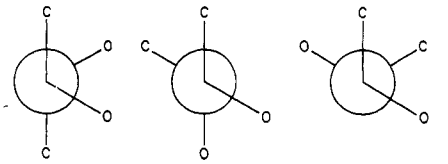
hexitol (**15b**) $J_{4,5} < J_{3,4}$. Both contain a considerable proportion of the planar form.

The hexaacetate (**20**) of D-glucitol assumes the $_2G^-$ form (ca. 60%), the $_3G^+$,$_4G^+$ form (ca. 40%), and very little of the planar form. The 2,3-diol (**20c**) and the 3,4-diol (**20a**) both have a much higher proportion (over 40%) of the planar form; $J_{2,3}$ is much smaller for the 2,3-diol and $J_{3,4}$ for the 3,4-diol than for the hexaacetate, suggesting the possible existence of hydrogen bonds between the hydroxyl groups.

(iv) 1,2-*erythro*-Diols. With one exception, the examples of this structural type all have the diol segment in the planar conformation when fully acetylated. Formation of a hydrogen bond in the diol would require a change into the sickle form. This does not happen; the diols are preponderantly in the planar form, the hydrogen bond not supplying sufficient energy for this change. Examples are 1,4,5-tri-*O*-acetylribitol (**12a**), 1,5,6-tri-*O*-acetyl-2-deoxy-D-*lyxo*-hexitol (**14b**), and 1,3,6-tri-*O*-acetyl-2-deoxy-D-*arabino*-hexitol (**17b**). The only exception is 1,2,3,4,7-penta-*O*-acetyl-*meso*-*glycero*-*gulo*-heptitol (**22d**), which has already been discussed; the heptaacetate assumes two sickle forms, of which the one capable of hydrogen-bond formation is favored by the diol.

(v) 1,4-Diols. There are only two examples of this type in the Moore collection. 1,3,4,6-Tetra-*O*-acetyl-D-mannitol (**19b**) is planar like the hexaacetate; there can be no hydrogen bond. For 1,3,4,6,7-penta-*O*-acetyl-*meso*-*glycero*-*gulo*-heptitol (**22c**), however, the $J_{3,4}$ value of 4.1 Hz suggests that some of the $_3G^-$ form is present, which would allow the formation of a hydrogen bond between O-2 and O-5.

The presence of two free hydroxyl groups therefore affects the conformation of partially acetylated alditols, by formation of an intramolecular hydrogen bond, in the following (decreasing) order: 1,3-*erythro*-diol, 1,3-*threo*-diol, 1,2-*threo*-diol, and 1,2-*erythro*-diol. The proportion of the hydrogen-bonded conformation, however, will depend on the configuration and conformation of the rest of the molecule, particularly on the number and nature of gauche interactions in the carbon chain. It appears that conformation A is more favorable for hydrogen-bond formation than conformation B. As already postulated by Mills,[7] conformation C is avoided by the molecules whenever possible.



Moore[8] noted that the coupling constants for vicinal methine protons generally become larger for anti (erythro) 1,2-protons and smaller for syn (threo) 1,2-protons when partially acetylated alditols were compared with fully acetylated alditols. The present paper explains this observation as being the consequence of the formation of hydrogen bonds in the partially acetylated alditols.

Synthesis of 3,4-Disubstituted 3,4-Dihydro-2-pyrones via 2-(Silyloxy)pyrylium Salts: Regioselective Introduction of Substituents into 2-Pyrones

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Silylation of 4,6-dimethyl- and 6-methyl-2-pyrone with *tert*-butyldimethylsilyl triflate affords the corresponding 2-(silyloxy)pyrylium triflates **2** quantitatively. Lithium diorganocuprates add regioselectively at position 4 of triflates **2** to give 4-substituted 2-(silyloxy)-4*H*-pyrans **4**. Compounds **4** react with electrophiles at position 3 to give 3-bromo- (**8**), 3-(silyloxy)- (**9**), 3-methylene- (**15**), and 3-(1-hydroxybutyl)-3,4-dihydro-2-pyrones (**16**).

Introduction

2-Pyrones and their dihydro derivatives play an important role in organic synthesis and occur in several types of natural products.[1] Most reported syntheses of 2-pyrones involve ring closure of a 5-keto acid derivative as the final step,[1] which imposes limitations on the substituents that can be attached to the 2-pyrone ring, especially at position 3. The direct addition of nucleophiles into 2-pyrones has had only limited success because of complex reactivities of 2-pyrones toward nucleophiles. For example, Grignard reagents attack position 2 or 4 of 2-pyrones, and the resulting adducts react further with the Grignard reagent to afford several products.[2] Ireland and coworkers have reported regioselective γ-addition of a Grignard reagent to 3-(methoxycarbonyl)-2-pyrone; the resulting adduct was used for the synthesis of lasalocid A.[3] The regioselective addition was attributed to stabilization of the carbanion generated at position 3 by the methoxycarbonyl group. Michael addition of pyrones with organocopper reagents is sluggish,[3] and our attempt to react 4,6-dimethyl-2-pyrone (**1a**) with lithium dibutylcuprate failed.

