Tetrahedron Letters, Vol. 34, No. 27, pp. 4277-4280, 1993
Printed in Great Britain

0040-4039/93 $6.00 + .00
Pergamon Press Ltd

Ring Expansion of an α-Bromoalkynol Camphor by Means of Iodine and Koser's Reagent

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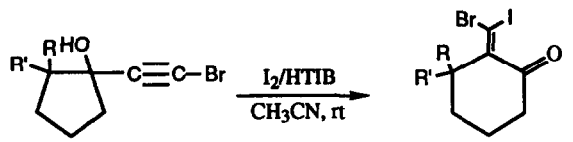
Abstract. The bromoethynyl adduct of camphor was treated with equimolar amounts of iodine and Koser's reagent (HTIB) to afford in good yield and in good stereospecificity a (Z)-bromoiodoenone, a synthon for enantiospecific syntheses.

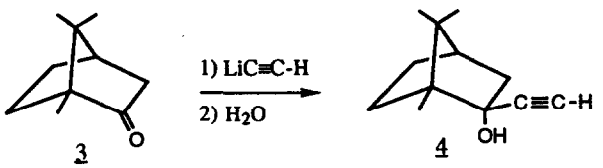
The reaction of α-alkynols with iodonium-producing reagents have come under scrutiny as of late, because they are novel modes of forming α-iodoenones, β-iodoenones and mixed β,β-bromoiodoenones.[1-4] Since such compounds are formed stereospecifically frequently, they are simple templates for the construction of more complex molecules via selective metal-catalyzed coupling reactions.[5] Recent noteworthy examples of these reactions are the ring expansions of α-alkynylcyclopentanols with iodine and Koser's reagent [6] (HTIB, [hydroxy(tosyloxy)iodo]benzene).[7]



1 2

	R	R'
a	H	H
b	CH3	CH3
c	CH3	H

The yields of these ring expansions ranged from 75 to 82%. The preponderances of Z-isomers vary from greater than 12/1 for 2a, through 7/1 for 2b to 3.3 for 2c. In this report we wish to present a significant extension of such expansions to a camphor-based system to obtain a product suitable for enantiospecific syntheses.



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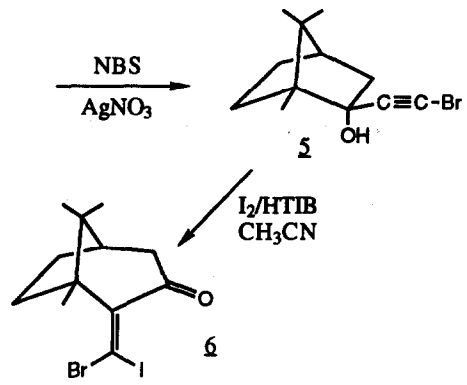
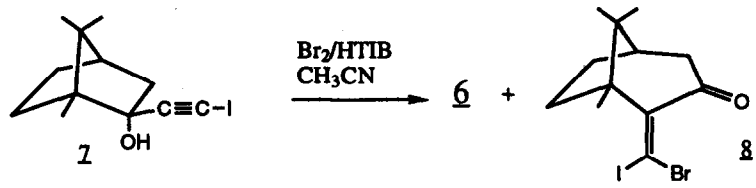


To this end, (1R)-(+)-camphor (3) was treated with lithium acetylide to afford 2-exo-ethynyl-1,7,7-trimethylbicyclo[2.2.1]heptan-2-ol (4). This low-melting solid (mp 57.5-59.5 °C; lit. 61-62 °C) had the same IR, ^{1}H-NMR and ^{13}C-NMR as reported by Lane and colleagues.[8] Compound 4 was treated with 1-bromo-2,5-pyrrolidinedione (NBS) and a catalytic amount of silver nitrate in acetone to form the bromoalkynol 5, 2-exo-bromoethynyl-1,7,7-trimethylbicyclo[2.2.1]heptan-2-ol in 90% yield.[9] This solid (mp 60.5-62.5 °C) had the following spectral properties: IR (nujol) 3480 (s), 2200 (w), 1060 (s), 1000 (m), 975 (m), 760 (m), 740 (m)cm^{-1}; ^{13}C-NMR ($CDCl_3$) δ 10.8, 21.5, 21.9, 27.4, 30.3, 33.0, 43.7, 45.9, 48.5, 54.4, 79.7, 84.7; GC/MS m/z (rel. int.) 177 (6, M^+-Br), 133 (18), 110 (40), 95 (100), 41 (33). Since the three absorbances in the ^{13}C-NMR spectrum of 5 assignable to the methyl carbons were the same as those of 4 (10.8, 21.5 and 21.9), there would appear to have been no isomerization of the exo-alkynyl group to its endo-isomer.

