of the isolated products (93% recovery) gave $[\alpha]^{21}_D = -10.8°$ or 64% inversion, suggesting that continued reaction in the presence of methanol caused racemization. Indeed, addition of methanol to (*S*)-(+)-α-naphthylphenylmethylmethoxysilane in the presence of $Rh_2(pfb)_4$ caused 80% racemization within 20 h at room temperature.

Acknowledgment. We are grateful to the Robert A. Welch Foundation and to the National Science Foundation for their support of this research. We wish to thank the Johnson Matthey Company for their loan of rhodium(III) chloride.

Registry No. 1, 1186-14-7; 1 (triethylsilyl ether), 129541-15-7; 2, 51916-47-3; 2 (triethylsilyl ether), 129541-16-8; 2 (*tert*-butyldimethylsilyl ether), 126680-66-8; 3, 1117-86-8; 3 (triethylsilyl ether), 129541-17-9; 3 (*tert*-butyldimethylsilyl ether), 129541-18-0; $Rh_2(pfb)_4$, 73755-28-9; Et_3SiH, 617-86-7; *t*-$BuMe_2SiH$, 29681-57-0; 1-octanol, 111-87-5; benzyl alcohol, 100-51-6; cholesterol, 57-88-5; glycidol, 556-52-5; (−)-nopol, 35836-73-8; (−)-menthol, 2216-51-5; (*E*)-3-phenyl-2-propen-1-ol, 4407-36-7; 2-octanol, 123-96-6; 3-buten-1-ol, 627-27-0; propen-1-ol, 4407-36-7; phenol, 108-95-2; (−)-borneol, 464-45-9; 1-butanol, 71-36-3; 1-pentanol, 71-41-0; 1-hexanol, 111-27-3; 2-methyl-1-propanol, 78-83-1; 2,2-dimethyl-1-propanol, 75-84-3; 2-butanol, 78-92-2; cyclohexanol, 108-93-0; (3-phenyl-1-propoxy)triethylsilane, 2290-40-6; (*E*)-3-phenyl-2-propen-1-yl triethylsilyl ether, 129541-12-4; (*S*)-(−)-α-naphthylphenylmethylsilane, 1025-09-8; (*R*)-(+)-α-naphthylphenylmethylsilane, 1025-08-7; (S)-(+)-α-naphthylphenylmethylmethoxysilane, 16544-83-5; 1-octyl triethylsilyl ether, 17957-36-7; benzyl triethylsilyl ether, 13959-92-7; cholesterol triethylsilyl ether, 7604-85-5; glycidol triethylsilyl ether, 17865-33-7; (−)-nopol triethylsilyl ether, 129541-13-5; (−)-menthoxytriethylsilane, 129541-14-6; (−)-borneol triethylsilyl ether, 129645-73-4; 2-octyl triethylsilyl ether, 17957-35-6; 3-buten-1-yl triethylsilyl ether, 13411-57-9; phenyl triethylsilyl ether, 5888-66-4; (*R*)-(−)-α-naphthylphenylmethylmethoxysilane, 3553-88-6.

Supplementary Material Available: ^1H NMR spectral data and ^1H NMR spectra for the triethylsilyl ethers shown in Tables I and IV (30 pages). Ordering information is given on any current masthead page.

[4 + 3] Cycloaddition Reaction of Some Silyl Enol Ethers Having a Conjugated Carbonyl Functionality

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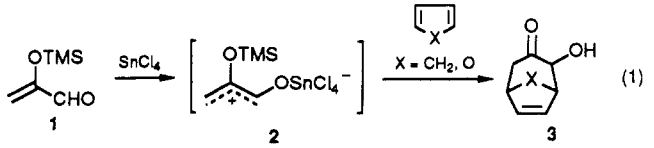
The Lewis acid catalyzed [4 + 3] cycloaddition reactions of 2-(trimethylsiloxy)propenal (**1**), with cyclopentadiene and furan were investigated. The vinylogous 4-(trimethylsiloxy)-2,4-pentadienal (**5**) reacted with cyclopentadiene in the presence of $SnCl_4$ at −78 °C to give 2-(formylmethyl)-substituted bicyclo[3.2.1]oct-6-en-3-one (**11**). This [4 + 3] cycloadduct arose as a result of the perispecific reaction at C_3 and C_5 rather than at C_2 and C_3 where the Diels–Alder reaction is normally expected to occur. With a homologous system, (1-(trimethylsiloxy)vinyl)oxirane (**7**, R = H) underwent a similar [4 + 3] cycloaddition reaction to give a 2-(hydroxymethyl)-substituted bicyclic product. In this case, trimethylsilyl triflate was a useful catalyst. The silyl enol ether **9**, conjugated with a 1,1-cyclopropanedicarboxylate was also reactive; thus, a catalyzed ring opening followed by the cycloaddition reaction gave a bicyclic diester. These cycloaddition reactions may be explained by the formation of a key oxyallyl cation-like intermediate and provide a method for constructing a functionalized bicyclo[3.2.1]octane system.

[4 + 3] Cycloaddition reactions have been extensively studied as a method for the formation of seven-membered rings.[1] Among the reliable 3C components in these reactions is the oxyallyl cation,[2] which was developed by Hoffmann.[3] Synthetic applications have been discussed in a recent review.[4]

Y= alkyl, silyl, metal, etc.