(1) (a) Stauton, J. *Compr. Org. Chem.* **1979**, *4*, 629. (b) Hepworth, J. D. *Compr. Heterocycl. Chem.* **1984**, *3*, 789.

(2) (a) Rouillier, P.; Gagnaire, D.; Dreux, J. *Bull. Soc. Chim. Fr.* **1966**, 689. (b) Montillier, J.-P.; Royer, J.; Dreux, J. *Bull. Soc. Chim. Fr.* **1970**, 1956. (c) Trolliet, M.; Longeray, R.; Dreux, J. *Tetrahedron* **1974**, *30*, 163. (d) Lhuste, P.; Morean, M.; Dreux, J. *Tetrahedron* **1984**, *40*, 1551 and references cited therein.

(3) Ireland, R. E.; McGavey, G. J.; Anderson, R. C.; Badoud, R.; Fitzsimmons, B.; Thaisrivongs, S. *J. Am. Chem. Soc.* **1980**, *102*, 6178.

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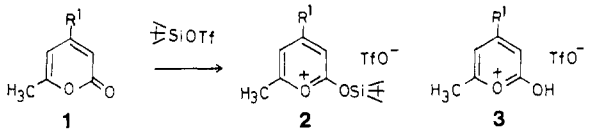
Table I. ^{1}H NMR Chemical Shifts of Ring Protons in 1-3[a]

compd	δ, ppm H-3	or	H-5	H-4
1a	5.87		5.94	-
2a	6.62		6.83	-
3a	6.80		6.93	-
1b	6.09		6.09	7.33
2b	6.59		6.69	7.91

[a] CD_3CN was used as a solvent.

We have found that the low reactivity of 2-pyrones toward organocopper reagents is enhanced by silylation with *tert*-butyldimethylsilyl triflate.[4] In this paper we describe the preparation of 2-(silyloxy)pyrylium salts **2**, addition of organocopper reagents at position 4 of **2**, and reactions of the resulting products **4** with some electrophiles.[5] The 4-alkenyl-3-bromo-3,4-dihydro-2-pyrones **8** obtained by bromination of **4** are useful intermediates for the preparation of 3-alkenyl-2-pyrones,[6] which are difficult to obtain by other methods.

Preparation of 2-(Silyloxy)pyrylium Salts 2. 2-(Silyloxy)pyrylium salts **2** were prepared by heating 2-pyrones with an equimolar amount of *tert*-butyldimethylsilyl triflate without solvent (eq 1). Triflates **2a**



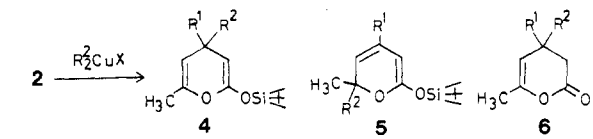
(1)

1a: R^1=Me
1b: R^1=H
2a: R^1=Me
2b: R^1=H
3a: R^1=Me

and **2b** were prepared by heating the mixtures at 110 °C for 1 h and at 0 °C for 10 min, respectively. Each reaction gave a homogeneous oil, which was used without purification for subsequent transformations.

The formation of **2** was clearly shown by the downfield shift of the signals of the ring protons of **2** compared with those of **1** (Table I). The difference in the chemical shifts between **2** and **1** was slightly less than that between the parent 2-pyrone (δ 6.38, 6.43, 7.56, 7.77) and the 2-methoxypyrylium salt (δ 7.56, 8.56).[7] The salts **2** were easily hydrolyzed by atmospheric moisture to *tert*-butyldimethylsilanol and the hydroxypyrylium salt **3**, which was also generated by addition of triflic acid to **1** (Table I). Salt **3** was characterized by the very low field hydroxy proton (δ 10.5). Pyrone **1** was regenerated from **2** and **3** by addition of triethylamine or 2,6-lutidine.

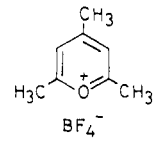
Reaction of 2 with Organocuprates $(R^2)_2CuX$. The results of the reaction of **2** with organocuprates are summarized in Table II. In most reactions, the substituent R^2 was introduced regioselectively at position 4 to produce 2-(silyloxy)-4*H*-pyrans **4**. These compounds are readily hydrolyzed on silica gel but could be isolated by chromatography on basic alumina. However, some of the nonvolatile hydrocarbons (homocoupling products of the cuprates) could not be separated (Table II, entries 1, 2, 6–10, 13, 14, 16). Although analytically pure samples of **4** could not be obtained, their ^{1}H NMR spectra confirmed the structural assignments. The C-3 proton in **4** appeared at δ 3.6–4.0 with rather large long-range coupling (J = 2–2.5 Hz) to the C-5 proton (δ 4.2–4.7, m).