The bromoalkynol 5 was then reacted with equimolar amounts of iodine and [hydroxy(tosyloxy)iodo]-benzene (Koser's reagent, HTIB) in acetonitrile at room temperature overnight. The ring-expanded product 6 (mp 50.5-51.5 °C) was formed in 60% yield (isolated; 85% by GC). The following spectral and analytical data are consistent with the structural assignment of 6 as 2-[(Z)-bromoiodomethylidene]-1,8,8-trimethylbicyclo[3.2.1]octan-3-one: IR (nujol) 1700 (s), 1560 (m), 1220 (m), 1200 (m), 960 (m), 770 (s) cm^{-1}; ^{1}H-NMR ($CDCl_3$) δ 0.88 (s, 3H), 0.96 (s, 3H), 1.04 (s, 3H), 1.52 (m, 2H), 1.77 (m, 2H), 2.01 (m, 1H), 2.14 (m, 1H), 2.57 (dt, 1H), 2.90 (dd, 1H); ^{13}C-NMR ($CDCl_3$) δ 14.5 (anti CH_3-8), 20.2 (syn CH_3-8), 24.6 (CH_3-1), 28.6 (C-7), 33.6 (C-8), 41.3 (C-6), 46.2 (C-1), 47.3 (C-5), 58.3 (C-4), 58.9 (CBrI), 144.5 (C-2), 203.1 (C-3); GC/MS m/z (rel. int.) 382/384 (M^+, 4), 354/356 ((M-CO)$^+$, 4), 227/229 ((M-CO-I)$^+$, 10) 148 ((M-CO-I-Br)$^+$, 24), 91 (34), 41 (100); anal. CH. The presence of a carbonyl in 6 is clear from the ^{13}C-NMR (203.1 ppm) and the IR spectra (1700 cm^{-1}). The mass spectral data has bearing on the alkene assignment. The pattern of M^+ (382/384)

followed by $(M\text{-}CO)^+$ (354/356) and $(M\text{-}CO\text{-}I)^+$ (227/229) is one that resembles the cracking pattern of Z-isomers of substituted 2-bromoiodomethylidene cyclohexanones.[7] The cracking pattern for the related E-isomers is M^+, then $(M\text{-}I)^+$ followed by $(M\text{-}I\text{-}CH_2CO)^+$. No such peaks are seen in the pattern of 6.



7 8

In contrast to the stereospecific ring expansions and shift induced by iodonium ions, similar reactions of iodoalkynols with bromine/HTIB have been shown to be devoid of any useful degree of sterospecificity of the bromonium ion. In the case of rearrangements of linear iodoalkynols with Br_2/HTIB, the principal product was not an E-isomer but the Z-isomer. Indeed, in the case of 3-iodo-1-phenylpropynol the Z-isomer was formed in 46% whereas the E-isomer's yield was 22%.[4] For 4-iodo-2-phenyl-3-butyn-2-ol and with half molar amounts of Br_2/HTIB in acetonitrile, the yield of the (Z)-4-bromo-4-iodo-3-phenyl-3-buten-2-one was 59% and that of the E-isomer was 10%.[3] In this work, similar behavior with bromine/HTIB in CH_3CN was observed with 2-exo-iodoethynyl-1,7,7-trimethylbicyclo[2.2.1]heptan-2-ol (7). Two major and several minor products were formed. Separations have been difficult and are incomplete but GC/MS data exhibit 6 to be one of the major products in at least 40% yield. A cracking pattern ascribable to an E-isomer (loss of iodine prior to loss of CO) such as 8 is observed for the other major product.

As in the other cases the mixture obtained by the reactions of bromine and iodoalkynols contrast sharply with the high yields and purity of the products of reactions between iodine /HTIB and bromoalkynols. Such Z-bromoiodoenones represent flexible entries to many substituted alkyl or aryl enones by means of selective couplings catalyzed by organometallic catalysts. Furthermore, if the coupling substituents are chiral, the products should be formed in high enantioselectivity in light of the proximate camphor-derived system. Mild cleavages such as with ozone would lend to a broad range of optically active ketones. The results of such on-going directions will be reported subsequently.

Acknowledgment

We are grateful for the financial support of the New York University Technology Transfer Fund.

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(Received in USA 12 March 1993; accepted 6 May 1993)