This type of intermediate is known to be accessible by an S_N1-like ionization in an allylic system by the reductive elimination of halogens from a halogenated ketone (in some cases directly from electronically equivalent cyclopropanone and alleneoxide).[3] An alternative approach was demonstrated in our previous work; 2-(trimethylsiloxy)-propenal (**1**) underwent cycloaddition to a diene as a 3C component rather than as a 2C dienophile, leading to a [4 + 3] cycloadduct **3**.[5,6] In this case, the activation of the carbonyl group by a Lewis acid lent positive character to the neighboring silyl enol ether, which gave rise to the key silyl oxyallyl cation intermediate **2** (eq 1).[5,6]



1 2 3 (1)

TMS = trimethylsilyl

It seemed reasonable to extend this [4 + 3] cycloaddition reaction to a silyl enol ether which is properly conjugated

(1) Recent examples in [4 + 3] cycloaddition methodologies: Hoffmann, H. M. R.; Eggert, U.; Gibbels, U.; Giesel, K.; Koch, O.; Lies, R.; Rabe, J. *Tetrahedron*, **1988**, *44*, 3899. Trost, B. M.; Schneider, S. *Angew. Chem., Int. Ed. Engl.* **1989**, *28*, 213. Gigneve, R. J.; Duncan, S. M.; Bean, J. M.; Purvis, L. *Tetrahedron Lett.* **1988**, *29*, 6071. Harmata, M.; Gamlath, C. B. *J. Org. Chem.* **1988**, *53*, 6154. Price, M. E.; Schore, N. E. *Tetrahedron Lett.* **1989**, *30*, 5865. Fukuzawa, S.; Fukushima, M.; Fujinami, T.; Sakai, S. *Bull. Chem. Soc. Jpn.* **1989**, *62*, 2348. Erden, I; Amputch, M. A. *Tetrahedron Lett.* **1987**, *28*, 3779. Davies, H. M. L.; McAfee, M. J.; Oldenburg, C. E. M. *J. Org. Chem.* **1989**, *54*, 930. Molander, G. A.; Schubert, D. C. *J. Am. Chem. Soc.* **1987**, *109*, 6877. Hassenrueck, K.; Martin, H. D. *Synthesis* **1988**, 569.

(2) Silyl oxyallyl cations: (a) Sakurai, H.; Shirahata, A.; Hosomi, A. *Angew. Chem. Int. Ed. Engl.* **1979**, *18*, 163. (b) Shimizu, N.; Tanaka, M.; Tsuno, Y. *J. Am. Chem. Soc.* **1982**, *104*, 1330.

(3) (a) Hoffmann, H. M. R. *Angew. Chem., Int. Ed. Engl.* **1973**, *12*, 819. (b) *ibid.* **1984**, *23*, 1.

(4) Mann. J. *Tetrahedron* **1986**, *42*, 4611.

(5) Sasaki, T. Ishibashi, Y. Ohno, M. *Tetrahedron Lett.* **1982**, *23*, 1693.

(6) Blackburn, C.; Childs, R. F.; Kennedy, R. A. *Can. J. Chem.* **1983**, *61*, 1981.

0022-3263/90/1955-6086$02.50/0

Table I. [4 + 3] Cycloaddition Reactions of 5, 7, and 9 with a Diene

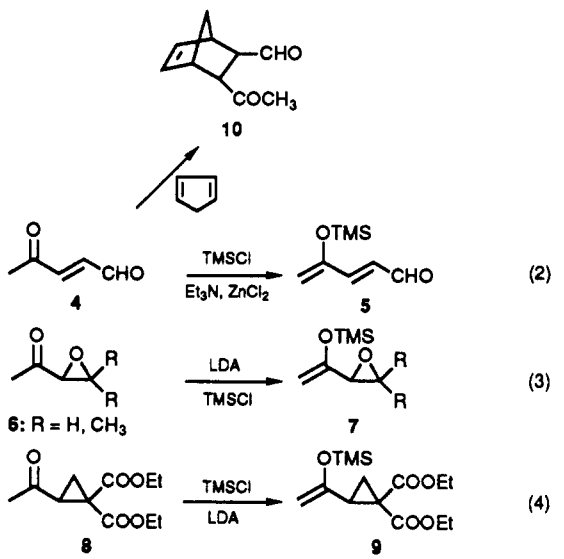
silyl enol ether	diene[a]	reaction conditions: cat.[b]	temp, °C	time, h	product	yield, % [endo/exo][c]
5	Cp	$SnCl_4$	−78	0.5	11	76 [4/1]
5	F	$SnCl_4$	−78	2	12	36 [1/0]
7	Cp	TMSOTf	−50	3	13	47 [3/2]
7	F	TMSOTf	−50	3	14	12 [3/2]
9	Cp	$TiCl_4$	0	3	16	55 [1/1]
9	F	$TiCl_4$	0	3	17[d]	15 [3/7]

[a] Cp, cyclopentadiene (5 equiv); F, furan (2 equiv). [b] $SnCl_4$ and $TiCl_4$ were employed in a stoichiometric amount (TMSOTf in 10 mol %). [c] The ratio was based on the relative amount isolated. In the cases of 16 and 17 it was estimated from ^1H NMR data in the inseparable mixture of products. [d] The open-chain adduct 18 was also obtained in 5% yield.

with a carbonyl function. To this end, we selected the following analogous systems: vinylogue, 4-(trimethylsiloxy)-2,4-pentadienal (**5**); homologue (oxirane), (1-(trimethylsiloxy)vinyl)oxirane (**7**); and cyclopropane analogue, 2-(1-(trimethylsiloxy)vinyl)cyclopropane-1,1-dicarboxylate (**9**).