(2)

4 5 6

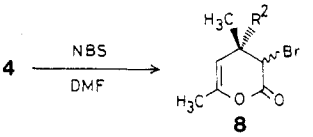
The following features of the reactions are apparent from Table II. (1) Only 4*H*-pyrans were obtained in reactions with aryl, alkenyl, and secondary alkyl cuprates. (2) primary alkyl or methyl cuprates gave mixtures of **4** and **5** (entries 9–12), but surprisingly, dimethylcuprate gave only **5j** in ether. (3) The geometry of the alkenyl group of the cuprates was completely retained in the reaction (entries 6 and 7).[8] (4) The lithium diorganocuprates reacted more efficiently than the cuprates prepared from Grignard reagents (entries 1 and 13). (5) Only hydrolyzed product **6l** was obtained in the reaction of the diisopropylcuprate prepared from a Grignard reagent (entry 15). Features 1, 2, and 4 are in contrast with our earlier finding that $R_2CuMgBr$ was as effective as R_2CuLi in reaction with 2,4,6-trimethylpyrylium tetrafluoroborate (**7**), in which the 1,2-adduct was a minor product in every case.[9] The difference probably reflects the lower reactivity of the silyloxy derivative **2** in comparison with **7**. Soft and bulky organocuprates prefer to attack position 4 selectively, as observed in the reactions of pyridinium salts with nucleophiles.[10]



7

It should be noted that the phosphine-complexed cuprates [(*E*)- and (*Z*)-$CH_3CH{=}CH]_2CuLi{\cdot}Bu_3P$, known to be effective for the conjugate addition to enones,[11] did not react with **2**.

Reaction of 4 with Electrophiles. We have recently found that 4-substituted 3-bromo-3,4-dihydro-2-pyrones **8** are useful precursors for the preparation of 3,4-disubstituted 2-pyrones.[6] We have now found that *N*-bromosuccinimide (NBS) in DMF reacts cleanly with **4** to give **8**.[12] The corresponding 5-bromo isomer was not detected (Table III). Bromination with bromine in DMF afforded a mixture of the 3- and 5-bromo derivatives.



(3)

8

The 3-bromo compound **8** was obtained as a mixture of diastereomers. From steric considerations, the major isomer was tentatively assigned trans stereochemistry, with the bromine atom trans to the introduced substituent R^2. This assignment was supported by the following facts. (1) An NOE of 8% was observed at H-3 (δ 4.25) and H-5 (δ 4.75) when a vinyl α-proton (δ 5.63) was irradiated in **8d** (major isomer), hence the vinyl group is cis to H-3 and

(4) For a preliminary communication on this subject, see: Kume, T.; Iwasaki, H.; Yamamoto, Y.; Akiba, K.-y. *Tetrahedron Lett.* **1987**, *28*, 6305.
(5) For reactions of silyl enol ethers and ketene silyl acetals, see: (a) Colvin, E. W. *Silicon in Organic Synthesis*; Butterworths: London, 1981; p 236. (b) Weber, W. P. *Silicon Reagents for Organic Synthesis*; Springer-Verlag: Berlin, 1983; p 206. (c) Brownbridge, P. *Synthesis* **1983**, 1. (d) Bakker, C. G.; Hazen, C. J. J. M.; Schreeren, J. W.; Nivard, R. J. F. *J. Org. Chem.* **1983**, *48*, 2736.
(6) Kume, T.; Akiba, K.-y. *J. Org. Chem.*, following paper in this issue.
(7) Piekle, W. H.; Dines, M. *J. Heterocycl. Chem.* **1969**, *6*, 313.
(8) Casey, C. P.; Boggs, R. A. *Tetrahedron Lett.* **1971**, 2455.
(9) Yamamoto, Y.; Kume, T.; Akiba, K.-y. *Heterocycles* **1987**, *26*, 1495.
(10) Akiba, K.-y.; Nishihara, Y.; Wada, M. *Tetrahedron Lett.* **1983**, *24*, 5269. Wada, M.; Nishihara, Y.; Akiba, K.-y. *Tetrahedron Lett.* **1985**, *26*, 3267. Akiba, K.-y.; Iseki, Y.; Wada, M. *Bull. Chem. Soc. Jpn.* **1984**, *57*, 1994.
(11) Posner, G. H. *Org. React. (N.Y.)* **1972**, *19*, 1.
(12) Reuss, R. H.; Hassner, A. *J. Org. Chem.* **1974**, *39*, 1785.

