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A STEREOSELECTIVE SYNTHESIS OF BROMOHOMOALLYLIC DERIVATIVES

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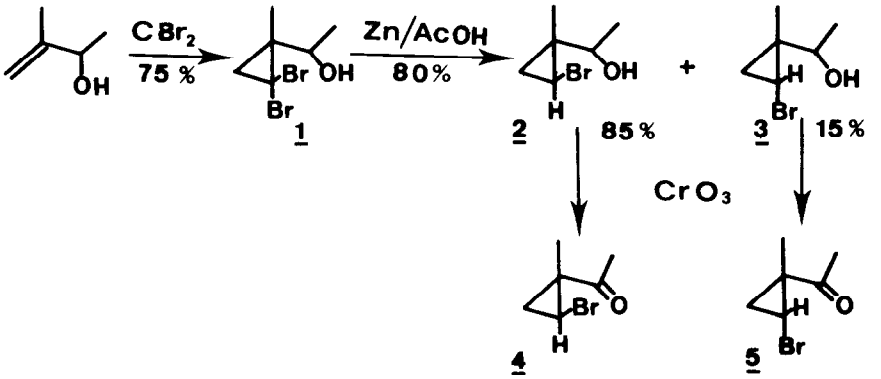
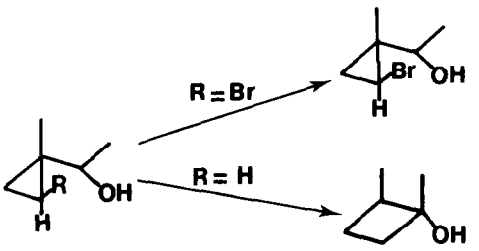
Perusal of the current chemical literature reveals an expanding interest in the stereoselective synthesis of trisubstituted ethylenic compounds Such interests are easily grasped since stereochemically pure olefins are often found in various natural products such as hormones, sex attractants, terpenes and marine products.

We now report a new rearrangement of the bromocyclopropylcarbinol 2 leading to the formation of the stereochemically pure E-isomer of bromohomoallylic derivatives 6 or 7. These compounds might be valuable intermediates in synthesis of trisubstituted olefins of non ambiguous stereochemistry.

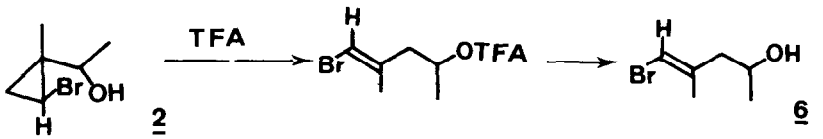
Gem-dibromocyclopropylcarbinol[2] 1 is obtained in good yield by dibromocarbene addition to the appropriate allylic alcohol (phase transfer method)[3]. Subsequent reduction by Zn/AcOH[4] is remarkably stereoselective resulting in a predominance of the cis-bromine substituted product 2 (overall yield 90 %). Stereochemistry of 2 and 3 is confirmed by oxidation (Jones reagent, quantitatively) to known bromocyclopropylketones 4 and 5 [5].



In solvolysis reactions bromine is a deactivating substituent. This is clearly illustrated by the acid catalysed isomerisation of (1-methylcyclopropyl)-methylcarbinol ($HClO_4$, 1M, room temp., 15 min.) which yields cyclobutanol [6] whereas a similar treatment of 2 results in no reaction even after several days.

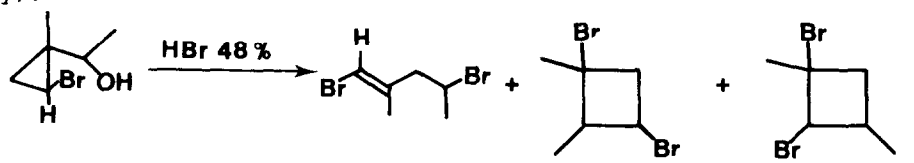


Isomerisation is observed when 2 is reacted with TFA (room temp. 1 min, quantitative yield). After saponification only E-1-bromo-2-methyl-1-penten-4 ol 6 is isolated [7]. A similar result is observed using H_3PO_4 (d=1.7, 100°C, 30 min.).



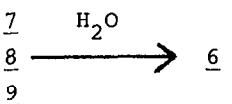
2 6

In contrast, treatment of 2 with HBr 48 % (100°C, 15 min., 70-80 %) results in a mixture of 7, 8 and 9 (bromide 7 is isolated pure by gas chromatography).

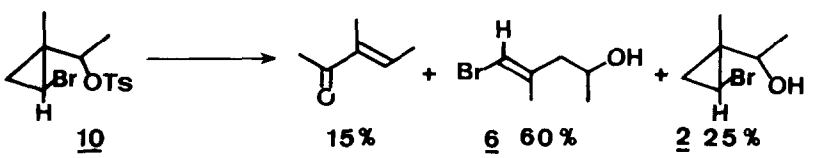


2 7 40% 8 30% 9 30%

Each of these bromides yields the homoallylic alcohol 6 after hydroly sis (pure water, 100°C, 4 hr.)