Results and Discussion

Starting silyl enol ethers were prepared by standard methods. 4-Oxo-2-pentenal (**4**) was synthesized by a furan ring-opening transformation with bromine. Since the old method depends on a two-step conversion,[7] a recently developed one-pot procedure was used.[8] The silylation was achieved by treating **4** with NEt_3–trimethylsilyl chloride (TMSCl)–$ZnCl_2$ in CH_3CN[9] to give **5** (eq 2). The silyl enol ethers **7** of 3,4-epoxy-2-butanone (**6**) and **9** of diethyl 2-acetylcyclopropane-1,1-dicarboxylate (**8**) were simply prepared by treatment with lithium diisopropylamide (LDA)–TMSCl;[10] in the latter case, a better yield was obtained by the reversed addition of LDA to a mixture of **8** and TMSCl (eqs 3 and 4).



The [4 + 3] cycloaddition reactions of the silyl enol ethers **5**, **7**, and **9** were carried out with 2–5-fold excess of a diene (cyclopentadiene and furan) in the presence of a Lewis acid under an atmosphere of nitrogen at low temperature (−78 °C to 0 °C). After the usual workup, the crude products were separated by silica gel chromatography and characterized by spectral and elemental analyses. The results are summarized in Table I.

First, the vinylogous system was examined with an interest in whether the [4 + 3] or the [4 + 2] cycloaddition reaction predominates. When the reaction of **5** with cyclopentadiene was conducted at −78 °C in the presence of $SnCl_4$, the product consisted of two stereoisomers (4:1). The mass spectral and elemental analyses suggested that these isomers had the necessary features of a 1:1 adduct. However, comparison with an authentic sample of the [4 + 2] cycloadduct **10**[11] from **4** and cyclopentadiene, eliminated the possibility of the formation of a normal Diels–Alder type product. The IR spectra indicated the presence of two carbonyl groups (1730 and 1710 cm^{-1}). Furthermore, in the ^1H NMR spectra, no signals due to an acetyl group were present, and the presence of a bridging ethenyl moiety and a formyl group was indicated by a AB quartet centered at δ 6.05 and a triplet at δ 9.84, respectively. These data confirmed that the products were [4 + 3] cycloadducts, bicyclo[3.2.1]oct-6-en-3-ones (**11**), the results of the perispecific reaction at C_3 and C_5. While each isomer exhibited a complex spectrum, more detailed structural and stereochemical assignments were made with the help of COSY and NOESY spectra. All of the protons were unambiguously assigned by the consideration of coupling patterns, and thus, resolved ^1H NMR spectral data are summarized in Table II. One of the bridge protons (C_8-H) resonated at higher field as a simple doublet due to a geminal coupling. This was assigned as anti to the C_6–C_7 bridge, because, in addition to NOESY data, J_{vic} was predicted to be nearly 0 (a model study), and no long-range coupling with equatorial C_2-H was observed.[12] Syn-C_8-H was slightly deshielded[12] and appeared as a complex multiplet due to geminal, vicinal, and long-range couplings. The signal due to the equatorial C_4-H appeared as a double triplet due to long-range coupling with syn-C_8-H, at higher field than that of the axial C_4-H. A proton α to the bridgehead (C_2-H) was useful in determining the stereochemistry of this bicyclic ring system. Although C_2-H coupled to C_1-H without much difference in coupling constant between axial and equatorial, splitting in the major isomer was observed as a double double doublet, showing only the vicinal coupling with C_1-H in addition to that with diastereotopic C_9-H; no *W*-path long-range coupling with syn-C_8-H was observed. This fact allowed us to assign the major isomer as the endo product. Furthermore, NOESY supported this; C_2-H was shown to correlate with anti-C_8-H to the same extent that axial-C_4-H did. At the side chain, the methylene protons (C_9-H) showed diastereotopic behavior[12] and appeared individually. In the same manner, the cycloaddition reaction of

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(8) Pikul, S.; Raczko, J.; Ankner, K.; Jurczak, J. *J. Am. Chem. Soc.* **1987**, *109*, 3981.
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(10) Mariano, J. P.; Hatanaka, N. *J. Org. Chem.* **1979**, *44*, 4467.
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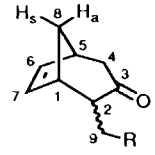
(12) Jackman, L. M.; Sternhell, S. *Application of Nuclear Magnetic Resonance Spectroscopy in Organic Chemistry*; Pergamon: Oxford, 1969.

Table II. ^{1}H NMR Spectral Data of 2-Substituted Bicyclo[3.2.1]oct-6-en-3-ones and 8-Oxa Derivatives[a]