Scheme I

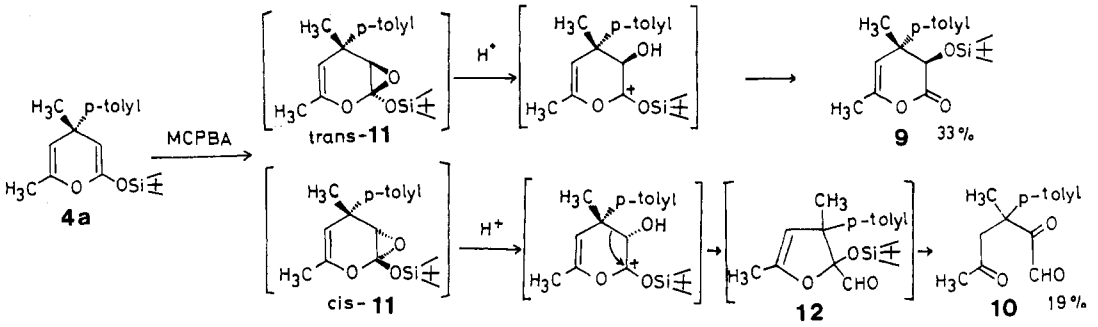


Table II. Synthesis of 2-(Silyloxy)-4*H*-pyrans 4 from 2 and Organocuprates

entry	2	organocuprate (1.2 equiv)	solvent	product	isolated yield, %	ratio 4/5
1	a	$(p\text{-}CH_3C_6H_4)_2CuLi$	THF/ether	4a	65	100/0
2	a	$(C_6H_5)_2CuLi$	THF/ether	4b	36	100/0
3	a	$(CH_3CH{=}CH)_2CuLi$[a]	THF/ether	4c	52[a]	100/0
4	a	$(CH_2{=}CH)_2CuLi$	THF/ether	4d	44	100/0
5	a	$[CH_2{=}C(CH_3)]_2CuLi$	THF/ether	4e	42	100/0
6	a	$[(E)\text{-}n\text{-}C_4H_9CH{=}CH]_2CuLi$	ether	4f	43[b]	100/0
7	a	$[(Z)\text{-}n\text{-}C_4H_9CH{=}CH]_2CuLi$	ether	4g	44[b]	100/0
8	a	$(sec\text{-}C_4H_9)_2CuLi$	ether/cyclohexane	4h	43	100/0
9	a	$(n\text{-}C_4H_9)_2CuLi$	ether/*n*-hexane	4i, 5i	65	57/43[c]
10	a	$(n\text{-}C_4H_9)_2CuLi$	ether/THF/*n*-hexane	4i, 5i	70	40/60[c]
11	a	$(CH_3)_2CuLi$	THF/ether	4j, 5j	53	38/62[c]
12	a	$(CH_3)_2CuLi$	ether	5j	50	0/100
13	a	$(p\text{-}CH_3C_6H_4)_2CuMgBr$	THF/ether	4a	28	100/0
14	a	$(p\text{-}CH_3OC_6H_4)_2CuMgBr$	THF/ether	4k	28	100/0
15	a	$(i\text{-}C_3H_7)_2CuMgBr$	THF/ether	6l	42	100/0
16	b	$(p\text{-}CH_3C_6H_4)_2CuLi$	THF/ether	4m	34	100/0
17	b	$[CH_2{=}C(CH_3)]_2CuLi$	THF/ether	4n	71	100/0

[a] Mixture of *E* and *Z* isomers. [b] The olefin geometry was retained. [c] The ratio was estimated from ^1H NMR data.

Table III. Bromination of 4 with NBS in DMF

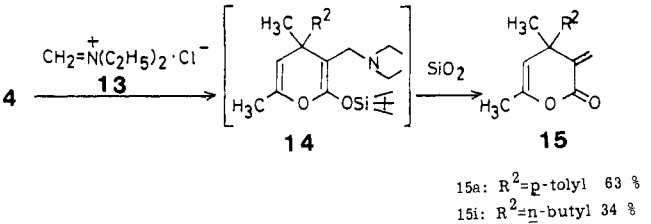
entry	R	ratio[a] *trans*-8/*cis*-8	product	yield, %
1	$p\text{-}CH_3C_6H_4$	85/15	8a	75
2	C_6H_5	86/14	8b	65
3	$p\text{-}CH_3OC_6H_4$	85/15	8k	80
4	(*E*)- and (*Z*)-$CH_3CH{=}CH$	*b*	8c	72
5	$CH_2{=}CH$	88/12	8d	56
6	$CH_2{=}C(CH_3)$	88/12	8e	57
7	$(E)\text{-}n\text{-}C_4H_9CH{=}CH$	89/11[c]	8f	92
8	$(Z)\text{-}n\text{-}C_4H_9CH{=}CH$	74/26[c]	8g	75

[a] Estimated from ^1H NMR data of the crude product. [b] Not determined. [c] Olefin geometry was retained completely.

trans to Br. (2) In the silver ion promoted rearrangement of **8** to the 3-substituted 2-pyrone,[6] R^2 of the major diastereomer migrated much faster than R^2 of the minor isomer (the neighboring-group participation is known to be favored by the trans σ-bond[13]). (3) In **8a–c**, isomerization of the minor diastereomer to the major one took place during purification by flash chromatography or TLC on silica gel. Thus the major diastereomer is kinetically and thermodynamically preferred. The trans/cis ratios in Table III are the kinetic ratios of the reactions.

Reaction of **4** with *m*-chloroperbenzoic acid (MCPBA) in hexane suspension at −30 to 0 °C afforded crystalline 3-(silyloxy)-2-pyrone **9** as a single diastereomer (33%) and α,δ-diketo aldehyde **10** (19%). The stereochemistry of **9** was also tentatively assigned as trans on the basis of stereochemical considerations. Possible mechanisms for the formation of **9** and **10** are shown in Scheme I. The initially formed epoxide *trans*-**11** undergoes acid-catalyzed ring opening followed by 1,4-silyl migration to give **9**. However, because of steric crowding in *cis*-**11**, skeletal contraction would be favored to give intermediate **12**, which hydrolyzes to **10** during workup.

