl compounds have become of interest in relation to the mode of reaction of "suicide enzyme inhibitors".[1] It is well-known that the allenic groups conjugated to an electron-withdrawing substituent readily undergo nucleophilic addition reactions. However, there have been conflicting reports on the regiochemical selectivity of the reaction.[2] Allenic ketones and esters were shown to yield β-alkoxy- and β-amino α,β-unsaturated adducts by their

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Table I. Regioselectivity of Addition of Thiols and Amines to Allenic Ketones

entry	substrate	R^1	R^2	Z	nuclphile	base	solv	yield,[a] %	2:3[b]
1	**1a**	Me	H	COEt	PhSH		C_6D_6	75	100[c]:trace
2	**1a**	Me	H	COEt	PhSH		$CDCl_3$		100[c]:trace
3	**1a**	Me	H	COEt	PhSH		CH_3CO_2H	47	100[c]:0
4	**1a**	Me	H	COEt	PhSH	Et_3N	C_6D_6	75	17:83
5	**1b**	Me	Me	COPr-*i*	PhSH		C_6D_6	82	83[c]:17
6	**1b**	Me	Me	COPr-*i*	PhSH	Et_3N	C_6D_6	93	7:93
7	**1c**	Ph	H	COMe	PhSH		$CDCl_3$	87	100[d]:0
8	**1c**	Ph	H	COMe	PhSH	Et_3N	$CDCl_3$	80	<5:>95
9	**1d**	Ph	Ph	COMe	PhSH		$CDCl_3$	(13)	
10	**1d**	Ph	Ph	COMe	PhSH	Et_3N	$CDCl_3$	80	0:100[e]
11	**1a**	Me	H	COEt	*p*-$NO_2C_6H_4SH$		C_6D_6	53	100[c]:0
12	**1a**	Me	H	COEt	*p*-$NO_2C_6H_4SH$	Et_3N	C_6D_6	79	0:100
13	**1b**	Me	Me	COPr-*i*	*p*-$NO_2C_6H_4SH$		C_6D_6	86	100[f]:trace
14	**1b**	Me	Me	COPr-*i*	*p*-$NO_2C_6H_4SH$	Et_3N	C_6D_6	90	0:100
15	**1b**	Me	Me	COPr-*i*	*p*-$NH_2C_6H_4SH$		C_6D_6	59	100[h]:trace
16	**1b**	Me	Me	COPr-*i*	*o*-$NH_2C_6H_4SH$		C_6D_6	72	88[i]:12
17	**1b**	Me	Me	COPr-*i*	2-PySH		$CDCl_3$	91	0:100
18	**1a**	Me	H	COEt	$PhNH_2$		C_6D_6	70	100[j]:0
19	**1b**	Me	Me	COPr-*i*	$PhNH_2$		C_6D_6	68	100[j]:0
20	**1c**	Ph	H	COMe	$PhNH_2$		$CDCl_3$	85	100[j,k]:0
21	**1d**	Ph	Ph	COMe	$PhNH_2$		$CDCl_3$	71	100[j,l]:0
22	**1b**[m]	Me	Me	COPr-*i*	pyrrolidine		C_6D_6	91	100:0
23	**1a**	Me	H	COEt	imidazole		C_6D_6	42	trace:100

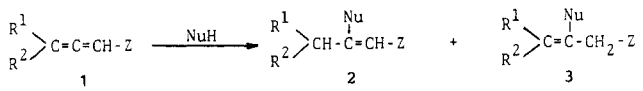
[a] Yields refer to isolated and purified products. Value in parentheses is a conversion percent. Satisfactory microanalytical and spectral data were obtained for the adducts. [b] Isomeric ratios **2**:**3** were obtained by peak integrals of NMR spectra of the crude products, α-CH= proton signal at δ 5.1–6.5 for **2** and α-CH_2 proton signal at δ 3.2–3.6 for **3**. [c] Mainly *E* isomer accompanied by a small amount of *Z* isomer. [d] *E* isomer, mp 57–60 °C. [e] mp 93–97 °C. [f] mp 45.5–47.0 °C. [g] mp 37–38 °C. [h] mp 102.5–106.0 °C. [i] mp 98.5–99.5 °C. [j] *Z* isomer. [k] mp 51–52 °C. [l] mp 136–138 °C. [m] A similar regiochemical result has been obtained in methanol solvent.[5]

