Silver Ion-induced Allylation of Furan with Cyclopropyl Halides

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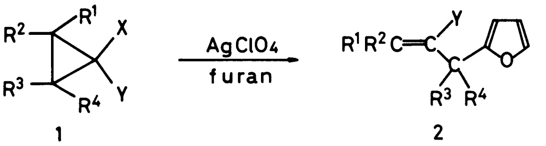
Synopsis. Allyl species generated from 1-bromo-2-phenylcyclopropane and seven different 1,1-dihalocyclopropanes with the aid of silver perchlorate reacted with furan in a regio- and stereoselective manner to give a series of 2-allylfuran derivatives in fair to good yields.

The S_N1 like reactions of cyclopropyl halides generally proceed *via* a stereoelectronically controlled ring-opening rearrangement to allyl cation intermediates.[1,2] Although this unique behavior of cyclopropyl halides provides a useful synthetic route to cyclic alkenes which are not readily accessible by other methods,[3] only a few examples have been reported on the reactions between the allyl species formed from cyclopropyl halides and substrates other than solvent nucleophiles.[4] Trapping of such the species by furan seems to be of synthetic interest in view of the fact that direct alkylation reactions of furan including allylation often cause extensive resinification.[5,6] We here report the results of the silver ion-induced reaction of furan with various cyclopropyl halides **1a—h**.



1 2

a R¹—R⁴=Me, X = Y = Br
b R¹—R³=Me, R⁴=H, X=Y=Br
c R¹=R²=Me, R³=R⁴=H, X=Y=Br
d R¹=Ph, R²=Me, R³=R⁴=H, X=Y=Br
e R¹=Ph, R²—R⁴=H, X=Y=Br
f R¹=n-Pr, R²—R⁴=H, X=Y=Br
g R¹—R⁴=Me, X = Y = Cl
h R¹=Ph, R²—R⁴=H, X=Br, Y=H

On exposure to silver perchlorate in THF/ether (1:3), 1,1-dibromo-2,2,3,3-tetramethylcyclopropane (**1a**) rapidly reacted with furan at room temperature to give 2-(2-bromo-1,1,3-trimethyl-2-butenyl)furan (**2a**) in 40% isolated yield together with 3-bromo-2,4-dimethyl-1,3-pentadiene (35%) which was shown to be the principal product in the absence of furan. Allyl species formed from cyclopropyl halides **1b—h** and silver perchlorate also reacted with furan to give the corresponding 2-allylfuran derivatives **2b—h** in moderate to good yields. The results are given in Table 1. Typical experimental procedure consists of treating a halide (**1**, 10 mmol) with silver perchlorate (2 equiv.) in THF/ether (1:3) in the presence of excess furan (*ca.* 5 equiv.) and calcium carbonate (as a buffer) at ambient temperature or under reflux.

Among 1,1-dihalocyclopropanes **1a—g**, ease of the reaction decreased in the order **1a**>**1b**≫**1c—g** and prolonged exposure to silver perchlorate was needed for the last series of halides. A marked difference in reactivity was also seen between the two stereoisomers of a cyclopropyl bromide **1h**. Thus, when a mixture of (*E*)-and (*Z*)-**1h** (1:1.47) was treated with silver perchlorate in the presence of furan in THF/ether (1:3) under reflux for 30 min, the (*E*)-isomer was completely consumed to give *trans*-**2h** in excellent yield, whereas the (*Z*)-isomer remained unchanged, in accord with the theoretical prediction.[1]

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Unsymmetrical halides **1b—f** and **1h** are expected to give a regioisomeric product **3** besides **2** but actually, furan preferentially reacted with the less heavily alkylated (or arylated) carbon site of the allyl species generated from these halides yielding **2** as the exclusive product. It should be noted, however, that the silver ion-induced reaction of these halides with methanol in place of furan gave the corresponding methyl ethers of type **3** as the major product.[7] Table 2 shows the change in regioselectivity in the silver ion-induced reaction of **1b** with various substrates. In contrast to methanol, *t*-butyl alcohol preferred the secondary carbon site rather than the tertiary site of the allyl species **4** formed from **1b**. Presumably, a small nucleophile such as methanol would preferentially react with the most electron positive site but the steric effects must be the major factor to control selectivity for bulky substrates including aromatic rings.