Scheme II



Reaction of **4a** and **4i** with iminium salt **13** (2 equiv) in THF at room temperature gave adducts **14**. Attempted chromatography of **14** on silica gel directly afforded α-methylene δ-lactone derivatives **15** in moderate yields (Scheme II). The intermediate adduct **14i** was detected by ^1H NMR in the crude reaction product of **4i** with **13**. The facile elimination of the amino group was unexpected in view of the reported two-steps conversion of similar Mannich bases to the corresponding α-methylene carbonyl compounds.[14] The elimination may be caused by steric crowding in **14** or by intramolecular reaction of the amino group with the silyl group. This reaction provides a facile route to α-methylene δ-lactone derivatives that may have useful biological activity.[15]

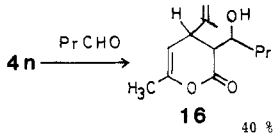
Compounds **4a–k**, which bear two substituents at position 4, did not react with other electrophiles examined. Thus Lewis acid catalyzed alkylation,[16] aldol condensa-

(13) Pelter, A.; Ward, R. S.; Balasubramanian, M. *J. Chem. Soc., Chem. Commun.* **1976**, 151.

(14) Danishefsky, S.; Prisvilla, M.; Lipisko, B. *Tetrahedron Lett.* **1980**, *21*, 805.

(15) For a review of the synthesis of α-methylene lactones, see: Grieco, P. A. *Synthesis* **1975**, 67.

tion,[17] and acylation induced by fluoride ion and triethylamine[18] were all unsuccessful, leading only to 2-pyrone **6**. On the other hand, **4n**, with only one substituent at position 4, reacted with butanal in the presence of $TiCl_4$ to give **16** in moderate yield (eq 4). Thus steric hindrance at position 4 severely retards the reactivity of **4** with electrophiles.



16 40 % (4)

Experimental Section

Melting points were taken on a Yanagimoto micro melting point apparatus and are uncorrected. IR, ^1H NMR, and mass spectra were obtained on Hitachi 215, Hitachi R-90H, and Hitachi RMU-6L spectrometers, respectively. High-resolution mass spectra were recorded on a JEOL D-300 spectrometer. Commercial *N*-bromosuccinimide (NBS) and *m*-chloroperbenzoic acid (MCPBA) were used without purification. Bromobenzene, *p*-bromoanisole, vinyl bromide, 1-bromopropene (*E* and *Z* mixture), 2-bromo-1-propene, *n*-butyl bromide, isopropyl bromide, and *N,N*-dimethylformamide (DMF) were distilled from CaH_2. (*E*)-1-Hexenyl bromide,[19] 4,6-dimethyl-2-pyrone,[20] *tert*-butyldimethylsilyl triflate,[21] tetrakis(tri-*n*-butylphosphine)copper(I) iodide,[22] and *N,N*-diethyl-*N*-methyleneammonium chloride[23] were prepared according to the literature. Phenyllithium,[24] vinyllithium,[25] 1-propenyllithium (*E* and *Z* mixture),[26] 2-propenyllithium,[26] and *n*-butyllithium[27] in ether were prepared as reported; the concentration was determined by titration with a standard solution of 2-butanol in xylene with *o*-phenanthroline as an indicator.[28] *n*-Butyllithium in hexane, *sec*-butyllithium in cyclohexane, and methyllithium in ether were obtained from Kanto Chemicals and Aldrich.

(*E*)-1-Hexenyllithium. A solution of (*E*)-1-hexenyl bromide (6.87 g, 42.2 mmol) in ether (28 mL) was added dropwise to small chips of lithium metal (0.537 g, 77.3 mg-atom) in ether (33 mL) with stirring under nitrogen. The addition of the bromide solution was continued slowly gentle reflux maintained (exothermic reaction). After addition was complete, the mixture was stirred for an additional 1 h at room temperature and allowed to stand overnight at −20 °C. The concentration was 0.468 M (78% of the theoretical).

Preparation of 2-(Silyloxy)pyrylium Salts 2a and 2b. General Procedure. Into a two-necked round-bottomed flask equipped with a rubber septum and a gas inlet tube with a stopcock was placed 2-pyrone **1a** or **1b** (12.0 mmol). *tert*-Butyldimethylsilyl triflate (2.75 mL, 12.0 mmol) was added dropwise to the compound via syringe. After addition was complete, the mixture was stirred at 110 °C for 1 h (**2a**) or at 0 °C for 10 min (**2b**). The resulting 2-(silyloxy)pyrylium salt (oil) was used directly for reactions with lithium diorganocuprates.

2-[(*tert*-Butyldimethylsilyl)oxy]-4,6-dimethylpyrylium trifluoromethanesulfonate (2a): ^1H NMR (CD_3CN) δ 0.46 (s, 6 H), 0.99 (s, 9 H), 2.37 (s, 3 H), 2.44 (s, 3 H), 6.62 (s, 1 H), 6.83 (s, 1 H).

2-[(*tert*-Butyldimethylsilyl)oxy]-6-methylpyrylium trifluoromethanesulfonate (2b): ^1H NMR (CD_3CN) δ 0.50 (s, 6 H), 1.02 (s, 9 H), 2.43 (t, *J* = 0.7 Hz, 3 H), 6.59 (dq, *J* = 9.0, 0.7 Hz, 1 H), 6.69 (dq, *J* = 7.0, 0.7 Hz, 1 H), 7.91 (dd, *J* = 7.0, 9.0 Hz, 1 H).