			C_4-H				C_8-H			
compd	C_1-H	C_2-H	equatorial	axial	C_5-H	C_6- and C_7-H	anti	syn	C_9-H	others
11 (endo)	2.81–2.98, m[b]	3.15, ddd (7.2, 6.0, 3.1)	2.37, dt (16.2, 2.8)	2.52, dd (16.2, 3.3)	2.81–2.98, m[b]	5.99 and 6.12, dd (5.8, 2.6)	1.96, d (11.0)	2.12–2.24, m	2.19 and 2.92, ddd (17.2, 6.0, 1.3) and (17.2, 7.2, 1.3)	9.84, t (1.3)[c]
11 (exo)	2.67–2.90, m[b]	2.67–2.90, m[b]	2.35, dt (18.2, 2.8)	2.47, dd (18.2, 3.8)	2.67–2.90, m[b]	6.10 and 6.13, d (5.4)	1.81, d (11.4)	1.91–2.03, m	2.61 and 2.78, ddd (17.6, 10.0, 1.6) and (17.6, 5.0, 1.6)	9.77, t (1.6)[c]
12 (endo)	4.95, dd (4.6, 1.5)	3.41, ddd (7.3, 5.8, 4.6)	2.36, dd (15.5, 1.2)	2.83, dd (15.5, 5.0)	5.07, ddd (5.0, 1.5, 1.2)	6.22 and 6.35, dd (6.1, 1.5)	–	–	2.14 and 2.86, ddd (17.7, 5.8, 0.9) and (17.7, 7.3, 0.9)	9.84, t (0.9)[c]
13 (endo)	2.80–2.85, m	2.67, ddd (8.4, 4.4, 3.2)	2.33, dt (16.2, 2.8)	2.47, dd (16.2, 3.4)	2.90–2.97, m	5.98 and 6.07, dd (5.8, 2.8)	1.89, d (11.0)	2.11–2.20, m	3.54 and 3.78, dd (11.3, 4.4) and (11.3, 8.4)	–[d]
13 (exo)	2.79–2.84, m	2.45–2.49, m	2.34, ddd (17.6, 3.4, 2.0)	2.48, dd (17.6, 3.9)	2.84–2.91, m	6.09 and 6.13, dd (5.4, 2.2)	1.90, d (11.2)	1.95–2.04, m	3.75 and 3.85, dd, (10.8, 6.6) and (10.8, 7.6)	–[d]
14 (endo)	4.99, d (4.4)	3.00, dt (5.8, 4.4)	2.31, d (15.8)	2.78, dd (15.8, 4.9)	5.06, d (4.9)	6.27 and 6.31, d (6.0)	–	–	3.73, d (5.8)	–[d]
14 (exo)	5.01, d (1.5)	2.45, t (6.0)	2.37, d (16.9)	2.78, dd (16.9, 5.3)	5.06, dd (5.3, 1.5)	6.30 and 6.35, dd (6.1, 1.5)	–	–	3.99, d (6.0)	–[d]
15	3.41, dd (4.6, 2.8)	–	2.34, dt (18.3, 2.8)	2.45, dd (18.3, 4.3)	2.93–2.96, m	5.98 and 6.10, dd (5.5, 2.8)	1.87, d (11.0)	2.17–2.22, m	5.06 and 5.80, d (1.7)	–
16 (endo-+exo)			(obscure)[f]			5.98–6.10, m			(obscure)[f]	3.52 (0.5 H), 3.71 (0.5 H)[e]
17[g] (endo)	4.91, dd (4.6, 1.4)		(obscure)[f]	2.75, dd (15.4, 4.8)	5.03, dd (4.8, 1.4)	6.26 and 6.32, dd (6.2, 1.4)	–	–	(obscure)[f]	3.67, dd (9.4, 5.8)[h]
17[g] (exo)	4.81, d (1.4)		(obscure)[f]	2.87, dd (16.4, 5.0)	5.01, dd (5.0, 1.4)	6.24 and 6.30 dd (6.2, 1.4)	–	–	(obscure)[f]	3.44, dd (7.8, 6.4)[h]

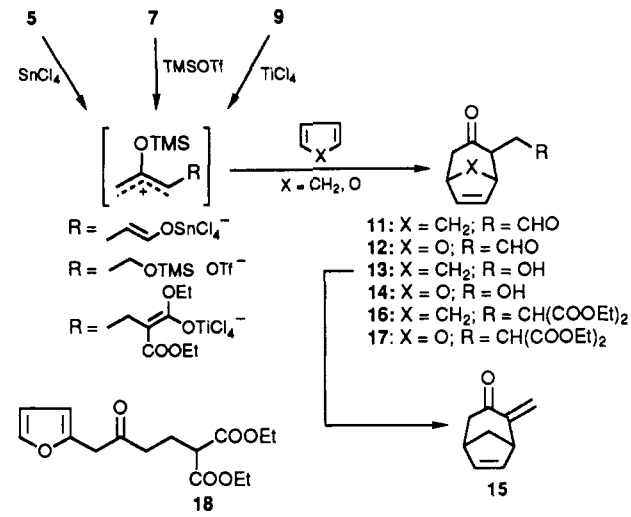
[a] The chemical shift in δ, coupling pattern, and coupling constant in hertz (in parentheses). [b] The signals overlapped with each other. [c] The aldehydic proton. [d] Analysis after D_2O exchange. [e] The methine proton at the side chain (dd, J = 8.6 and 6.4 Hz and J = 7.8 and 6.3 Hz, respectively); in addition, ethyl protons appeared around at δ 4.13–4.28 and 1.23–1.32. [f] These signals were not isolated from each other, which made the full assignment impossible. [g] Assignment for the endo and exo mixtured products. [h] In addition, ethyl protons appeared in the reasonable region; see the footnote *e*.

5 with furan gave a corresponding 8-oxa derivative **12**; in this case a single isomer was obtained in a fair yield. The structure of the product was likewise elucidated. Because of the lack of the C_8-methylene bridge, the ^1H NMR was comparatively uncomplicated, and the stereochemistry was easily deduced from the vicinal coupling constant as discussed above.[13] The value of $J_{1,2}$ = 4.6 Hz was attributed to the endo product.