reactions with alkoxides and amines, respectively.[3-5] The addition of thiols to an allenic ester preferentially gave α,β- or β,γ-unsaturated adduct depending on the concentration of base catalyst.[6] It has also been shown that the Michael addition of benzenethiol and imidazole, and of triethylamine-catalyzed phenol and acetic acid to a secosteroidal allenic ketone gave unconjugated adducts. On the other hand, pyrrolidine and methanol gave α,β-unsaturated ketones, in which reaction the Michael addition was accompanied by transannular cyclization.[7] More recently, it was reported that the imidazole moiety of *N*-acetylhistidine methyl ester added to an allenic thio ester to give the β-substituted β,γ-unsaturated thio ester.[8] In this paper we report on the regioselectivity of the addition of thiols and amines to allenic ketones and esters.

Results

The substrate allenic ketones 4,5-heptadien-3-one (**1a**) and 2,6-dimethyl-4,5-heptadien-3-one (**1b**) were easily prepared from 5-chloro-5-hepten-3-one and 5-chloro-2,6-dimethyl-5-hepten-3-one,[9] respectively, by treating them with 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU). 5-Phenyl- (**1c**) and 5,5-diphenyl-3,4-pentadien-2-one (**1d**) were synthesized from (triphenylphosphoranylidene)acetone and phenyl- or diphenylacetyl chloride by a modification of the route used by Lang for the synthesis of ethyl 2,3-pentadienoate.[10] Some of the substrates are chiral, but in this work racemic mixtures were used.

Scheme I



a: R^1 = Me, R^2 = H, Z = COEt
b: R^1, R^2 = Me, Z = COPr-*i*
c: R^1 = Ph, R^2 = H, Z = COMe
d: R^1, R^2 = Ph, Z = COMe
e: R^1 = Me, R^2 = H, Z = CO_2Me
f: R^1, R^2 = Me, Z = CO_2Me
g: R^1, R^2 = Me, Z = CN

m: Nu = PhS-
n: Nu = *p*-$NO_2C_6H_4S$-
o: Nu = *p*-$NH_2C_6H_4S$-
p: Nu = *o*-$NH_2C_6H_4S$-
q: Nu = Pyridin-2-yl
r: Nu = PhNH-
s: Nu = Pyrrolidin-1-yl
t: Nu = Imidazol-1-yl

The addition reactions to allenic ketones **1** were carried out in NMR tubes on a 1.0–1.5-mmol scale (1/nucleophile = 1:1 or 1/nucleophile/Et_3N = 1:1:1) in benzene-d_6 or chloroform-*d*, unless otherwise specified. The progress of a given reaction was monitored by ^1H NMR spectroscopy. The reactions of γ-monosubstituted allenic ketones **1a** and **1c** were usually completed within 0.5–3 h, while a little more time was required for **1b**. These reactions occurred almost quantitatively and no byproducts were detected by NMR. The products were β-substituted α,β-unsaturated ketone **2** and/or β,γ-unsaturated ketone **3** (Scheme I). These isomeric adducts were easily distinguished by their ^1H NMR spectra, **2** showing α-vinyl proton at δ 5.1–6.5 and **3** showing α-methylene protons at δ 3.2–3.6. The isomeric product ratios did not change after the mixture was al-

