Tetrahedron Letters,Vol.29,No.31,pp 3825-3828,1988 0040-4039/88 $3.00 + .00
Printed in Great Britain Pergamon Press plc

SYNTHESIS OF 3-ARYL- OR 3-ALKENYL-4,6-DIMETHYL-2-PYRONES BY SILVER ION PROMOTED REARRANGEMENT OF 4-ARYL- OR 4-ALKENYL-3-BROMO-4,6-DIMETHYL-3,4-DIHYDRO-2-PYRONES

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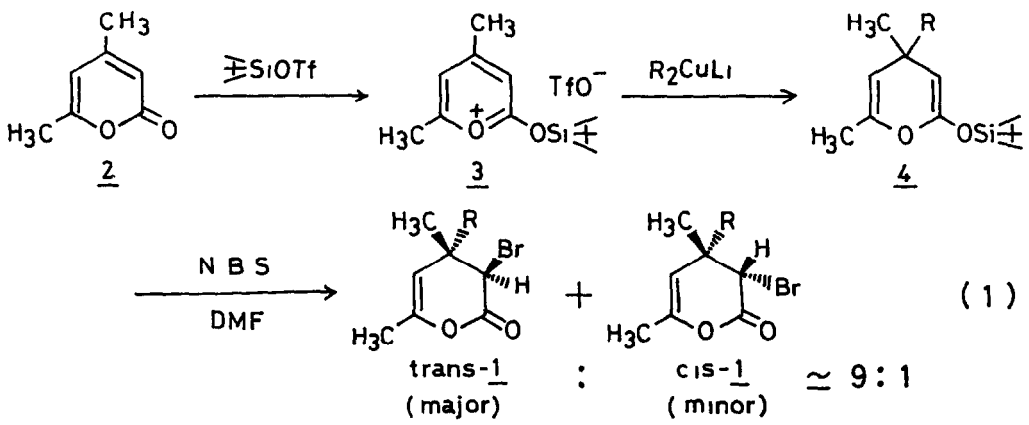
Abstract: Debromination of 4-aryl- or 4-alkenyl-3-bromo-4,6-dimethyl-3,4-dihydro-2-pyrone (1) with $AgSbF_6$ in dichloromethane or 1,2-dichloroethane induced rearrangement of the aryl or alkenyl group to the 3-position to afford the corresponding 3-substituted 2-pyrone (6) in high yield.

In a continuation of our study on the regiospecific introduction and transformation of substituents on oxygen-containing heterocyclic systems via pyrylium salts,[1] we now found that 3-aryl- or 3-alkenyl-2-pyrones (6) were readily prepared from silver ion promoted rearrangement of the corresponding 4-aryl- or 4-alkenyl-3-bromo-4,6-dimethyl-3,4-dihydro-2-pyrones (1) (scheme I). This reaction represents a novel synthesis of 3-substituted 2-pyrones which have been hardly obtained from usual synthetic method of 2-pyrone derivatives.[2]

A variety of the 4-aryl- or 4-alkenyl-3-bromo-4,6-dimethyl-3,4-dihydro-2-pyrones (1)[3] were readily prepared as a mixture of diastereoisomers (major:minor = 9:1) according to the recently reported procedure shown in eq 1.[1b] Compounds 1 (1.35 mmol) were treated with $AgSbF_6$ (463 mg, 1.35 mmol) in 4 ml of dichloromethane or 1,2-dichloroethane in the presence of 2,6-lutidine



(0.17 ml, 1.40 mmol) at room temperature with stirring. The mixture was filtered on Celite and the Celite was washed with dichloromethane (25 ml x 2). The resulting filtrate was washed with water (25 ml x 2) and dried over $MgSO_4$. The solvent was removed in vacuo and the residue was chromatographed on silica gel (n-hexane:ethyl acetate=7:3) to give 6.[4] The results are summarized in Table 1. Thus the 3-alkenyl-2-pyrone derivatives (6d-6g) must be useful

