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FORMATIONS of β,β-DIHALOENONES FROM HALOGENATED TERTIARY ALKYNOLS

Geetha J. Angara, Pakorn Bovonsombat and Edward McNelis*

Department of Chemistry, New York University, New York, New York 10003

Abstract. Halogenated alkynols react with N-halosuccinimides and catalytic amounts of Koser's reagent to afford mixed β,β-dihaloenones, useful templates for aryl and alkyl substituted enones.

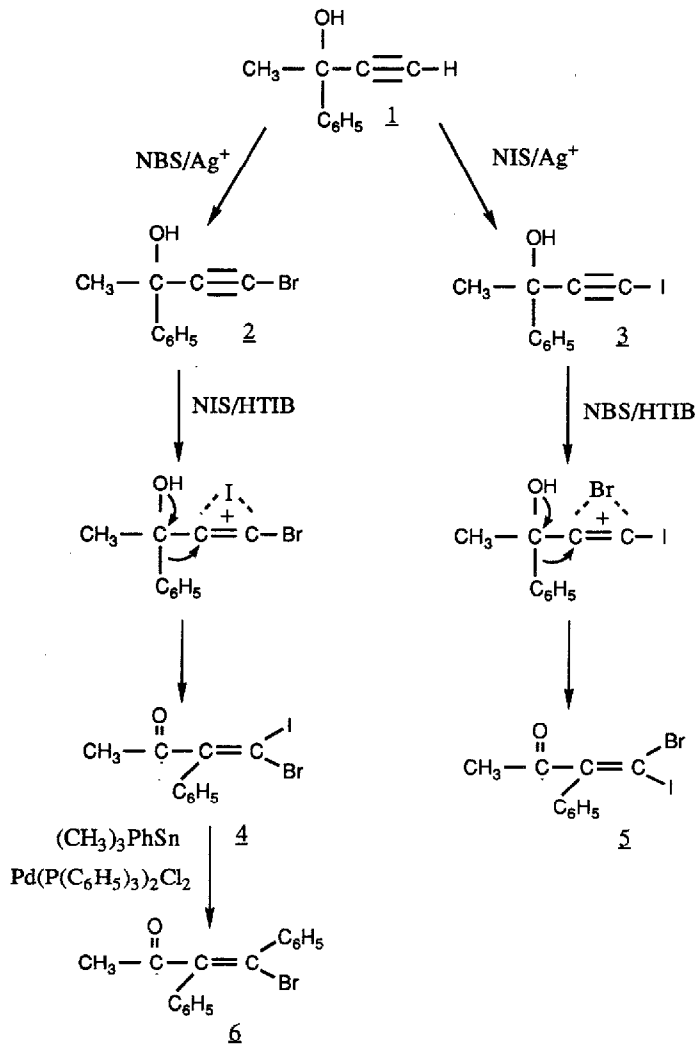
We have been examining the conversions of alkynols to haloenones with a variety of halogenating agents. Secondary alkynols were converted to α-iodoenones in high yield by a reaction with N-iodosuccinimide (NIS) and catalytic quantities of acids, such as [hydroxy(tosyloxy)iodo]benzene (HTIB or Koser's reagent).[1] Tertiary alkynols were transformed to β-iodoenones via group shift by means of iodine and oxides of iodine.[2] Herein we report reactions of halogenated alkynols to mixed β,β-dihaloenones, potential templates for selective exchanges for aryl or alkyl groups via catalyses involving palladium or its complexes.[3]

The general approach to these compounds is shown in the scheme. The halogenated alkynols 2 and 3 can be prepared in high yield from the alkynol 1 by either N-bromosuccinimide (NBS) or NIS with catalytic amounts of silver salts in acetone.[4] There are two useful combinations of reagents for the conversion of 2 to the Z-isomer 4: NIS and catalytic amounts of HTIB; iodine and stoichiometric amounts of HTIB. Their value for the electrophilic iodination of alkylaromatics has been presented lately.[5] Corresponding reagents involving NBS and bromine can be used for selected brominations.

