Hydroalumination-Brominolysis of Vinylalkynols: A Novel Entry to (*E*)- and (*Z*)-Bromoalkadienols, and Bromoallenols

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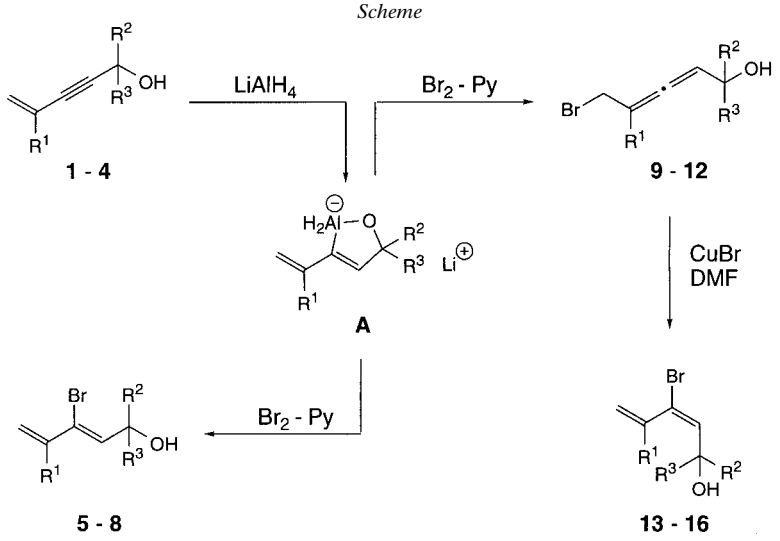
Hydroalumination-brominolysis of vinylacetylenic alcohols **1**–**4** provides a novel entry to synthetically useful (*E*)- and (*Z*)-bromoalkadienols, and bromoallenols, which are otherwise hardly accessible. An electrophilic cleavage of cyclic intermediate **A** follows competing mechanistic pathways, giving rise to isomeric (*Z*)-bromodienols **5**–**8** and allenic alcohols **9**–**12**. The latter are stereoselectively converted to (*E*)-bromoalkadienols **13**–**16** by CuBr-catalyzed anionotropic rearrangement.

1. Introduction. – Hydroalumination of the C≡C bond provides facile access to alkenylaluminum species, which can be converted, both stereo- and chemoselectively, into a variety of useful organic products [1]. In particular, electrophiles, like I_2, cleave C_{sp2}–metal bonds with retention of configuration, yielding respective (*E*)-iodoalkenes [2a]. The stereochemical outcome varies for propargyl and homopropargyl alcohols and ethers [2b–e], depending upon the substrate and the structure of the alkylaluminum hydride (mostly, >95% (*E*)- or (*Z*)). Hydroalumination of vinylalkynols, on the contrary, lacks selectivity, affording, upon iodinolysis, isomeric iodoalkadienols [3]. The present study was undertaken for two major reasons. First, using Br_2 as a cleaving agent should enhance the synthetic potential of the hydroalumination-halogenolysis reaction. Second, replacement of commonly used I_2 with Br_2 might improve the kinetic stability of intermediate products, thus making their isolation and structural characterization more feasible.

Results and Discussion. – The hydroalumination of vinylalkynols **1**–**4** follows, at the addition step, the selectivity pattern of the parent reaction with propargyl alcohols as substrates [2]. The incoming entities, *i.e.*, hydride ion and metal atom, are introduced to the C≡C bond *trans* to each other to form a proposed cyclic intermediate **A**. The electrophilic ring-opening with Br_2-pyridine complex occurs with a high stereoselectivity to afford (*Z*)-bromoalkadienols **5**–**8** as minor products. For comparison, hydroalumination of 1-(trimethylsilyl)alk-1-ynes with $(i\text{-}Bu)_2AlH$ and subsequent bromination gives vinyl bromides with a hydride ion and Br-atom disposed *cis* to each other [4]. The presence of the vinyl group in intermediate **A** creates a new mechanistic

Scheme



1, **5**, **9**, **13**: $R^1 = R^2 = R^3 = H$; **2**, **6**, **10**, **14**: $R^1 = R^2 = H$, $R^3 = Me$;
3, **7**, **11**, **15**: $R^1 = H$, $R^2 = R^3 = Me$; **4**, **8**, **12**, **16**: $R^1 = Me$, $R^2 = H$, $R^3 = i\text{-}Pr$.