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Table II. Addition of Benzenethiol and Aniline to Allenic Esters and a Nitrile

entry		Substrate R¹	R²	Z	nuclphile	base	reactn conditions solv	temp, °C	reactn time	conversn, %	yield,[a] %	2:3[b]
24	**1e**	Me	H	CO_2Me	PhSH		$CDCl_3$	50	4 days	100	61	67[c]:33
25	**1e**	Me	H	CO_2Me	PhSH	Et_3N	$CDCl_3$	30–38	5 min	100	51	0:100
26	**1f**	Me	Me	CO_2Me	PhSH		$CDCl_3$	50	5 days	70	67	9:91
27	**1f**	Me	Me	CO_2Me	PhSH	Et_3N	$CDCl_3$	30–38	4 days	85	23	0:100
28	**1g**	Me	Me	CN	PhSH		$CDCl_3$	30–38	9 days	0		
29	**1g**	Me	Me	CN	PhSH	Et_3N	$CDCl_3$	50	5 min	100	54	0:100
30	**1e**	Me	H	CO_2Me	$PhNH_2$		$CDCl_3$	50	19 h	100	41	100[d]:0
31	**1g**	Me	Me	CN	$PhNH_2$		$CDCl_3$	30–38	7 days	0		

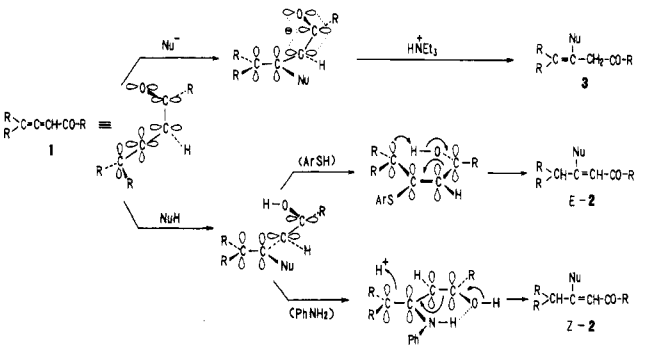
[a] Yields refer to isolated and purified products. Satisfactory microanalytical and spectral data were obtained for the adducts. [b] Isomeric ratios **2**:**3** were obtained by peak integrals of NMR spectra of the crude products: α-CH= proton signal at δ 5.1–5.8 for **2em** and at δ 4.7–4.8 for **2em** and **2fm** and α-CH_2 proton signal at δ 3.2–3.3 for **3**. [c] A mixture of *E*:*Z* = 75:25. [d] *Z* isomer.

lowed to stand overnight. The reactions of **1d** proceeded more slowly: the reaction with aniline progressed 71% after 2 days and 80% after 3 days and that with benzenethiol less than 13% after 2 days. The results are summarized in Table I.

In the reaction with benzenethiol or *p*-nitrobenzenethiol, **2** was the main or exclusive product. This regioselectivity was not affected by the solvents, benzene, chloroform, and acetic acid. In contrast, **3** was the main product when an equivalent amount of triethylamine was added. The products obtained, **2am**, **2bm**, and **2an**, were mixtures of geometrical isomers, one of which was a minor component. The vinyl proton signals of the major isomers appeared at higher magnetic field than those of the minor isomers. Since these shifts seemed to be due to long-range shielding by the benzene ring, the major products were assigned the *E* configuration. Reactions of **1** with aniline or pyrrolidine gave **2** whether triethylamine was present or not, but imidazole and 2-pyridinethiol gave only **3**. The other α,β-unsaturated adducts **2**, except the adducts of aniline, were single geometrical isomers and expected to have the *E* configuration. The α,β-unsaturated adducts of aniline were characterized by their amine proton signals, which appeared at δ 12–13. The IR spectra of these adducts indicated carbonyl absorption at 1600 cm^{-1}, at a lower frequency than the 1680 cm^{-1} of the thiol adducts. These facts indicate that there is hydrogen bonding between amino and carbonyl groups and that the adducts have the *Z* configuration.[4] When **1a** or **2am** was treated with triethylamine or **3am** with acetic acid or benzenethiol or **2cm** or **3cm** with benzenethiol and triethylamine, no isomerization was observed under the reaction conditions. Thus the isomeric ratios of the products do not result from secondary isomerization but evidently reflect the regioselectivities of the addition reactions.