Scheme I

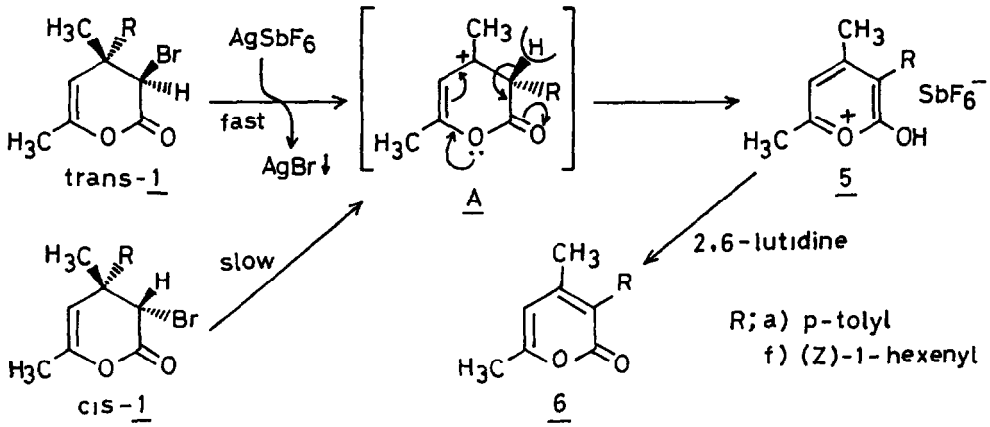


Table 1. Yield of 6 by the rearrangement of 1 with $AgSbF_6$[a)]

Bromide (1)	R	Ratio trans-1 / cis-1	react. time	conv. %	yield of 6 %
a	p-tolyl	≥97 / 3[b)]	15 min.	100	ca.100
b	p-anisyl	85 / 15	15 min.	88[c)]	80
c	phenyl	80 / 20	15 min.	57	47
d	1-propenyl[d)]	≥97 / 3[b)]	15 min.	100	84
e	(E)-1-hexenyl	≥97 / 3[b)]	15 min.	100	90
f	(Z)-1-hexenyl	93 / 7[b)]	15 min.	93	93
g i)	2-propenyl	∿97 / 3[b)]	23 hr.	60	48
ii)[e)]		76 / 24	12 hr.	81	58
h	vinyl	≥97 / 3[b)]	12 hr.	-[f)]	-[f)]

a) Dichloromethane was used as a solvent except for entries a and g-ii, where 1,2-dichloroethane was used. All the reactions were carried out at room temperature. b) The ratio (≥ 97 / 3) indicates that only one diastereomer was detected by ^1H NMR. c) Only cis diastereomer was recovered. d) A mixture of (E)- and (Z)-1-propenyl groups. e) Reaction temperature was 50 °C. f) Complex mixture.

compounds for further transformation by modification of the vinyl group. It must be noted that the 3-vinyl derivatives polymerized rather easily, especially the compounds with (E)-geometry such as 6e did start to polymerize when a pale yellow oil of 6e was stood at room temperature. 6f and 6g were rather stable in comparison with 6e,[5] but 6 should be stored refrigerated in solution.

The rearrangement from 1 to 6 had the following characteristics: (i) for the aryl groups, electron donating substituents such as methyl and p-methoxy groups substantially increased the rate and yield of the rearrangement, (ii) in the case of alkenyl groups, the rate of migration was much faster in those with an alkyl group at β-position than those without β-alkyl groups. For example, 1d, 1e and 1f were completely converted to the corresponding 6 at room temperature within 15 min, whereas 4-(2-propenyl) (1g) and 4-vinyl (1h) compounds required much longer reaction time and resulted in lowered yield of 6, (iii) the major diastereomer (trans-1) reacted quickly and only the minor diastereomer of 1 (cis-1)[6] was recovered when a mixture of the diastereomers was used as a starting material.

In order to explore the mechanism of the present rearrangement, first we cautiously explored the stereochemistry of the migrating alkenyl group and found that (E)- (1e) and (Z)-hexenyl (1f) groups were transferred with 100 % retention of the stereochemistry.[7] Second we tried to detect the cationic intermediate (5) during the reaction. Bromides 1a and 1f were reacted with $AgSbF_6$ in dichloromethane-d_2 at room temperature and the insoluble silver bromide was filtered. ^1H NMR analysis of the solution showed a very low field proton (δ 10.07 and 9.83, respectively) and significant low field shift in the proton at C-5 and two methyl protons on the ring,[8] showing the formation of 2-hydroxypyrylium salts 5a and 5f, respectively. These were converted to the corresponding 6 by the addition of 2,6-lutidine.

A plausible mechanism which accounts for these observation is shown in scheme I. The concerted nature of the debromination and migration was clearly supported by the facts that the stereochemistry of the migrating alkenyl groups was retained and cis-1 did not take part in the migration. The above mentioned characteristics of (i) and (ii) indicate that the significant cationic nature was involved in the transition state and the stabilization of the cationic intermediates effected profoundly on the rate of migration. After the neighboring group migration, enolization of A gave stable 2-hydroxypyrylium salt 5. Finally, deprotonation of 5 by 2,6-lutidine afforded 6.