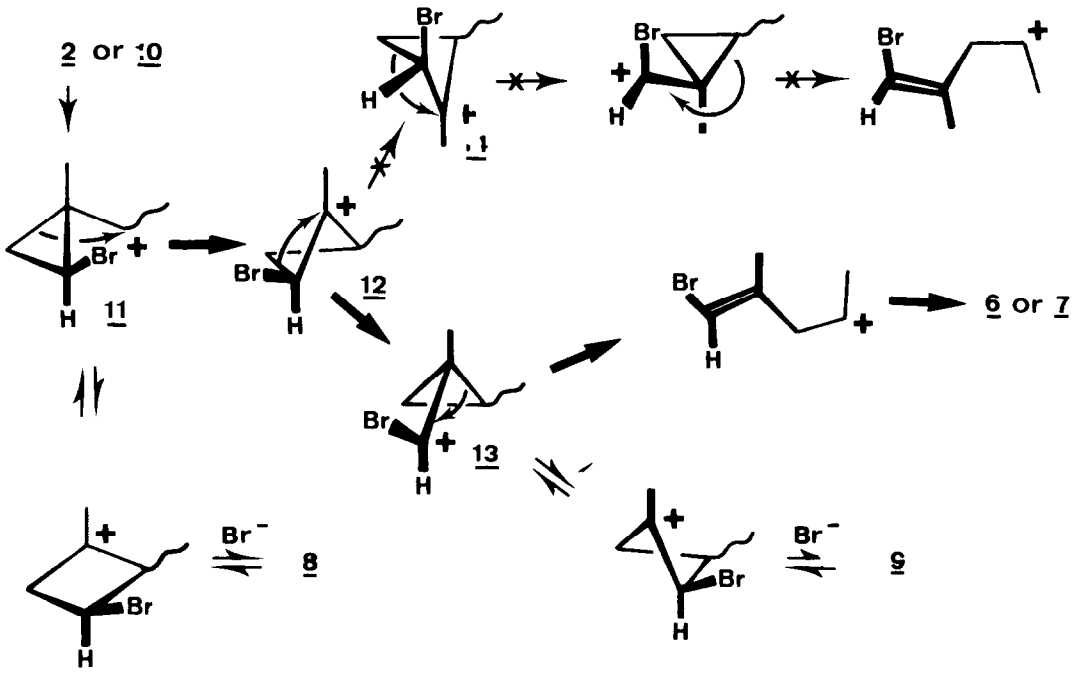
Alcohol 6 is the main product of the tosylate 10 hydrolysis (pure water, buffer $CaCO_3$, 100°C, 4 hr, 80 %, crude product).



10 15% 6 60% 2 25%

It has been long established that the cyclopropyl group acts as a carbonium ion stabilising group and induces carbon scrambling between the ring and exocyclic atoms [8].

In spite of the complexity of solvolysis reactions, the main (or only) product of isomerisation of the bromide 2 is a homoallylcarbinyl derivative which is exclusively the E-isomer. A similar result was observed by Schleyer et al. with deuterium labeled cyclopropylcarbinyl mesylates [9]. If one assumes that cyclopropylcarbinyl ions have a bisected conformation and a finite barrier to rotation about the 1-1' bond, we may propose the following scheme.



The observed stereochemistry for 6 and 7 excludes an inversion of configuration for each step as the transformation 11⟶12⟶13 is acomplished with retention of configuration. If the process with inversion of configuration 11⟶12⟶14 occurred, the Z-isomer would be formed.

This stereoselective synthesis of bromohomoallylic alcohol is an alternative to the Julia-Johnson synthesis [1d] since different homoallylic alcohols of definite stereochemistry may be obtained by the reaction of 6 with an alkylcuprate [10].

References

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C. Santelli and M. Bertrand, Bull. Soc. Chim. Fr., I974, 605.
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4 - Reduction with Zn/AcOH [a] seems a more convenient method -with a high regioselectivity- than tri-n-butyltin hydride [b].
a) K. Hoffmann, S.F. Orochena, S.M. Say, G.A. Jeffrey, J. Amer. Chem. Soc., I959, 81, 992.
b) L.K.H. Sydnes, Acta Chem. Scan., I978, ser.B, 32, 47.
For another method of preparation of monohalogenocyclopropylcarbinol see R. Barlet and M. Vincens, Tetrahedron, I977, 33, 1291.
5 - R. Barlet, Thesis, Grenoble, France, I976.
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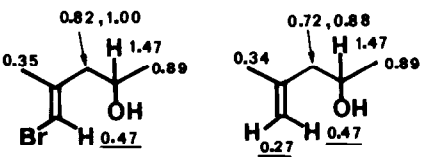
7 - Compound 6 NMR (δ/TMS, $CDCl_3$, 100MHz) d. 1.195, J = 6 Hz (3H) ; broad s. 1.83 (3H) ; broad d. 2.24, J = 6 Hz (2H) ; sext. 3.94, J = 6 Hz (1H) ; broad s. 5.99 (1H).
7 NMR (δ/TMS, CCl_4, 60 MHz) d. 1.7, J = 6,8 Hz (3H) ; broad s. 1.83 (3H) ; broad d. 2.66, J = 7.2 Hz (2H) ; sext. 4.2 (1H) ; 6.08 broad s. (1H).
MS m/e : 81 (100 %), 161-163 (60 %) , 240-242-244 (10-12-10 %).
Stereochemistry of 6 or 7 was established using shift reagent EuFOD by comparison with induced shift on 2-methyl-1-penten-4-ol.
(21 mg EuFOD/65 mg alcohol/0,5 ml $CDCl_3$).



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