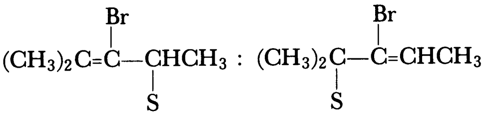
It is also worth stating that besides the stereospecific conversion of (*E*)-**1h** to *trans*-**2h**, the formation of **2** from **1d—f** was highly stereoselective yielding a single

TABLE 1. SILVER ION-INDUCED REACTION OF FURAN WITH CYCLOPROPYL HALIDES

Halide	Conditions[a]	Yield/% of **2** (*Z*/*E*)[b]
1a	rt, 1 h	40[c]
1b	rt, 1 h	76
1c	reflux, 6 h	73
1d	reflux, 6 h	73 (8.7)
1e	reflux, 6 h	61 (*Z*)[d]
1f	reflux, 6 h	54 (*Z*)[e]
1g	reflux, 6 h	60[f]
1h[g]	reflux, 0.5 h	37, 93 (*E*)[h]

a) Reactions were carried out in THF/ether (1:3) by stirring a mixture of **1**, silver perchlorate (2—3 equiv), furan (*ca.* 5 equiv), and calcium carbonate under conditions given. b) Isolated yield. c) 3-Bromo-2,4-dimethyl-1,3-pentadiene was also formed (35%). d) A mixture of **2e** and **3e** in the ratio 8.4:1. e) A mixture of **2f** and **3f** in the ratio 24:1. f) 3-Chloro-2,4-dimethyl-1,3-pentasiene was also formed (25%). g) (*Z*)/(*E*)=1.47. h) Corrected for the recovery of (*Z*)-**1h** which remained unchanged.

Table 2. Regioselectivity in the silver ion-induced reactions of **1b**[a)]

Nucleophile (S-H)	 $(CH_3)_2C{=}C(Br){-}CH(S)CH_3$: $(CH_3)_2C(S){-}C(Br){=}CHCH_3$
Furan	≈100:0
Anisole[b)]	≈100:0
MeOH[c)]	36:64
i-PrOH[c)]	54:46
t-BuOH[c)]	80:20

a) Reaction were carried out in THF/ether (1:3) using **1b**, silver perchlorate, and a nucleophile in the molar ratio 1:2:5 (0 °C, 45 min). b) A mixture of *p*- and *o*-isomers (1.9:1) was obtained in 82% yield. c) The corresponding ethers were formed in high yields.

stereoisomer or near so. The (*Z*)-structure may be deduced for the abundant isomer from the reported stereochemical observation on the Ag(I)-induced solvolysis of 1,1-dihalocyclopropanes.[2)] This was in fact true and the reductive dehalogenation of **2e** with LAH in boiling THF[8)] gave *trans*-**2h** as the principal product. These results are explicable in terms of the stereocontrolled ring-opening formation of (*Z*)-allyl cations from **1d**—**f** in preference to the isomeric (*E*)-cations.[1,9)]

Experimental

NMR spectra were determined in carbon tetrachloride using a Hitachi R-600 spectrometer. IR spectra were recorded on a Hitachi 260-10 spectrophotometer.

Silver Perchlorate-Induced Reaction of Furan with Cyclopropyl Halides. The following procedure for the preparation of 2-(2-bromo-1,3-dimethyl-2-butenyl)furan (**2b**) is representative.