Although alkyl or phenyl substituents at the γ-position of allenic ketones have little effect on the regioselectivity of addition, changing the activating groups of the allenes had significant effects on the regioselectivity as well as the reactivity. The results of addition reactions to allenic esters and to the allene 4-methyl-2,3-pentadienenitrile are summarized in Table II. As shown in Table II, the reaction with esters was slower than with the ketones, and the nitrile reacted either very much slower than the esters or did not react at all under the reaction conditions. However, aniline gave the α,β-unsaturated adducts **2** and triethylamine-catalyzed thiols gave the β,γ-unsaturated adducts **3**, as did their reactions with the allenic ketones. The β,γ-unsaturated adduct **3** became predominate over **2** on going from a monomethyl to a dimethyl-substituted allenic ester. The α,β-unsaturated adduct **2em** was quite stable, and no isomerization was observed after standing at 50 °C for 7 days whether in the presence of benzenethiol or not. In contrast, when **3em** was treated with benzenethiol in chloroform solution at 50 °C, a small amount of **2em** was detected by its ^1H NMR spectrum after 3 days, and ca. 30% of **3em** was isomerized to **2em** after 6 days. Product **2em** obtained by the addition reaction may be the result of such a slow isomerization. However, the product ratio, **2em**/**3em** = 7:3, exceeds the value expected only from the isomerization, and the ratios were also found to be almost constant throughout the reaction. It appears that the addition of thiols to allenic esters has a tendency to produce **2** and that the regiochemical selectivity is inferior to that of the allenic ketones.

Scheme II



Information on the structures of the nucleophiles was obtained by ^1H NMR and IR spectroscopy. In the NMR spectrum of an equivalent mixture of *p*-nitrobenzenethiol and triethylamine, the SH proton signal at δ 3.87 was not observed, but an ammonium proton signal at δ 10.60 was exhibited. 2-Pyridinethiol also showed a broad signal for ammonium proton at δ 13.7. Thus *p*-nitrobenzenethiol in the presence of triethylamine, and 2-pyridinethiol itself, obviously form inter- and intramolecular salts under the reaction conditions. On the other hand, the SH proton signal of benzenethiol was shifted from δ 3.34 to 5.51 by the addition of an equivalent amount of triethylamine, and it shifted further on addition of excess triethylamine. The IR spectrum of the mixture ($CHCl_3$ solution) showed that the S–H stretching band at 2580 cm^{-1} was greatly diminished and a new absorption for N–H stretching appeared at 2300 cm^{-1}. These spectral data indicate that benzenethiol in the presence of triethylamine exists in an equilibrium state between free thiol and its salt. In the cases of *o*- and *p*-aminobenzenethiols, the SH proton signals appeared at δ 3.17 and 3.0, respectively; thus these thiols did not form salts in spite of the presence of a basic amino group.

Discussion

The addition of thiols or amines to allenic ketones and esters is promoted by initial attack of nucleophiles at the β-C, followed by protonation either at the α-C or the γ-C.

Protonation at the α-C would give the β,γ-unsaturated adducts **3**, while protonation at the γ-C would afford the α,β-unsaturated adducts **2** (Scheme II).

When the nucleophile is an anionic species, attack at the β-C initially leads to a dienolate. The two double bonds of the resulting dienolate do not form a single π system but are orthogonal to each other. As a result, this intermediate could be protonated at the γ-C only after a 90° rotation about the α,β-single bond. There is, however, no analogous stereoelectronic barrier for protonation at the α-C. If protonation takes place before the rotation has been completed, the β,γ-unsaturated adducts would be obtained. Imidazole appeared to be different among the nucleophiles studied. Although it is not an anionic salt, its behavior seems to be like one. It is well-known that the basic and nucleophilic properties of imidazole are due to its pyridine-type nitrogen and that some ionic structures appear to be important in order to account for its reactivity and properties. Imidazole, therefore, should behave similarly to pyridinethiol and should give the β,γ-unsaturated adduct **3at**.