Reaction of 2-(Silyloxy)pyrylium Salts 2 with Lithium Diorganocuprates. General Procedure. (Table II, entries 1–6.) To a cold (−70 °C) suspension of cuprous iodide (2.74 g, 14.4 mmol) in 23 mL of THF was added dropwise the organolithium reagent in ether/THF (ca. 1/5–3/5). After addition was complete, the mixture was warmed to −30 °C and stirred for ca. 1 h and then cooled to −70 °C. The resulting cuprate solution was rapidly transferred to a cold (−70 °C) suspension of a (silyloxy)pyrylium salt **2** in ether (24 mL) through a double-ended needle. The mixture was allowed to warm to room temperature and then poured into ice-cooled 5% aqueous Na_2CO_3 (150 mL). The mixture was filtered through Celite. The filtrate was extracted with ether (150 mL × 2), and the organic extracts were combined, dried over 4A molecular sieves under a nitrogen atmosphere, and evaporated to give the crude product. Flash chromatography [basic Al_2O_3, *n*-pentane/ethyl acetate = 19/1–19/5 (v/v) as an eluent] afforded the 4-substituted 4,6-dimethyl-2-[(*tert*-butyldimethylsilyl)oxy]-4*H*-pyran **4**. Quick operation was necessary to avoid decomposition of **4** on the column.

2-[(*tert*-Butyldimethylsilyl)oxy]-4,6-dimethyl-4-[(*Z*)-1-hexenyl]-4*H*-pyran (4g). (Table II, entry 7.) To a slurry of 27.0 mmol of **2a** in ether (30 mL) was added 32.1 mmol of ethereal lithium di[(*Z*)-1-hexenyl]cuprate solution, which was prepared at −78 °C according to the literature.[29] The resulting mixture was warmed to room temperature. After workup and purification as above, **4g** (3.69 g, 44%) was obtained as a pale yellow oil containing 2.4 g of (*Z,Z*)-5,7-dodecadiene (the yield of **4g** was calculated from ^1H NMR data of the mixture). The ^1H NMR spectrum showed no peak assignable to the *E* isomer (vide infra). ^1H NMR ($CDCl_3$): δ 0.19 (s, 6 H), 0.95 (s, 9 H), 0.73–1.00 (m, 3 H), 1.13 (s, 3 H), 1.10–1.50 (m, 4 H), 1.76 (d, *J* = 1.0 Hz, 3 H), 1.95–2.34 (m, 2 H), 3.83 (d, *J* = 2.0 Hz, 1 H), 4.36–4.48 (m, 1 H), 5.15–5.58 (m, 2 H).

2-[(*tert*-Butyldimethylsilyl)oxy]-4,6-dimethyl-4-*sec*-butyl-4*H*-pyran (4h). (Table II, entry 8.) To 1.37 g (7.2 mmol) of cuprous iodide in 20 mL of ether at −78 °C was added 13.75 mL of 1.05 M (14.4 mmol) *sec*-butyllithium. The dark mixture was warmed to −48 °C and then stirred for 35 min. The blue-black solution was recooled to −78 °C and rapidly transferred to a suspension of **2** (6.0 mmol) in 12 mL of ether at −78 °C. The reaction mixture was allowed to warm to room temperature, followed by the usual workup and purification to give 761 mg (43%) of **4h** as a mixture of diastereomers. ^1H NMR (acetone-d_6): δ 0.19 (s, 6 H), 0.96 (s, 9 H), 0.61–1.13 (m, 9 H), 1.04 (s, 3 H), 1.76 (br s, 3 H), 3.64, 3.69 (d, *J* = 2.2 Hz, 1 H), 4.26–4.42 (m, 1 H).

Reaction of 2a with Cuprate Prepared from Grignard Reagents. General Procedure. (Table II, entries 13 and 14.) A cuprate in 115 mL of THF/ether (v/v = 12/11) was prepared from 15.0 mmol of cuprous iodide and 30 mmol of Grignard reagent and added to 16.0 mmol of **2a** in 25 mL of ether at −78 °C. The resulting mixture was allowed to warm to room temperature, followed by the usual workup and purification to give 4*H*-pyran **4** as a mixture with the biaryl.

4-Isopropyl-4,6-dimethyl-3,4-dihydro-2-pyrone (6l). A reaction procedure similar to that used above was employed. Analysis of the crude product by ^1H NMR revealed that **6l** was mainly produced while no signal that could be assigned to the corresponding 2-(silyloxy)-4*H*-pyran was observed. Purification by flash column chromatography on silica gel [*n*-hexane/ethyl acetate = 9/1 (v/v) as an eluent] afforded **6l** in 42% yield as a pale yellow oil. ^1H NMR ($CDCl_3$): δ 0.89 (d, *J* = 6.6 Hz, 6 H), 1.01 (s, 3 H), 1.25–1.90 (m, 1 H), 1.88 (d, *J* = 1.3 Hz, 3 H), 2.25 (dd, *J* = 15.6, 0.7 Hz, 1 H), 2.52 (d, *J* = 15.6 Hz, 1 H), 4.83 (m, 1 H). The chemical shifts were identical with the reported data.[2b] Mass spectrum: *m/z* 168 (M^+), 125 (base peak), 112, 97, 55.