alternative: an electrophilic substitution accompanied by a double-bond shift S_E2' or S_Ei' [5], resulting in bromoallenols **9**–**12**. In fact, the regioselectivity of bromination is highly sensitive toward structural changes. Thus, the transition from primary alcohol **1**, *via* secondary **2**, to tertiary alcohol **3** is accompanied by a significant increase in the concentration of allenic isomers, from 62 to 85% (total yields vary in the range of 58–76%). The highest mark of 95% was achieved with substrate **4** bearing an isopropenyl group. A conceptually analogous preference for allenic species undergoing introduction of a Me group at the terminal C=C bond has been observed in electrophilic acylation reactions of conjugated enynes [6]. The (*Z*)-bromoalkadienols **5**–**8** and bromoallenols **9**–**12**, although relatively unstable, can be separated by column chromatography. The latter were stereoselectively converted to (*E*)-bromoalkadienols **13**–**16** when treated with catalytic quantities of CuBr [7] at ambient temperature (53–58%). Thermal isomerization, on the contrary, occurs stereochemically random: distillation of allene **12** yields (*Z*)-configured **8** and (*E*)-configured **16** in the ratio of 2:5. The stereochemical assignment of trisubstituted C=C bond in isomeric bromoalkadienols **5**–**7** and **13**–**15** was carried out on the basis of the chemical shift of the H-atom ($R^1 = H$). In NMR spectra of (*E*)-bromoalkadienols **13**–**15**, it suffers significant downfield shift due to the electronegativity of an O-atom occupying a neighboring vertex of the imaginary hexagon. The magnitude of the shift is structurally dependent and varies in the range of 0.29–1.08 ppm.

Based on these data, we conclude that hydroalumination-iodinolysis of vinylalkynols [3], although stereochemically random, might still be selective at the ring-opening step, affording (*Z*)-iodoalkadienols as a single stereoisomer. The respective iodoallenols supposedly undergo *in situ* 'thermal' isomerization to yield the mixtures of (*Z*)- and (*E*)-iodoalkadienols. The enhanced stability of bromoallenols **9**–**12** is an

advantage of the process we studied; it made this class of organic compounds synthetically available, and it also allowed us to detect the formation of mechanistically significant rearranged products.

Financial assistance from the *U. S. Civilian Research and Development Foundation* (CRDF Award No. AC1-954), College of Science and Mathematics, Office of Graduate Studies, Research and International Programs, and University Corporation, California State University Northridge is gratefully acknowledged. *H. G.*, *G. P.*, and *S. H. B.* wish to thank the *National Foundation of Science and Advanced Technologies*, Armenia, for financial support (NFSAT Award ACH-005-98).

Experimental Part

1. *General*. Vinylalkynols **1**–**4** have been synthesized according to the protocol in [8]. TLC: silica-gel plates *Silufol UV-254*, hexane Et_2O, 1:1, visualization $KMnO_4$. Column chromatography (CC): *Silicagel L40/100*. MS: *VG-7070* spectrometer; CI with NH_3 CH_4. IR Spectra: *UR-20* spectrometer; ν in cm^{-1}. ^{1}H-NMR Spectra (300 MHz): *Varian Mercury-300* spectrometer; δ in ppm rel. to Me_4Si (=0 ppm), J in Hz; (D_6)acetone as a solvent.