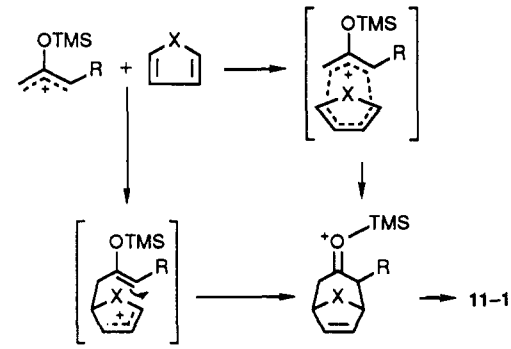
This type of catalyzed cycloaddition reaction was then extended to the homologous system, a silyl enol ether having an oxirane ring (which is regarded as a homolog of a carbonyl group). The action of a catalyst on an oxirane ring could induce ring opening to form an oxyallyl cation-like intermediate, which could promote a [4 + 3] cycloaddition reaction. In this case, the reaction of **7** (R = H) with cyclopentadiene at −50% °C proceeded as expected. The best yield (47%) was obtained by using 10 mol % of trimethylsilyl triflate (TMSOTf) as a catalyst.[14] Other Lewis acids such as $TiCl_4$, $SnCl_4$, and $BF_3{\cdot}Et_2O$ gave poorer yields (16–32%). The cycloadduct was characterized as 2-(hydroxymethyl)bicyclo[3.2.1]oct-6-en-3-one (**13**), primarily by elemental and mass spectral analyses in addition to IR spectral inspections which indicated the presence of hydroxyl (3430 cm^{-1}) and carbonyl groups (1705 cm^{-1}). Conclusively, the ^1H NMR spectrum established the bicyclic ring structure by comparison to that of **11** (Table II). Again, the products consisted of a 3:2 isomeric mixture. The first major fraction (chromatography) was assigned as the *endo* product based on the lack of long-range coupling (vide supra). From the same reaction with furan, a separable 3:2 isomeric mixture was obtained; the major product was determined to be the *endo*-**14** by the larger coupling constant (4.4 Hz) of C_2-H. Two findings are noted here. The cycloadduct **13** underwent quantitative dehydration to give the α-methylene ketone **15** upon standing at room temperature. Also, dimethyl-substituted oxirane **7** (R = CH_3) did not afford the cycloadduct under the same conditions. This may be attributed to the steric effect; more alkyl substituents resulted in less cycloaddition reactivity as is often observed in the Diels–Alder reaction.[15]

1,1-Cyclopropanedicarboxylate is known to undergo ring opening which is effected by activation with a Lewis acid.[16] This methodology can be applied to the generation of an oxyallyl cation-like intermediate. Such a system was realized in the silyl enol ether conjugated with 1,1-cyclopropanedicarboxylate. Thus, **9** was treated with cyclopentadiene in the presence of a Lewis acid at 0 °C. For an effective Lewis acid to initiate ring opening, $EtAlCl_2$ was reported to be useful;[16] however, in this case, $TiCl_4$ was found to be a better catalyst. Essentially the same type of reaction occurred to give a 1:1 cycloadduct as supported by mass spectral and elemental analyses. Furthermore, the IR and ^1H NMR spectra satisfied the structure requirements of the expected product, 2-bis(ethoxycarbonyl)ethyl-substituted bicyclo[3.2.1]oct-6-en-3-one (**16**), showing carbonyl absorptions at 1720–1740 cm^{-1} and endo olefinic signals at δ 6.0 and the disappearance of an acetyl group. However, exo and endo products were not

Scheme I



Scheme II



separable, and, therefore, from the highly complex ^1H NMR spectrum, no definite assignment could be made, although the endo/exo ratio was estimated by integration of distinct signals for the methine protons at the side chain in each isomer (Table II). With furan, the corresponding 8-oxa derivative **17** was obtained in a lower yield, but again it consisted of two inseparable stereoisomers. Nonetheless, the ^1H NMR spectrum of this mixture was partially resolved except for C_2-H, endo-C_4-H, and C_9-H; the peak area ratio of C_1-H showed that endo/exo = 3/7. In this case, an open-chain product **18** was obtained in 5% yield, arising from a Friedel–Crafts type reaction. This might be formed from the common intermediate without the cyclization. These results are illustrated in Scheme I.

In conclusion, based on the [4 + 3] cycloaddition reaction of α-siloxypropenal, a similar type of the reaction was examined using the analogous systems **5**, **7**, and **9**. It has been shown that such silyl enol ethers give rise to 2-substituted bicyclo[3.2.1]oct-6-en-3-ones (8-oxa derivatives) by the [4 + 3] cycloaddition to cyclopentadiene (or furan), if the key oxyallyl cation-like intermediate is induced by the action of a Lewis acid on a carbonyl group. Mechanistically, appreciable stereoselectivity was not observed, though the endo product was predominant in all cases except **16** and **17**.[17] This is in contrast to the exo preference which had previously been found in the reaction

(13) (a) Hoffmann, H. M. R.; Clemens, K. E.; Smithers, R. H. *J. Am. Chem. Soc.* **1972**, *92*, 3940. (b) Takaya, H.; Makino, S.; Hayakawa, Y.; Noyori, R. *Ibid.* **1978**, *100*, 1765.

(14) TMSOTf was reported to catalyze oxirane ring opening: Murata, S.; Suzuki, M.; Noyori, R. *J. Am. Chem. Soc.* **1979**, *101*, 2738. Simchen, G. *Synthesis* **1982**, 1.

(15) Caruthers, W. *Some Modern Methods of Organic Synthesis*, 3rd ed.; Cambridge University Press: Cambridge, 1986, Chapter 3.

(16) Beal, P. B.; Dombrosk, M. A.; Snider, B. B. *J. Org. Chem.* **1986**, *51*, 4391.

