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Conversions of Phenylalkynylcyclopentanols to α-Iodoenones

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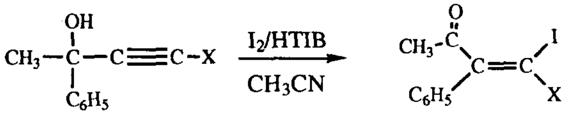
Abstract: N-Iodosuccinimide and catalytic amounts of Koser's reagent react with phenylalkynylcyclopentanols to afford α-iodoenones. No ring expansions occur.

Recently we reported the reactions of tertiary bromoethynylalkynols with iodine and [hydroxy(tosyloxy)iodo]benzene (HTIB or Koser's reagent). In the case of a linear alkynol 1a, the product was a (Z)-β,β-dihaloenone 2a.[1]

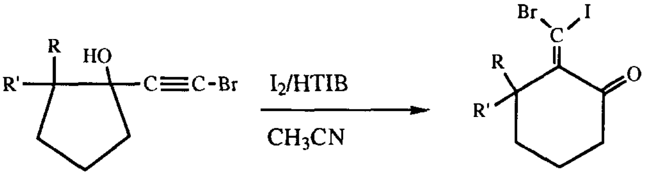


1

2

X = a, Br ; b, C_6H_5

For the cyclopentyl systems 3, the same reagents effected ring expansions to 4 with a predominance of Z-isomers.[2]

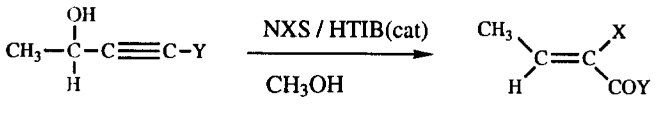


3

R, R' = H or CH_3

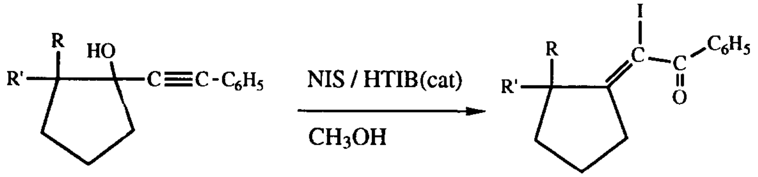
4

These mixed β,β-dihaloenones could be used as templates for stereospecific exchanges via organometallic modes such as the Stille reaction.[3] We are now reporting that efforts to extend these reactions to phenylalkynyl alcohols to form the analogous β-halo-β-phenylenones have led to a different pathway for cyclopentanols.



5 Y = C_2H_5 or C_6H_5 6

In the linear system the alkynol 1b with iodine and iodic acid in methanol was converted to the β-iodoenone 2b which was mixed with lesser amounts of an α-iodoenone.[4] Such α-iodoenones 6 are the principal products of secondary alkynol (5) reactions with N-halosuccinimides and catalytic amounts of HTIB.[5]



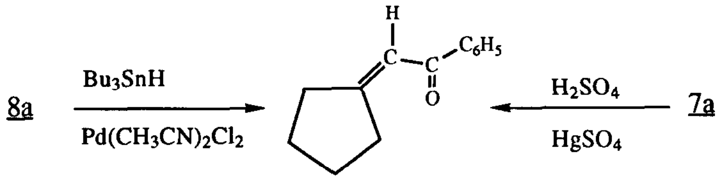
7 8

a, R = R' = H
b, R = H; R' = CH_3
c, R = R' = CH_3

When compound 7a was treated with equimolar amounts of iodine and HTIB in acetonitrile as in the bromoalkynol case, an unresolved mixture was obtained. With an equimolar amount of 1-iodo-2,5-pyrrolidinedione (NIS) and a tenth molar amount of HTIB in methanol, however, 7a was converted to 8a in 56% yield (80% by GC). The spectral data that support the assignment of 2-(cyclopentylidene)-2-iodo-1-phenylethanone are as follows: GC/MS m/z (rel. int.) 312 (31, M^+), 185 (54, M-I), 105 (35, $C_6H_5CO^+$), 77 (100, $C_6H_5^+$); ^{1}H-NMR ($CDCl_3$) δ 1.78-1.84 (m, 4H, C-3' and C-4'), 2.25 (t, 6.6Hz, 2H, C-2' syn to I), 2.54 (t, 6.9Hz, 2H, C-5'), 7.47 (t, 6Hz, 2H, meta), 7.62 (d, 6Hz, 1H, para), 7,91 (d, 6Hz, 2H, ortho); ^{13}C-NMR ($CDCl_3$) δ 25.2 (C-3'), 28.5 (C-4'), 34.0 (C-2'), 40.8 (C-5'), 85.6 (C-2), 128.5, 128.6, 129.7, 133.2, 133.3, 134.6, 158.8 (C-1'), 192.8 (C-1); IR (neat) 1670 cm^{-1} (CO) ; anal.CH.