Reaction of 2-(Silyloxy)-4*H*-pyrans 4 with *N*-Bromosuccinimide (NBS) in *N,N*-Dimethylformamide. General

(16) For a review of Lewis acid induced α-alkylation of carbonyl compounds, see: Reetz, M. T. *Angew. Chem., Int. Ed. Engl.* **1982**, *21*, 96.
(17) Mukaiyama, T.; Banno, K.; Narasaka, K. *J. Am. Chem. Soc.* **1974**, *96*, 7503.
(18) Rathke, M. W.; Sullivan, D. F. *Tetrahedron Lett.* **1973**, 1297.
(19) Zweifel, G.; Whitney, C. C. *J. Am. Chem. Soc.* **1967**, *89*, 2753.
(20) Anschutz, R.; Bendix, P.; Kerp, W. *Justus Liebigs Ann. Chem.* **1890**, *259*, 148.
(21) Corey, E. J.; Cho, H.; Rucker, C.; Hua, D. H. *Tetrahedron Lett.* **1981**, *22*, 3455.
(22) Kauffman, G. B.; Teter, L. A. *Inorg. Synth.* **1963**, *7*, 9.
(23) Rochin, C.; Babot, O.; Dunogues, J.; Duboudin, F. *Synthesis* **1986**, 228.
(24) Jones, R. G.; Gilman, H. *Org. React. (N.Y.)* **1951**, *6*, 353.
(25) Seyferth, D.; Weiner, M. A. *J. Am. Chem. Soc.* **1961**, *83*, 3583.
(26) Brande, E. A.; Coles, J. A. *J. Chem. Soc.* **1951**, 2078.
(27) Jones, R. G.; Gilman, H. *Org. React. (N.Y.)* **1951**, *6*, 352.
(28) Watson, S. C.; Eastham, J. F. *J. Organomet. Chem.* **1967**, *9*, 165.
(29) (a) Alexakis, A.; Cahiez, G.; Normant, J. F. *J. Organomet. Chem.* **1979**, *177*, 293. (b) Alexakis, A.; Cahiez, G.; Normant, J. F. *Org. Synth.* **1983**, *62*, 1.

Procedure. To 10.0 mmol of **4** in 20 mL of DMF at −30 °C was added dropwise a solution of NBS (10.0 mmol) in 10 mL of DMF. After addition was complete, the reaction mixture was slowly warmed to 0 °C and poured into ice-cooled water (80 mL). The mixture was extracted with ether (3 × 50 mL), and the organic layers were collected, washed with water (4 × 30 mL), and dried over $MgSO_4$. The solvent was removed in vacuo, and the residue was separated by flash column chromatography on silica gel with *n*-hexane/ethyl acetate [19/1 (v/v)] to afford **8**. The trans/cis ratio was determined by ^1H NMR of the mixture before chromatography.

Reaction of 4a with *m*-Chloroperbenzoic Acid (MCPBA). A solution containing 1.8 mmol of **4a** in 7.0 mL of *n*-hexane was added dropwise to a precooled (−30 °C), stirred solution of 1.8 mmol of MCPBA in 7.0 mL of *n*-hexane. After addition was complete, the resulting slurry was stirred for 1 h at −30 °C and then warmed to room temperature for 1 h. After filtration of the mixture to remove the bulk of the *m*-chlorobenzoic acid formed in the reaction, the solvent was removed in vacuo to give 620 mg of crude product. Part of the crude product (203 mg) was separated by TLC (SiO_2, *n*-hexane/ethyl acetate = 9/1 as an eluent) to give **9** (67 mg, 33%) and **10** (26 mg, 19%).

Reaction of 4 with an Iminium Salt (13). General Procedure. To a suspension of 2.48 mmol of *N,N*-diethyl-*N*-methyleneammonium chloride (**13**) in 2.0 mL of THF was added 1.31 mmol of **4** in 2.0 mL of THF at room temperature. The reaction mixture was stirred for 9 h and then poured into 25 mL of ice-cooled 5% aqueous Na_2CO_3. The mixture was extracted with CH_2Cl_2. The organic layer was dried over $MgSO_4$ and evaporated to give the crude product, which was purified by TLC (*n*-hexane/ethyl acetate = 8/2 as an eluent).

4-*n*-Butyl-4,6-dimethyl-3-methylene-3,4-dihydro-2-pyrone (15i). The ^1H NMR spectrum of the crude product indicated that 4-*n*-butyl-3-[(*N,N*-diethylamino)methyl]-4,6-dimethyl-4*H*-pyran (**14i**) was mainly produced, but **14i** underwent deamination during purification by TLC (*n*-hexane/ethyl acetate = 9/1) to afford **15i** (34%).