(17) Formally, the extented U-configurational or compact *W*-configurational transition state may give endo product, if the class A (Hoffmann's definition) reaction would operate. Regardless of the mechanism, the exo preference in **17** may be explained by a steric effect; bulkiness of a cyclopropanedicarboxylate moiety seems to result in less hindered extended *W*-configurational approach.

of 1 with furan;[5] the oxygen-chelation as assumed in 2[3b] is not likely in the analogous systems. At present the precise mechanism cannot be proposed (concerted or stepwise?:[3] Scheme II). However, bond formation with a diene at the terminus of a silyl enol ether should give a zwitterionic intermediate, which may collapse into a cyclized product; otherwise an open-chain product is formed from this intermediate as observed with 18.[2b,3]

Experimental Section

Infrared (IR) spectra were determined as thin films. ^1H NMR spectra were determined at 200 or 500 MHz in $CDCl_3$ and mass spectra at 70 eV. Chromatographic separations were carried out on silica gel columns (Fuji-Davison BW-300) eluted with the solvent noted. The solvents used for reactions were dried and distilled: CH_2Cl_2 ($CaCl_2$), THF (Na–Ph_2CO), CH_3CN (CaH_2).

(*E*)-4-(Trimethylsiloxy)-2,4-pentadienal (5). The starting aldehyde 4 was prepared by the reported procedure.[8] To a solution of 2-methyfuran (805 mg, 9.8 mmol) and pyridine (1.7 mL, 21 mmol) in 85/15 (v/v) of CH_3CN/H_2O (100 mL) cooled at −20 °C was added a solution of bromine (1.574 g, 9.8 mmol) in the same mixed solvent (12 mL), and the mixture was stirred at room temperature for 2 h. After the solution was concentrated and saturated with NaCl, the products were extracted with ether. The combined ethereal extracts were dried by passing through a Na_2SO_4 column and evaporated to leave a yellow oil, which was subjected to trap-to-trap distillation [90 °C (oven temperature)/2 mmHg] to give 4 (520 mg, 54%). To a solution of 4 (980 mg, 10 mmol) in CH_3CN (20 mL) containing a trace of $ZnCl_2$ was added TMSCl (1.5 mL, 12 mmol) and NEt_3 subsequently at 0 °C under an atmosphere of nitrogen, and the mixture was stirred at room temperature for 5 h. After evaporation of the solvent, hexane (20 mL) was added to the residue and resulting precipitates were filtered off under a nitrogen stream. The solvent was evaporated to leave an oil, which was subjected to trap-to-trap distillation [70 °C (oven temperature)/1 mmHg] to give 5 (1.02 g, 60%): IR 2720, 1690, 1625, 1250, 850 cm^{-1}; ^1H NMR δ 0.25 (s, 9 H), 4.77 and 4.81 (d, J = 1.0 Hz, each 1 H), 6.38 (dd J = 15.2 and 8.2 Hz, 1 H), 6.92 (d, J = 15.2 Hz, 1 H), 9.66 (d, J = 8.2 Hz, 1 H).

(1-(Trimethylsiloxy)ethenyl)oxirane (7, R = H). To a solution of LDA (16.7 mL of 1.5 M solution in cyclohexane, 25 mmol) in THF (30 mL) was added a solution of 6 (R = H)[18] (1.958 g, 22.8 mmol) in THF (3 mL) at −78 °C under an atomosphere of nitrogen, and stirring was continued for 1 h. Then, TMSCl (6.35 mL, 50 mmol) was added to this solution, and the mixture was warmed up gradually to room temperature and stirred for further 30 min. After replacement of the solvent with hexane, precipitates were removed by filtration under a nitrogen stream. The filtrate was passed through a short Florisil column and evaporated to leave an oil, which was subjected to trap-to-trap distillation [150 °C (oven temperature)/60 mmHg] to give 7 (R = H) (1.912 g, 53%): IR 1650, 1260, 850 cm^{-1}; ^1H NMR δ 0.21 (s, 9 H), 2.75 and 2.88 (dd, J = 6.4 and 3.2 Hz, each 1 H), 3.27 (t, J = 3.2 Hz, 1 H), 4.37 and 4.53 (d, J = 1.5 Hz, each 1 H). For R = CH_3, the similar treatment of 3,4-epoxy-4-methyl-2-pentanone gave 7 (R = CH_3) in 80% yield: IR 1640, 1250, 840 cm^{-1}; ^1H NMR 0.21 (s, 9 H), 1.25 and 1.35 (s, each 3 H), 2.88 (s, 1 H), 4.22 (br s, 2 H).

Diethyl 2-(1-(Trimethylsiloxy)ethenyl)cyclopropane-1,1-dicarboxylate (9). To a solution of 8[19] (456 mg, 2 mmol) and TMSCl (1.52 mL, 12 mmol) in THF (4 mL) was added LDA (1.67 mL of 1.5 M solution in cyclohexane) at −78 °C under an atomosphere of nitrogen, and stirring was continued for 3 h. The mixture was allowed to warm gradually to room temperature and worked up as above. Trap-to-trap distillation [150 °C (oven temperature)/1 mmHg] gave 9 (288 mg, 48%): IR 1730, 1630, 1260, 850 cm^{-1}; ^1H NMR 0.18 (s, 9 H), 1.26 and 1.28 (t, J = 7.2 Hz, each 3 H), 1.44 (dd, J = 9.0 and 4.5 Hz, 1 H), 1.75 (dd, J = 7.5 and 4.5 Hz, 1 H), 2.48 (dd, J = 9.0 and 7.5 Hz, 1 H), 4.16 and 4.18 (q, J = 7.2 Hz, each 2 H), 4.17 and 4.31 (d, J =1.4 Hz, each 1 H). The yield was lowered to less than 40‰ when the addition was reversed.

These silyl enol ethers 5, 7, and 9 obtained as above were used for next cycloaddition reactions without further purification.