References and Notes

1.(a) Y. Yamamoto, T. Kume, K-y. Akiba, Heterocycles, 26, 1495 (1987). (b) T. Kume, H. Iwasaki, Y. Yamamoto, K-y. Akiba, Tetrahedron Lett., 28, 6305 (1987). (c) H. Iwasaki, T. Kume, Y. Yamamoto, K-y. Akiba, Tetrahedron Lett., 28, 6355 (1987).

2.For a review of synthesis of 2-pyrone derivatives, see (a) J. Stauton, in "Comprehensive Organic Chemistry", P. G. Sammes Ed., Pergamon Press, Oxford, England, 1979, Vol. 4, Part 18.2, pp 638-644. (b) J. D. Hepworth, in "Comprehensive Heterocyclic Chemistry", A. J. Boulton and A. McKillop Ed., Pergamon Press, Oxford, England, 1984, Vol.3, Part 2.24.3, pp 789-799.

3.^{1}H NMR ($CDCl_3$) 1a (major isomer, assigned as trans): δ 1.59 (s, 3H), 2.06 (d, 3H, J=1.3 Hz), 2.31 (s, 3H), 4.61 (d, 1H, J=1.5 Hz), 4.92-5.06 (m, 1H), 6.97-7.31 (m, 4H). 1f (major isomer, assigned as trans): δ 0.90 (brt, 3H, J=6.4 Hz), 1.15-1.47 (m, 4H), 1.33 (s, 3H), 1.94 (d, 3H, J=1.1 Hz), 1.98-2.30 (m, 2H), 4.41 (d, 1H, J=1.3 Hz), 4.89-5.05 (m, 1H), 5.16 (dt, 1H, J=12 Hz, 1 Hz), 5.37 (dt, 1H, J=12 Hz, 6.8 Hz).

4.All new compounds displayed satisfactory ^{1}H NMR (90 MHz), IR, and Mass spectra, and complete spectroscopic details of the derivatives will be given in our full paper. ^{1}H NMR ($CDCl_3$) 6a: δ 1.99 (s, 3H), 2.22 (d, 3H, J=0.7 Hz), 2.36 (s, 3H), 5.94 (brs, 1H), 7.17 (brs, 4H). 6f: δ 0.69-1.03 (brt, 3H), 1.03-1.56 (m, 4H), 1.71-2.06 (brdt, 2H), 2.03 (d, 3H, J=0.9 Hz), 2.21 (s, 3H), 5.60-6.08 (m, 3H). ^{13}C NMR (CD_2Cl_2) 6f: δ 14.10 (q), 19.78 (q), 20.16 (q), 22.81 (t), 29.68 (q), 31.56 (q), 107.11 (d), 119.15 (s), 121.33 (d), 136.53 (d), 151.29 (s), 158.90 (s), 162.22 (s).

5.We assume that the stability in 6f compared with 6e may be due to the steric factors in the crystal or in the conjugation between the vinyl group and the pyrone ring.

6.We could not determine the exact structure of the two diastereomers of 1 from these spectral data, but we assigned cis geometry to the recovered diastereomer because of the lower ratio in the equilibrium of 1 and the resistance to the migration.

7.Structural assignment was supported by homo nuclear decoupling.

8.^{1}H NMR (CD_2Cl_2) 5a: δ 2.35 (s, 3H), 2.40 (s, 3H), 2.64 (d, 3H, J=0.7 Hz), 7.16 (d, 2H, J=8.6 Hz), 7.16 (brq, 1H), 7.34 (d, 2H, J=8.6 Hz), 10.07 (s, 1H). 5f: δ 0.70-1.03 (brt, 3H), 1.03-1.65 (m, 4H), 1.76-2.05 (brdt, 2H), 2.47 (s, 3H), 2.66 (brs, 3H), 5.95 (dd, 1H, J=12, 1 Hz), 6.18 (dt, 1H, J=12, 7 Hz), 7.13 (brs, 1H), 9.83 (s, 1H). ^{13}C NMR (CD_2Cl_2) 5f: δ 13.98 (q), 19.59 (q), 22.21 (q), 22.64 (t), 29.90 (t), 31.12 (t), 114.60 (d), 117.10 (s), 117.40 (d), 142.53 (d), 166.19 (s), 168.01 (s), 171.43 (s).

9.A Grant-in-Aid for Special Project Research (No. 61111004) is acknowledged for the partial support of this research.

(Received in Japan 24 February 1988)