In contrast to the anionic nucleophiles, the Michael-type addition of a neutral nucleophile molecule leads to a β-substituted dienol, which should be fairly stable and would form a single π system by a rotation about the α,β-single bond. This conjugated dienol could form an α,β-unsaturated carbonyl compound by proton transfer to the γ-C via a six-membered cyclic transition state.[11] If one assumes that such intramolecular proton transfer takes place, it is reasonable that the α,β-unsaturated ketone products, except the adducts of aniline, would be predominately the *E* isomers. It also follows from these assumptions that the addition of benzenethiol to a secosteroidal allenic ketone would not give an α,β-unsaturated product but rather an β,γ-unsaturated adduct,[7] because the conjugated dienol formed initially cannot lead to the six-membered cyclic transition state for proton transfer. Since the dienol-type adducts obtained from allenic esters are less stable than those from allenic ketones, protonation at the α-C competes well with protonation at the γ-C and the regioselectivity to give α,β-unsaturated products becomes lower than with allenic ketones. Comparison of entry 1 with 5 and 24 with 26 shows a clear tendency for methyl substitution at the γ-position to favor the formation of β,γ-unsaturated products. Thermodynamic stabilities of α,β- and β,γ-unsaturated ketones and carboxylic esters have been studied extensively and have shown that the introduction of one or two γ-methyl groups to a propenyl carbonyl system increases the relative thermodynamic stability of the β,γ-unsaturated isomers.[12] The present results indicate that the regioselectivity of the protonation is also influenced by the thermodynamic stabilities of the products.

The above explanations do not account for the observation that aniline afforded the *Z*-α,β-unsaturated adducts. In this case, possibly a strong hydrogen bond between the amino group and the initially formed dienol oxygen stabilizes the *Z* configuration, and proton transfer to the γ-C then occurs intermolecularly.

Experimental Section

^1H and ^{13}C NMR spectra were taken on JEOL PMX-60 and on JNM-FX100 spectrometers, respectively, in $CDCl_3$ unless otherwise specified, with Me_4Si as an internal standard. IR spectra were measured with a Hitachi EPI-G2 spectrometer. High-resolution mass spectra were provided by Hitachi Research Laboratory, Naka. VPC analyses were performed on Hitachi 163 and 263 gas chromatographs using 3 mm × 2 m columns packed with Silicone SE-30 30% on Shimalite and DEGS 5% or PEG-20M 20% on Chromosorb-W. The products were purified by medium-pressure column chromatography on silica gel (Merck Kieselgel 60). Melting and boiling points are uncorrected.

4,5-Heptadien-3-one (1a). To a stirred and ice-cooled solution of 5-chloro-5-hepten-3-one[9] (1.6 g, 10.9 mmol) in ether (30 mL) was added dropwise a solution of 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU, 1.67 g, 11.0 mmol) in ether (20 mL) under argon. After 10 min, the mixture was percolated through a short silica gel column, and the column was successively eluted with ether (300 mL). The combined solutions were distilled under reduced pressure, giving **1a** (0.95 g, 79.2%): bp 86–96 °C (34 mmHg) (Kugelrohr apparatus); ^1H NMR δ 1.08 (t, *J* = 8 Hz, 3 H), 1.74–1.93 (m, 3 H), 2.65 (q, *J* = 8 Hz, 2 H), 5.39–5.81 (m, 2 H); ^{13}C NMR δ 8.22 (q), 12.74 (q), 32.06 (t), 89.83 (d), 95.93 (d), 201.55 (s), 212.94 (s); IR (neat) 1955, 1685 cm^{-1}; exact mass calcd for $C_7H_{10}O$ (M^+) 110.0732, found 110.0743.