Reaction of 4n with *n*-Butanal in the Presence of $TiCl_4$. To a suspension of *n*-butanal (0.15 mL, 1.65 mmol) and $TiCl_4$ (0.18 mL, 1.65 mmol) in 20 mL of CH_2Cl_2 was added 1.65 mmol (439 mg) of **4n** in 10 mL of CH_2Cl_2 at −78 °C. After the reaction mixture was stirred for 1 h at −78 °C, 2 mL of water was added to the mixture, which was then warmed to room temperature. The organic layer was washed with aqueous saturated NaCl solution, and the water layer was extracted with ether. The combined organic layer was dried over $MgSO_4$ and evaporated to give the crude product, which was purified by TLC (*n*-hexane/ethyl acetate = 8/2 as an eluent) to give 3-(1-hydroxybutyl)-6-methyl-4-(2-propenyl)-3,4-dihydro-2-pyrone (**16**) as a pale yellow oil (40%).

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Supplementary Material Available: Table 4 listing ^1H NMR data for **4** and **5**, Table 5 listing IR data and elemental analyses or HR mass spectral data for **8**, Table 6 listing ^1H NMR and mass spectral data for **8**, Table 7 listing IR data and elemental analyses or HR mass spectral data for **9**, **15**, and **16**, and Table 8 listing ^1H NMR and mass spectral data for **9**, **10**, and **14–16** (7 pages). Ordering information is given on any current masthead page.

Silver Ion Promoted Rearrangement of 4-Aryl- and 4-Alkenyl-3-bromo-4,6-dimethyl-3,4-dihydro-2-pyrones

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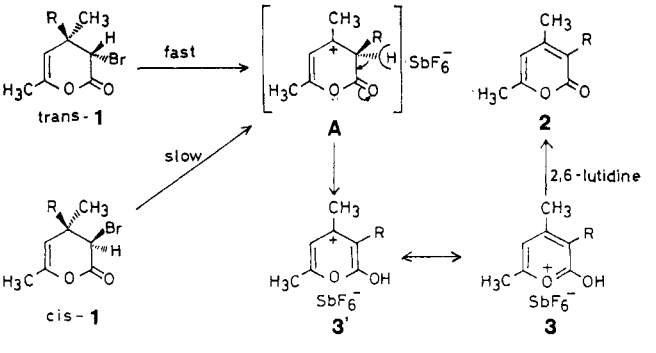
Debromination of 4-aryl- or 4-alkenyl-3-bromo-4,6-dimethyl-3,4-dihydro-2-pyrone **1** with $AgSbF_6$ in CH_2Cl_2 or $ClCH_2CH_2Cl$ induced migration of the aryl or alkenyl group, giving the corresponding 3-substituted 2-pyrones **2**. A 2-hydroxypyrylium salt **3** was detected in the reaction mixture by ^1H and ^{13}C NMR and was converted to **2** by treatment with 2,6-lutidine. Evidence that the rearrangement of **1** to **3** is concerted is provided by the complete retention of stereochemistry in the migrating alkenyl group and by trans specificity of the starting **1**. The 3-alkenyl group of **2** can be epoxidized with MCPBA.

Introduction

Although 2-pyrones are useful synthesis intermediates,[1] general methods for preparing 3-substituted 2-pyrones are lacking.[2] In particular, the 2-pyrone ring does not survive direct substitution at C-3 under basic conditions.[3]

Scheme I



α-Aryl and α-alkenyl carbonyl compounds can be synthesized by Favorskii,[4] pinacol,[5] or Wagner–Meerwein[6]

(1) (a) Shusherina, N. P. *Russ. Chem. Rev.* **1974**, *43*, 851. (b) Ireland, R. E.; Anderson, R. C.; Badoud, R.; Fitzsimmons, B. J.; McGarvey, G. J.; Thaisrivongs, S.; Wilcox, C. S. *J. Am. Chem. Soc.* **1983**, *105*, 1988. (c) Corey, E. J.; Watt, D. S. *J. Am. Chem. Soc.* **1973**, *95*, 2303. (d) Jung, M. E.; Hagenah, J. A. *J. Org. Chem.* **1987**, *52*, 1889. (e) Posner, G. H.; Wettlaufer, D. G. *Tetrahedron Lett.* **1986**, *27*, 667. (f) Posner, G. H.; Wettlaufer, D. G. *J. Am. Chem. Soc.* **1986**, *108*, 7373. (g) Boger, D. L.; Mullican, M. D. *J. Org. Chem.* **1984**, *49*, 4033; **1984**, *49*, 4045. (h) Dieter, R. K.; Fishpaugh, J. R. *J. Org. Chem.* **1987**, *52*, 923. (i) Poulton, G. A.; Cyr, T. D. *Can. J. Chem.* **1982**, *60*, 2821. (j) Carpenter, T. A.; Jenner, P. J.; Leeper, F. J.; Stauton, J. *J. Chem. Soc., Chem. Commun.* **1980**, 1227. (k) Posner, G. H.; Harrison, W.; Wettlaufer, D. G.; *J. Org. Chem.* **1985**, *50*, 5041.

(2) For a review of synthesis of 2-pyrone derivatives, see: Hepworth, J. D. *Compr. Heterocycl. Chem.* **1984**, *3*, 789.

(3) Harris, T. M.; Wachter, M. P.; Wiseman, G. A. *J. Chem. Soc., Chem. Commun.* **1969**, 177.

(4) Tsuchihashi, G.; Kitajima, K.; Mitamura, S. *Tetrahedron Lett.* **1981**, *22*, 4305.

0022-3263/89/1954-1935$01.50/0