General Procedure for the [4 + 3] Cycloaddition Reaction. To a solution of a silyl enol ether (1 mmol) and a diene (2–5 mmol) in CH_2Cl_2 (2 mL) was added a catalyst (1 mmol for $SnCl_4$ and $TiCl_4$ and 10 mol % for TMSOTf) by a syringe under an atmosphere of nitrogen and stirring was continued (for time and temperature, see Table I). The reaction mixture was poured into ice–water and diluted with ether (then neutralized with $NaHCO_3$ for 13 and 14). The separated organic layer was washed with water and dried over Na_2SO_4. After evaporation of the solvent, the oily products were separated by silica gel chromatography [elution: hexane/EtOAc (v/v), 85/15 for 11 and 16; 70/30 for 12, 13 and 17; 60/40 for 14]; the endo product was obtained as the first fraction except for 16 and 17, which were inseparable. The yield and endo/exo ratio were listed in Table I.

3-Oxobicyclo[3.2.1]oct-6-ene-2-ethanal (11) (endo): IR 2740, 1730, 1710 cm^{-1}; mass spectrum, m/e (relative intensity) 164 (molecular ion, 2), 136 (25). 122 (15), 107 (10), 91 (90), 79 (100), 66 (75). Anal. Calcd for $C_{10}H_{12}O_2$: C, 73.15; H, 7.37. Found: C, 73. 08; H, 7.31. **11 (exo):** IR 2730, 1720, 1710 cm^{-1}; mass spectrum, m/e (relative intensity) 164 (molecular ion, 2), 136 (25), 122 (15), 107 (11), 91 (90), 79 (100), 66 (75). Anal. Calcd for $C_{10}H_{12}O_2$: C, 73.15; H, 7.37. Found: C, 73.02; H, 7.30.

3-Oxo-8-oxabicyclo[3.2.1]oct-6-ene-2-ethanal (12) (endo): IR 2750, 1730, 1720 cm^{-1}; mass spectrum, m/e (relative intensity) 166 (molecular ion, 7), 138 (10), 137 (40), 123 (8), 119 (12), 109 (18), 95 (59), 81 (100), 68 (61). Anal. Calcd for $C_9H_{10}O_3$: C, 65.04; H, 6.08. Found: C, 64.74; H, 6.35.

2-(Hydroxymethyl)bicyclo[3.2.1]oct-6-en-3-one (13) (endo): IR 3430, 1705 cm^{-1}; mass spectrum, m/e (relative intensity) 152 (molecular ion, 9), 134 (7), 121 (4), 106 (12), 91 (64), 79 (100), 66 (61). Anal. Calcd for $C_9H_{12}O_2$: C, 71.03; H, 7.95. Found: C, 71.25; H, 7.73. **13 (exo):** IR 3430, 1705 cm^{-1}; mass spectrum, m/e (relative intensity) 152 (molecular ion, 7), 134 (4), 106 (13), 91 (88), 79 (100), 66 (65). Anal. Calcd for $C_9H_{12}O_2$: C, 71.03; H, 7.95. Found: C, 71.21; H, 7.88.

2-(Hydroxymethyl)-8-oxabicyclo[3.2.1]oct-6-en-3-one (14) (endo): IR 3450, 1715 cm^{-1}; mass spectrum, m/e (relative intensity) (no molecular ion), 136 (39), 123 (9), 108 (8), 107 (11), 95 (13), 81 (100), 68 (30). Anal. Calcd for $C_8H_{10}O_3$: C, 62.33; H, 6.54. Found: C, 62.22; H, 6.32. **14 (exo):** IR 3400, 1710 cm^{-1}; mass spectrum, m/e (relative intensity) (no molecular ion) 136 (24), 123 (6), 108 (5), 107 (8), 95 (10), 81 (100), 68 (22). Anal. Calcd for $C_8H_{10}O_3$: C, 62.33; H, 6.54. Found: C, 62.26; H, 6.39.

Diethyl ((3-oxobicyclo[3.2.1]oct-6-en-2-yl)methyl)-propanedioate (16) (endo and exo mixture): IR 1740 (s), 1730, 1720 (s) cm^{-1}; mass spectrum, m/e (relative intensity) 294 (molecular ion, 24), 249 (34), 203 (18), 175 (31), 160 (71), 134 (61), 92 (95), 91 (74), 79 (100), 66 (53). Anal. Calcd for $C_{16}H_{22}O_5$: C, 65.29; H, 7.53. Found: C, 65.26; H, 7.43.

Diethyl ((3-oxo-8-oxabicyclo[3.2.1]oct-6-en-2-yl)propanedioate (17) (endo and exo mixture): IR 1740 (s), 1735 (s) cm^{-1}; mass spectrum m/e (relative intensity) 296 (molecular ion, 5), 251 (25), 205 (27), 177 (21), 160 (20), 136 (60), 108 (48), 81 (100), 68 (45). Anal. Calcd. for $C_{15}H_{20}O_6$: C, 60.80; H, 6.80. Found: C, 60.94; H, 6.66.

For the ^1H NMR spectra of these compounds, see Table II.

2-Methylenebicyclo[3.2.1]oct-6-en-3-one (15). When 13 was allowed to stand at room temperature for 2 weeks, quantitative dehydration afforded 15: IR 1705, 1630 cm^{-1}; mass spectrum, m/e (relatively intensity) 134 (molecular ion, 12), 105 (15), 92 (26), 91 (52), 66 (100). Anal. Calcd. for $C_9H_{10}O$: C, 80.56; H, 7.51. Found: C, 80.42; H, 7.47. See also Table II for the ^1H NMR spectrum.