2,6-Dimethyl-4,5-heptadien-3-one (1b). 5-Chloro-2,6-dimethyl-5-hepten-3-one[9] (1.93 g, 10 mmol) was treated with DBU (1.54 g, 10 mmol) as above, yielding **1b** (1.12 g, 81%) after purification by column chromatography (silica gel, 30–50% ethyl acetate/hexane): ^1H NMR δ 1.09 (d, *J* = 7 Hz, 6 H), 1.86 (d, *J* = 3 Hz, 6 H), 3.08 (sept, *J* = 7 Hz, 1 H), 5.58 (sept, *J* = 3 Hz, 1 H); ^{13}C NMR δ 19.08 (q), 19.32 (q), 36.64 (d), 94.05 (d), 99.57 (s), 205.89 (s), 210.30 (s); IR (neat) 1955, 1675 cm^{-1} [lit.[5] 1950, 1640 cm^{-1}; bp 75 °C (2 kPa)]; exact mass calcd for $C_9H_{14}O$ (M^+) 138.1045, found 138.1021. Anal. Calcd for $C_9H_{14}O$: C, 78.21; H, 10.21. Found: C, 78.16; H, 10.45.

5-Phenyl-3,4-pentadien-2-one (1c). **1c** was prepared from (triphenylphosphoranylidene)acetone[13] (8.0 g, 25 mmol), phenylacetyl chloride (3.9 g, 25 mmol), and triethylamine (2.55 g, 25 mmol) by the method reported for synthesizing allenic esters.[10] The yield was 1.45 g (37%) after chromatography on a silica gel column (5% ethyl acetate/hexane): ^1H NMR δ 2.25 (s, 3 H), 6.06 (d, *J* = 6 Hz, 1 H), 6.23 (d, *J* = 6 Hz, 1 H), 7.25 (s, 5 H); ^{13}C NMR δ 26.72 (q), 98.52 (d), 101.04 (d), 127.22 (d), 128.16 (d), 128.98 (d), 131.80 (s), 197.67 (s), 215.70 (s); IR (neat) 1940, 1680 cm^{-1} (lit.[14] 1928 cm^{-1}). Anal. Calcd for $C_{11}H_{10}O$: C, 83.52; H, 6.37. Found: C, 83.70; H, 6.42.

5,5-Diphenyl-3,4-pentadien-2-one (1d). **1d** was prepared in the same way as **1c** from diphenylacetyl chloride, yield 59%: ^1H NMR δ 2.30 (s, 3 H), 6.16 (s, 1 H), 7.28 (s, 10 H), (lit.[15] δ 2.25, 6.10, 7.30); ^{13}C NMR δ 26.09 (q), 99.98 (d), 113.66 (s), 128.40 (d), 128.69 (d), 133.86 (s), 197.79 (s), 215.05 (s); IR (neat) 1935, 1690 cm^{-1} (lit.[14] 1690, 1930 cm^{-1}). Anal. Calcd for $C_{17}H_{14}O$: C, 87.15; H, 6.02. Found: C, 86.64; H, 5.88.

Methyl 2,3-pentadienoate (**1e**),[10,16] methyl 4-methyl-2,3-pentadienoate (**1f**),[10,17] and 4-methyl-2,3-pentadienenitrile (**1g**)[18] were prepared by the reported methods.

Typical Procedure for the Addition Reactions. Solutions of **1a** (139 mg, 1.26 mmol) in 0.4 mL of benzene-d_6 and of benzenethiol (163 mg, 1.48 mmol) in 0.2 mL of benzene-d_6 were mixed in an NMR tube. (When the reaction was carried out in the presence of triethylamine, 1 equiv of which was added to the mixture.) The mixture was kept at 30–38 °C, and progress of the

(11) A similar six-membered cyclic transition state has been proposed for reketonization of (*Z*)-1-butadienol to *cis*-crotonaldehyde, and a moderate activation energy, 14.2 kcal/mol, was calculated by the INDO semiempirical method: Dannenberg, J. J.; Rayez, J. C. *J. Org. Chem.* **1983**, *48*, 4723–4727. The quasi-cyclic six-membered structure of hydrogen bonding between CO and CH groups was also posturated by the $\nu_{C=O}$ vibration of homologous ketones $CH_3(CH_2)_nCOR$: Dusart, O.; Piekarski, C.; Piekarski, S. *J. Chim. Phys. Phys.-Chim. Biol.* **1976**, *73*, 832–836.