Into a stirred mixture of silver perchlorate (4.05 g, 20 mmol), furan (3.5 g), and calcium carbonate (2 g) in THF/ether (1:3, 20 ml) was added a solution of 1,1-dibromo-2,2,3-trimethylcyclopropane (**1b**, 2.36 g, 9.8 mmol) in ether (2 ml) during the period of 15 min at room temperature. The mixture was stirred for additional 45 min at ambient temperature and quenched with saturated sodium chloride solution. A crude oil obtained after usual workup was distilled to give an allylfuran **2b** (1.76 g, 76%): bp 95—98 °C (14 Torr: 1=Torr 133.3 Pa); IR 3130, 1650, 1505, 1150, 1080, 1010, 910 and 740 cm^{-1}; NMR δ=1.40 (3H, d, J=7 Hz), 1.92 (6H, s), 4.17 (1H, q, J=7 Hz), 6.00 (1H, m), 6.20 (1H, m), and 7.24 (1H, m). Found: C; 52.31, H; 5.74%. Calcd for $C_{10}H_{13}BrO$: C; 52.42, H; 5.72%.

Similarly, furan derivatives **2a** and **2c**—**h** were obtained and characterized. They showed IR bands near 3130, 1640, 1505, 1150, 1010, 920, and 730cm^{-1} and NMR signals of the furan ring protons near δ=6.0, 6.2, and 7.2. **2a**: NMR δ=1.20 (3H, s), 1.52 (6H, s), and 1.84 (3H, s). **2c**: bp 97—98 °C (17 Torr); NMR δ=1.90 (6H, s), 3.80 (2H, s) (Found: C; 50.22, H; 5.20%). **2d** (as a mixture of (*E*)- and (*Z*)-isomers in the ratio 1:8.7): bp 114—117 °C (3 Torr); NMR (signals of the less abundant isomer were shown in italics.) δ=*2.17* (s) and 2.21 (s) (together 3H), 3.66 (s) and *3.97* (s) (together 2H), and 7.22 (5H, s). **2e**+**3e** (8.4:1): bp 123—126 °C (2 Torr); NMR for **2e** δ=3.90 (2H, s), 6.72 (1H, s), and 7.2—7.6 (5H, m) (Found: C; 59.03, H; 4.14%), and for **3e** δ=4.99 (1H, s), 5.45 (1H, s), 5.67 (1H, s), and 7.26 (5H, s). **2f**+**3f** (24:1): bp 96—100 °C (14 Torr); NMR for **2f** δ=0.92 (3H, t, J=7 Hz), 1.44 (2H, m), 2.18 (2H, q, J=7 Hz), 3.70 (2H, s), and 5.19 (1H, t, J=6 Hz) (Found: C; 52.18, H; 5.74%), and for **3f** δ=0.95—2.0 (7H, m), 3.56 (1H, t, J=7 Hz), 5.45 (1H, broad s), and 5.65 (1H, broad s). **2g**: bp 85—87 °C (15 Torr); NMR δ=1.23 (3H, s), 1.52 (6H, s), and 1.86 (3H, s) (Found: C; 66.60, H; 7.68%). **2h**: NMR δ=3.51 (2H, d, J=5 Hz), 5.98 (1H, m) 6.18—6.32 (2H, m), 6.60 (1H, d, J=16 Hz), and 7.2—7.4 (6H, m).

*Reduction of **2b**, **2e**, and **2f** with LAH.* A mixture of **2b** (1.28 g, 15.6 mmol) and LAH (0.5 g) in THF (10 ml) was heated under reflux for 5 h. A crude oil (801 mg) obtained after workup was distilled to give 2-(1,3-dimethyl-2-butenyl)furan (450 mg): bp 105—109 °C (92 Torr); IR 1590, 1010, and 730 cm^{-1}. NMR δ=1.27 (3H, d, J=7 Hz), 1.70 (6H, s), 3.65 (1H, m), 5.15 (1H, d, J=8 Hz), 5.85 (1H, m), 6.15, (1H, m), and 7.20 (1H, m) (Found: C; 79.82, H; 9.42%).

Similarly, **2e** and **2f** were reduced to **2h** and 2-(2-hexenyl)furan, respectively. NMR of the latter compound: δ=1.90 (3H, t, J=7 Hz), 1.42 (2H, m), 2.00 (2H, m) , 3.30 (2H, m), 5.4—5.6 (2H, m), 5.87 (1H, m), 6.16 (1H, m), and 7.20 (1H, m).

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