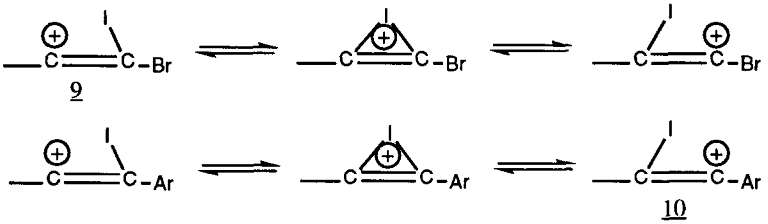
These data can not be assigned to a cyclohexanone, a possible product if there were a ring expansion. Such a structure would be the analogue of the bromoalkynol product 4 and would feature an absorption at 200-210 ppm in the ^{13}C-NMR for the carbonyl and an absorption at 2.7 ppm in the ^{1}H-NMR for methylene protons when adjacent to a carbonyl. Most informative for product 8a is the major appearance of a benzoyl fragment at 105 and its related phenyl fragment at 77 in the mass spectrum. Its ^{1}H-NMR spectrum exhibits the two hydrogen multiplets close to 8 ppm assignable to the ortho protons of a benzoyl group.

To put the structural designation on a firmer footing, 8a was treated with the deiodinating combination of $Pd(CH_3CN)_2Cl_2$ and Bu_3SnH to afford 2-cyclopentylidene-1-phenylethanone. This substance was identical to material prepared from the mercuric sulfate catalyzed hydration of 7a.[6]

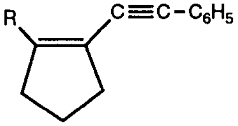


In order to test the stereochemical aspects of this reaction, the methyl (7b) and the dimethyl (7c) isomers were examined. When 2-methyl-1-phenylethynylcyclopentanol (7b) was mixed with NIS/ HTIB (catalytic) in methanol at room temperature for 18 hours, the reaction products was E/Z 8b (IR 1670 cm^{-1}, CO) obtained in 65% yield after silica chromatograpy (85% by GC). The GC/MS data contained the strong benzoyl fragment as well as the M^+ ion of 326. An E/Z ratio of 2/1 was assigned on the basis of the ratio of the methyl groups - 0.92 ppm for the Z-isomer and 1.24 ppm for the E-isomer in the ^1H-NMR spectrum. The ^{13}C-NMR spectrum displayed two carbonyl lines at 194.0 and 194.2 ppm. Similar events took place when 2,2-dimethyl-1-phenylethynylcyclopentanol (7c) reacted with NIS/HTIB(cat.) in methanol to give 8c (IR 1670 cm^{-1}, CO). The Z/E ratio of 8c was 1.5. The yield was 50% (90% by GC). Again the mass spectrum's base peak had the benzoyl mass of 105 with its concomitant peak of 77 along with the parent of 340 (28%). In the ^1H-NMR the methyl peaks of 1.05 and 1.42 were assigned to the Z- and E-isomers, respectively, and the telltale ortho protons were seen at 7.94 and 8.0 ppm. The benzoyl carbonyls in the ^{13}C-NMR spectrum appeared at 192.9 and 194.8 ppm.

In all of these series an unsymmetrically bridged iodonium species might be involved. Such vinyl cations should favor a site of greater charge stabilization.[7] For bromine-containing alkynes, the charge should be on the carbon not bearing the bromine (9), whereas for phenyl-containing alkynes the charge should be on the carbon bearing the phenyl (10). This latter stabilization is reflected in the milder reaction conditions - NIS/HTIB(catalytic) rather than I_2 / HTIB(stoichiometric).



Variations of solvent and acidic catalyst were not helpful in efforts to increase the ratios of geometric isomers. For example, when the HTIB catalyst was replaced with p-toluenesulfonic acid (TsOH) in the NIS treatment of 7b in methanol, the iodoenones were mixed with nearly equal amounts of starting material and the dehydrated starting material, 2-methyl-1-phenylethynylcyclopentene (11a). This latter compound was the sole product when 7b was reacted with NIS/TsOH(cat.) in acetonitrile. The identification of the cyclopentene was made through a GC/MS spectrum: 182 (100, M^+), 167 (64), 152 (36), 115 (28). Similarly, 7a was converted completely to phenylethynylcyclopentene (11b) by treatment with NIS/TsOH (catalytic) in acetonitrile: GC/MS, 168 (100%, M^+), 152 (48), 115 (18).



11 a, R = CH_3; b, R = H

The value of these alkyliodoeneones as synthons is not necessarily diminished by the low isomer ratios. For example, with LDA they could serve as Michael adducts to non-halogenated enones to afford vinylcyclopropanes suitable for [2+3] intermolecular annulation as demonstrated by Hudlicky for α-bromo-α,β-unsaturated esters.[8] Inverse adition to LDA/ eneones would lead to bisannulations as shown by Hagiwara and colleagues.[9]

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