When 4-bromo-2-phenyl-3-butyn-2-ol (2) (1mmol) was treated with NIS (1mmol) and HTIB (0.1mmol) in acetonitrile (10ml) for 18 hours at room temperature, (Z)-4-bromo-4-iodo-3-phenyl-3-buten-2-one (4) was formed in greater than 95% selectivity on a 72% conversion. The use of p-toluenesulfonic acid in place of HTIB gave a higher conversion of 93% with 94% selectivity to 4. A 95% conversion of 2 to 4 with 89% selectivity was obtained by the use of half-molar quantities of iodine and HTIB in acetonitrile at room temperature. The product 4 was a low-melting solid (53-

5°C) that was more often an oil: ^{1}H NMR ($CDCl_3$) δ 2.30 (s, 3H), 7.2-7.4 (m, 5H); ^{13}C NMR ($CDCl_3$) δ 28.6, 53.0, 127.9, 128.9, 129.0, 136.0, 200.5; IR ($CHCl_3$) 1690, 1580, 1380, 1240, 1170 cm^{-1}; Anal. CH; mass spectrum M/z (relative intensity) 350/352 (M^+, 14), 228 ($C_6H_5C_2I$, 72), 180/182 ($C_6H_5C_2Br$, 29), 101 ($C_6H_5C_2$, 19), 43 (CH_3CO, 100).

Proposed pathways for β,β-dihaloenones



Consistent with the assignment of 4 as the (Z)-isomer was its conversion to (E)-4-bromo-3,4-diphenyl-3-buten-2-one (6) by means of trimethylphenylstannane (equimolar) and $Pd(P(C_6H_5)_3)_2Cl_2$ (2 mole%) in THF at room temperature for 6 hours in 80% yield. Compound 6 had the following ^1H NMR: δ 2.28 (s, 3H), 7.35-7.4 (m, 5H) and 7.42-7.64 (m, 5H). This pattern was in contrast to that of the known (Z)-4-iodo-3,4-diphenyl-3-buten-2-one whose aromatic protons are situated at 7.0 (s, 5H), 7.1-7.25 (m, 3H) and 7.50-7.75 (m, 2H).[2] The splitting of a phenyl *anti* to an acetyl group in an enone system can be further exemplified by (Z)-3-bromo-4-phenyl-3-buten-2-one whose aromatic protons absorb at 7.2-7.5 (m, 3H) and 7.7-8.0 (m, 2H).[6]

The solvent for the NIS/HTIB system is important. When methanol was used, 4 was mixed with ethers. In ethyl acetate the reaction proceeded moderately well (70% yield) after a refluxing for six hours. There were no reactions in ether, dimethylformamide, dimethyl sulfoxide or N-methylpyrrolidinone.

Since NBS is usually less reactive than NIS, the preparation of the (E)-isomer 5 was not as straightforward. When 4-iodo-2-phenyl-3-butyn-2-ol (3) was treated with NBS and catalytic amounts of HTIB in acetonitrile at reflux for three hours, neither 5 nor 4 was detected. The same reagents in methanol at room temperature for eighteen hours afforded a complex mixture with four major products. Two of these were methoxylated - the methyl ether and the bromomethoxylated forms of 3. The other two were the enones 4 and 5 in the ratio of 1:2, respectively. The combined yields of enones did not exceed 15%. When 3 was treated with half-molar quantities of bromine and HTIB in acetonitrile at room temperature overnight, the conversion of 3 was 90% and the selectivities for 4 and 5 were 59% and 10%, respectively. The (E)-isomer 5 was not isolated. In the GC/MS it displayed the following pattern, M/z (relative intensity): 350/352 (M^+, 20), 271 (M^+-Br, 62), 223/225 (M^+-I, 30), 144 (31), 127 (31), 115 (61), 101 (23), 43 (CH_3CO, 100).

The presence of 4 in the reactions of 3 and the absence of 5 in the reactions of 2 indicate stereospecificity induced by an iodonium attack on an alkyne bond prior to the shift of the phenyl group. Such specificity by the corresponding bromonium species and 3 could have led to a more open vinyl cation that converted to a bridged iodonium ion that favored the formation of 4 over 5 in the acetonitrile medium.

The synthetic potential of the original scheme resides then with the 2 to 4 pathway and not the 3 to 5 pathway. The (Z)-isomer 4 represents a flexible starting material for subsequent chemistry as foreshadowed by the conversion of 4 to 6. It can serve as a template whereby the iodine and then the bromine can be replaced at will

by aryl or alkyl groups or their acyl forms via organometallic steps involving tin and palladium.[7]

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