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reaction was monitored by ^1H NMR spectroscopy. After 3 h, signals of the substrates disappeared. The spectrum did not change after the mixture was allowed to stand overnight. Although no peak attributable to byproducts could be observed, a small amount of diphenyl disulfide was detected by VPC. The isomeric ratio of the products (**2am**/**3am**) was determined by peak integrals of ^1H NMR spectrum (4-CH= proton signal at δ 5.60 for (*E*)-**2am** and δ 6.34 for (*Z*)-**2am**, and 4-CH_2 proton signal at δ 3.30 for (*E*)-**3am** and δ 3.25 for (*Z*)-**3am**) and also by VPC. The crude product was purified by medium-pressure column chromatography (silica gel, 0.5–1% ethyl acetate/hexane), giving 5-(phenylthio)-4-hepten-3-one (**2am**) (194 mg, 74.8%, *E*/*Z* = 8:2). The *E* isomer could be isolated pure, but the *Z* isomer was obtained only as a mixture with the *E* isomer: ^1H NMR (*E*) δ 0.96 (t, *J* = 8 Hz, 3 H), 1.23 (t, *J* = 8 Hz, 3 H), 2.23 (q, *J* = 8 Hz, 2 H), 2.85 (q, *J* = 8 Hz, 2 H), 5.60 (s, 1 H), 7.48 (s, 5 H), (*Z*) δ 0.97 (t, *J* = 8 Hz, 3 H), 1.15 (t, *J* = 8 Hz, 3 H), 2.17 (q, *J* = 8 Hz, 2 H), 2.56 (q, *J* = 8 Hz, 2 H), 6.34 (s, 1 H), 7.17–7.78 (m, 5 H); IR (neat) 1680 cm^{-1}. Anal. Calcd for $C_{13}H_{16}OS$: C, 70.87; H, 7.31; S, 14.55. Found: C, 70.59; H, 7.45; S, 14.32.

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Registry No. **1a**, 108425-53-2; **1b**, 58442-43-6; **1c**, 74143-89-8; **1d**, 36144-55-5; **1e**, 22377-44-2; **1f**, 17039-96-2; **1g**, 2861-04-3; (*E*)-**2am**, 109244-74-8; (*Z*)-**2am**, 109244-75-9; (*E*)-**2an**, 109244-77-1; (*Z*)-**2an**, 109244-78-2; (*Z*)-**2ar**, 109244-80-6; (*E*)-**2bm**, 109244-82-8; (*Z*)-**2bm**, 109244-83-9; (*E*)-**2bn**, 109244-85-1; (*E*)-**2bo**, 109244-87-3; (*E*)-**2bp**, 109244-88-4; (*Z*)-**2br**, 109244-91-9; (*E*)-**2bs**, 109244-92-0; (*E*)-**2cm**, 109244-93-1; (*Z*)-**2cr**, 109244-95-3; (*Z*)-**2dr**, 109244-97-5; (*Z*)-**2em**, 109244-99-7; (*E*)-**2em**, 109244-98-6; (*Z*)-**2er**, 109245-01-4; (*E*)-**2fm**, 109245-02-5; (*Z*)-**2fm**, 109245-09-2; **2gm**, 109245-04-7; **2gr**, 109245-05-8; (*E*)-**3am**, 109244-76-0; (*Z*)-**3am**, 109245-06-9; (*E*)-**3an**, 109244-79-3; (*Z*)-**3an**, 109245-07-0; **3at**, 109244-81-7; **3bm**, 109244-84-0; **3bn**, 109244-86-2; **3bp**, 109244-89-5; **3bq**, 109244-90-8; **3cm**, 109244-94-2; **3dm**, 109244-96-4; (*E*)-**3em**, 109245-00-3; (*Z*)-**3em**, 109245-08-1; **3fm**, 109245-03-6; **3gm**, 85895-39-2; PhSH, 108-98-5; *p*-$NO_2C_6H_4SH$, 1849-36-1; *p*-$NH_2C_6H_4SH$, 1193-02-8; *o*-$NH_2C_6H_4SH$, 137-07-5; 2-PySH, 73018-10-7; $PhNH_2$, 62-53-3; $EtCOCH_2C(Cl)$=CHMe, 80060-10-2; *i*-$PrCOCH_2C(Cl)$=CMe_2, 80060-11-3; Ph_3P=CHCOMe, 1439-36-7; $PhCH_2COCl$, 103-80-0; $Ph_2CHCOCl$, 1871-76-7; pyrrolidine, 123-75-1; imidazole, 288-32-4.