2. *General Procedure: Synthesis of (*Z*)-3-Bromopenta-2,4-dien-1-ols* **5**–**8** *and 5-Bromopenta-2,3-dien-1-ols* **9**–**12**. Under N_2, a soln. of alcohol (**1**–**4**, 10 mmol) in dry THF (2 ml) was added dropwise to a suspension of $LiAlH_4$ (0.46 g, 12 mmol) in dry THF (10 ml) at 0°. The mixture was stirred at 20° (2 h), then quenched with AcOEt (0.18 g, 2 mmol) at 0°. After 30 min, the mixture was cooled (−10°), treated with a soln. of Br_2 (2.08 g, 13 mmol) and pyridine (1.19 g, 15 mmol) in dry THF (2 ml), stirred for another 30 min, and quenched consecutively with H_2O (0.46 ml), aq. NaOH (15%, 0.46 ml), and H_2O (1.38 ml). The precipitate was filtered off and extracted with Et_2O (3 × 5 ml). Combined Et_2O extracts were washed with dil. HCl, sat. aq. Na_2CO_3, and brine, and dried ($MgSO_4$). The solvents were stripped off under reduced pressure, the residue was filtered through silica to yield mixtures of **5**–**8** and **9**–**12**. Total yield, ratio by NMR: **5**/**9**, 76%, 38:62; **6**/**10**, 59%, 26:74; **7**/**11**, 58%, 15:85; **8**/**12**, 70%, 5:95. Satisfactory microanalysis data were obtained for C, H, and Br. IR: **5**–**8**: 3400 (O–H), 3100 (CH_2=C), 1620 (C=C); **9**–**12** 3400 (O–H), 1950–1970 (C=C=C). Individual products were isolated by CC with hexane/acetone, 39:1 to 9:1.

*(*Z*)-3-Bromopenta-2,4-dien-1-ol* (**5**): 25%. TLC: R_f 0.56. ^{1}H-NMR: 4.10 (br. *s*, OH); 4.33 (*d*, *J* = 5.4, CH_2); 5.23 (*d*, *J* = 10.5, CH=); 5.53 (*d*, *J* = 16.5, CH=); 6.29 (*t*, CH=); 6.44 (*dd*, CH=). HR-CI-MS (CH_4): 162.957554 ($C_5H_6O^{81}Br$, $[M-H]^+$; calc. 162.958155).

*(*Z*)-4-Bromohexa-3,5-dien-2-ol* (**6**): 8%. TLC: R_f 0.50. ^{1}H-NMR: 1.24 (*d*, *J* = 6.3, Me); 4.10 (br. *s*, OH); 4.72 (*quint.*, CH); 5.24 (*d*, *J* = 10.5, CH=); 5.54 (*d*, *J* = 16.3, CH=); 6.16 (*d*, *J* = 7.5, CH=); 6.44 (*dd*, CH=). HR-CI-MS (NH_3): 176.006721 ($C_6H_{11}N^{79}Br$, $[M+NH_4-H_2O]^+$; calc. 176.007486).

*(*Z*)-4-Bromo-2-methylhexa-3,5-dien-2-ol* (**7**): 3%. TLC: R_f 0.49. ^{1}H-NMR: 1.48 (*s*, 2 Me); 5.17 (*d*, *J* = 10.5, CH=); 5.54 (*d*, *J* = 16.5, CH=); 6.40 (*dd*, CH=); 6.46 (*s*, CH=).

*(*Z*)-5-Bromo-2-methylhepta-4,6-dien-3-ol* (**8**): This compound could not be isolated from the mixture **8**/**12** due to its low concentration. The authentic sample was obtained by distillation of **12** (b.p. 94–86°/2 mm Hg), affording isomers **8** and **16** in the ratio of 2:5. TLC: R_f 0.70. ^{1}H-NMR: 0.93 (*d*, *J* = 6.6, Me); 0.97 (*d*, *J* = 6.6, Me); 1.81 (*m*, CH); 2.02 (*s*, Me); 4.33 (*dd*, *J* = 8.1, 6.0, CH); 5.19 (br. *s*, CH_2=); 6.11 (*d*, CH=).

5-Bromopenta-2,3-dien-1-ol (**9**): 12%. TLC: R_f 0.45. ^{1}H-NMR: 3.57 (*s*, OH); 4.00–4.08 (*m*, CH_2Br, CH_2O); 5.54 (*m*, CH=C=CH).

6-Bromohexa-3,4-dien-2-ol (**10**): 12%. TLC: R_f 0.41. ^{1}H-NMR: 1.24 (*d*, *J* = 6.3, Me); 1.25 (*d*, *J* = 6.3, Me); 4.03 (*dd*, *J* = 7.9, 1.9, CH_2Br); 4.31 (*quint. d*, *J* = 6.3, 2.4, CH); 5.54 (*m*, CH=C=CH). HR-CI-MS (NH_3): 176.006674 ($C_6H_{11}N^{79}Br$, $[M+NH_4-H_2O]^+$; calc. 176.007486).