Diethyl [4-(2-Furyl)-3-oxobutyl]propanedioate (18). In the case of the reaction of 9 with furan, a byproduct 18 which was eluted after 17, was obtained in 5%: IR 1740, 1510, 865 cm^{-1}; ^1H NMR δ 1.26 (t, J = 7.0 Hz, 6 H), 2.15 (q, J = 7.2 Hz, 2 H), 2.57 (t, J = 7.2 Hz, 2 H), 3.38 (t, J = 7.2 Hz, 1 H), 3.71 (s, 2 H), 4.18 (q, J = 7.0 Hz, 2 H), 6.19, 6.35, and 7.37 (dd, J = 3.2 and 1.0 Hz, J = 3.2 and 2.0 Hz, and J = 2.0 and 1.0 Hz, respectively, each 1 H). Anal. Calcd for $C_{15}H_{20}O_6$: C, 60.80; H, 6.80. Found: C, 60.88; H, 6.79.

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3-Acetylbicyclo[2.2.1]hept-5-ene-2-carboxaldehyde (10). A solution of **4** (98 mg, 1 mmol) and cyclopentadiene (132 mg, 2 mmol) was stirred in benzene (2 mL) at room temperature for 30 min. After evaporation of the solvent, **10** was obtained nearly quantitatively as a ca. 1:1 endo and exo mixture of stereoisomers: IR 2720, 1710 cm^{-1}; ^1H NMR δ 1.26–1.55 (m, 2 H), 2.18 and 2.26 (s, each 1.5 H), 2.85–3.50 (m, 4 H), 6.02–6.31 (m, 2 H), 9.58 and 9.83 (s, each 0.5 H). Anal. Calcd for $C_{10}H_{12}O_2$: C, 73.15; H, 7.37. Found: C, 73.20; H, 7.35.

Registry No. **4**, 34218-21-8; **5**, 129492-01-9; **6** (R = H), 4401-11-0; **7** (R = H), 129492-02-0; **8**, 719-00-6; **9**, 129492-03-1; **10** (isomer 1), 129568-34-9; **10** (isomer 2), 129568-35-0; *endo*-**11**, 129492-04-2; *exo*-**11**, 129492-12-2; *endo*-**12**, 129492-05-3; *endo*-**13**, 129492-06-4; *exo*-**13**, 129492-13-3; *endo*-**14**, 129492-07-5; *exo*-**14**, 129492-14-4; **15**, 129492-08-6; *endo*-**16**, 129492-09-7; *exo*-**16**, 129492-15-5; *endo*-**17**, 129492-10-0; *exo*-**17**, 129492-16-6; **18**, 129492-11-1; TMSOTf, 27607-77-8; $SnCl_4$, 7646-78-8; $TiCl_4$, 7550-45-0; cyclopentadiene, 542-92-7; furan, 110-00-9.

A New Route to N-Monosubstituted Thioamides Utilizing Phosphoramidothionates as Reagents for the Thioamidation of Carboxylic Acids

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Several *N*-monosubstituted thioamides have been synthesized from the corresponding carboxylic acid chlorides and primary amines by a new procedure. The procedure utilizes a commercially available and inexpensive organophosphorus reagent (dimethyl chlorothiophosphate) to derivatize the amine, form the carboxamide bond, and accomplish the thionation of the carbonyl by an intramolecular rearrangement. The phosphoryl group is then cleaved from the resulting thiocarbonyl phosphoryl mixed imide by a simple hydrolysis. Thioamides (RCSNHR′) containing a variety of functionality (R = simple alkyl, phenyl, bulky alkyl, cycloalkylalkyl, α,β-unsaturated, and alkyl with remote keto, ester, or amide carbonyl groups; R′ = methyl, benzyl, allyl) have been prepared by this method in generally high overall yields (50–80%). Competing thionation of remote carbonyl groups or epimerization of a chiral center containing a proton α to a ketone group was not observed.

Introduction

In addition to their wide use in agriculture, medicine, etc., thioamides (thiocarboxamides) undergo an assortment of chemical transformations[1] which make them attractive for synthetic applications. Recent papers have reported new methods for their oxidation to carbonyl compounds,[2] reduction to amines,[3] and conversions to nitriles,[4] thioimidates,[5] and amidines.[6] Numerous heterocycles have been generated by virtue of the dipolar nature of thioamides.[7] Other cyclization reactions have utilized electrophile-induced addition to olefins,[8] photochemistry,[9] and a novel trimethyl phosphite induced addition to an α-diketone.[10] Thioenolate anions of thioamides have been employed in a variety of condensation reactions[11] and stereoselective Michael additions to α,β-unsaturated ketones.[12]

A number of methods for the synthesis of thioamides have been reported.[1,13] Recently, N-substituted thioamides have been prepared from aliphatic ketones (extended Willgerodt–Kindler reaction),[14] nitroacetamides,[15] imine oxides,[16] α-keto acids,[17] orthoformates,[18] dimethyl thioformamide,[19] and unsubstituted thioamides.[20] From carboxylic acids, thioamides are most commonly generated by forming a carboxamide (via the acid chloride) and then treating with thionation agents such as phosphorus pentasulfide or Lawesson's reagent.[21] Treating acid chlorides with Lawesson's reagent followed by addition of an amine has also been described.[22]

We would like to report an alternative procedure for the synthesis of thioamides from carboxylic acids (via acid chlorides) and amines. The procedure utilizes a readily available phosphorochloridothionate reagent to derivatize the amine, form the carboxamide bond, and accomplish the thionation of the carbonyl by an *intramolecular* rearrangement. The resulting phosphoryl group is then cleaved by a simple hydrolysis. Scheme I shows the general pathway. The procedure uses rather mild conditions and

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