Supplementary Material Available: Spectral and analytical data for the addition products (*E*)- and (*Z*)-**2am**, (*E*)-**2bm**, (*E*)-**2cm**, **2an**,**ar**,**bn**,**bo**,**br**,**bs**,**cr**,**dr**,**em**,**er**, and **3am**,**an**,**at**,**bm**,**bn**,**bp**,**bq**,**cm**,**dm**,**em**,**fm**,**gm** (8 pages). Ordering information is given on any current masthead page.

Binding Properties of 1-Pyrenesulfonic Acid in Water

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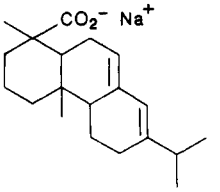
Experiments are described with 1-pyrenesulfonic acid (1-PSA), an unconventional surfactant of the type Ar_n–X where Ar_n is a polycyclic aromatic and X is a water-solubilizing entity. Little is known about the properties of such compounds when dissolved in water at relatively high concentrations (up to 0.1 M). Tensiometry, fluorescence spectroscopy, UV spectrophotometry, NMR spectroscopy, and kinetics were all used to characterize the aqueous 1-PSA systems. 1-PSA dimerizes but resists forming stacks or other multimolecular aggregates ("micelles"); possible reasons for this are discussed. Although possessing a "tail" which is less hydrophobic than those of common aliphatic surfactants, 1-PSA is capable of binding guests tightly (e.g., K_{assoc} with phenol blue = 3×10^4 M^{-1}). It does so as a monomer which has a large aromatic surface exposed to water. Thus, binding processes can be exploited without the complication of micellization; design of an enzyme mimic was attempted on this basis. Ar_n–X compounds have other attractive features: their "tails" are electronically active, and a wide variety of distinctive shapes are readily available.

Conventional surfactants possess a polar head-group attached to a long hydrocarbon chain. Basic research into the chemistry of surfactants has centered around the head-group, the main role of the hydrocarbon tail being to assemble the head-groups and to induce what is known as "micellar chemistry". Generally, a chain of 10 or more carbons suffices for the purpose. But as a result of this philosophy, we know surprisingly little about micellar properties as a function of the hydrophobic portion of the surfactant. For example, we do not know (and cannot even predict) how the catalytic properties of a hexadecyltrimethylammonium bromide micelle[1] would be affected by a phenolic unit at the chain terminus or an amino group at position-5 or an *n*-hexyl attached near the center of the tail. The reason for scarcity of structure–activity data of this type is clear: the necessary compounds are not readily available. A wealth of useful information lies in wait for those willing to overcome the synthetic difficulties.

Although basic research has relied largely on straight-chain surfactants, industrial chemistry has produced an imaginative array of nonlinear materials. For example, tall oil contains 30–50% rosin acids (e.g., abietic acid) whose salts display surfactant-like behavior with good wetting properties.[2]



Naphthalenesulfonic acid–formaldehyde condensates are used as setting agents for powdered pesticides, paints, and other formulations.[3] Surfactants can also be obtained by

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