6-Bromo-2-methylhexa-3,4-dien-2-ol (**11**): 19%. TLC: R_f 0.39. ^{1}H-NMR: 1.30 (*s*, Me); 1.31 (*s*, Me); 3.30 (br. *s*, OH); 4.04 (*m*, CH_2Br); 5.58 (*m*, CH=C=CH). HR-CI-MS (NH_3): 190.022417 ($C_7H_{13}N^{79}Br$, $[M+NH_4-H_2O]^+$; calc. 190.023136).

7-Bromo-2-methylhepta-4,5-dien-3-ol (**12**): 70%. TLC: R_f 0.67. ^{1}H-NMR: 0.93 (*td*, *J* = 6.6, 2.4, Me); 1.72 (*m*, CH); 1.80 (*d*, *J* = 2.9, Me); 1.81 (*d*, *J* = 2.8, Me); 3.43 (br. *s*, OH); 3.84 (*td*, *J* = 6.5, 1.1, CH); 4.08 (*m*, CH_2Br); 5.21 (*m*, C=C=CH). HR-CI-MS (NH_3); 218.054220 ($C_9H_{17}N^{79}Br$, $[M+NH_4-H_2O]^+$; calc. 218.054436).

3. *General Procedure: Synthesis of (*E*)-Bromoalkadienols* **13**–**16**. A soln. of bromoallenol (**9**–**12**, 3 mmol) in dry DMF (1 ml) was added to a suspension of CuBr (43 mg, 0.3 mmol) in dry DMF (4 ml) at r.t. The mixture was stirred for 15 h, treated with H_2O (3 ml), and filtered off. The filtrate was extracted with Et_2O (3 × 10 ml);

combined Et_2O fractions were washed with dil. HCl, sat. aq. Na_2CO_3 solns., and brine, and dried ($MgSO_4$). The solvents were evaporated; the residue was chromatographed (silica gel; hexane/acetone, 29:1) to afford (*E*)-bromoalkadienols **13**–**16** (samples contain fractional amounts of DMF).

*(*E*)-3-Bromopenta-2,4-dien-1-ol* (**13**): 53%. TLC: R_f 0.45. ^{1}H-NMR: 3.62 (br. *s*, OH); 4.26 (*d*, *J* = 6.9, CH_2); 5.37 (*d*, *J* = 10.5, CH=); 5.58 (*d*, *J* = 16.2, CH=); 6.25 (*t*, CH=); 6.73 (*dd*, CH=).

*(*E*)-4-Bromohexa-3,5-dien-2-ol* (**14**): 55%. TLC: R_f 0.41. ^{1}H-NMR: 1.23 (*d*, *J* = 6.3, Me); 4.75 (*dq*, *J* = 8.6, CH); 5.35 (*d*, *J* = 10.4, CH=); 5.58 (*d*, *J* = 16.0, CH=); 6.10 (*d*, CH=); 6.75 (*dd*, CH=). HR-CI-MS (NH_3): 176.006685 ($C_6H_{11}N^{79}Br$, $[M + NH_4 - H_2O]^+$; calc. 176.007486).

*(*E*)-4-Bromo-2-methylhexa-3,5-dien-2-ol* (**15**): 58%. TLC: R_f 0.55. ^{1}H-NMR: 1.38 (*s*, 2 Me); 4.17 (*s*, OH); 5.27 (*d*, *J* = 10.5, CH=); 5.49 (*d*, *J* = 16.5, CH=); 6.23 (*s*, CH=); 7.48 (*dd*, CH=). HR-CI-MS (NH_3): 190.022680 ($C_7H_{13}N^{79}Br$, $[M + NH_4 - H_2O]^+$; calc. 190.023136).

*(*E*)-5-Bromo-2-methylhepta-4,6-dien-3-ol* (**16**): 54%. TLC: R_f 0.67. ^{1}H-NMR: 0.87 (*d*, *J* = 6.6, Me); 0.94 (*d*, *J* = 6.9, Me); 1.66 (*m*, CH); 1.90 (*s*, Me); 3.96 (*dd*, *J* = 9.6, 6.9, CH); 5.11 (br. *s*, CH_2=); 5.93 (*d*, CH=). HR-CI-MS (NH_3): 218.029789 ($C_9H_{15}O^{79}Br$, $[M]^+$; calc. 218.030626).

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Received May 24, 2000