A New Synthesis of 3-Chloro Butenolides via Rearrangement of 3,3-Dichloro Beta Lactones

T. Howard Black & Todd S. McDermott

Department of Chemistry, Eastern Illinois University, Charleston, Illinois, 61920

Available online: 24 Oct 2006

To cite this article: T. Howard Black & Todd S. McDermott (1990): A New Synthesis of 3-Chloro Butenolides via Rearrangement of 3,3-Dichloro Beta Lactones, Synthetic Communications, 20:19, 2959-2964

To link to this article: http://dx.doi.org/10.1080/00397919008051512

Full terms and conditions of use: http://www.tandfonline.com/page/terms-and-conditions

This article may be used for research, teaching and private study purposes. Any substantial or systematic reproduction, re-distribution, re-selling, loan, sub-licensing, systematic supply or distribution in any form to anyone is expressly forbidden.

The publisher does not give any warranty express or implied or make any representation that the contents will be complete or accurate or up to date. The accuracy of any instructions, formulae and drug doses should be independently verified with primary sources. The publisher shall not be liable for any loss, actions, claims, proceedings, demand or costs or damages.
whatsoever or howsoever caused arising directly or indirectly in connection
with or arising out of the use of this material.
A NEW SYNTHESIS OF 3-CHLORO BUTENOLIDES VIA REARRANGEMENT OF 3,3-DICHLORO BETA LACTONES

T. Howard Black* and Todd S. McDermott

Department of Chemistry, Eastern Illinois University
Charleston, Illinois 61920

4,4-Dialkyl 3,3-dichloro oxetan-2-ones rearrange under Lewis acid catalysis, accompanied by loss of HCl, to afford 4,5-dialkyl 3-chloro butenolides.

We have recently been investigating the reactions of beta lactones under the influence of Lewis acid catalysis.1 When the lactone ring oxygen is bonded to a secondary carbon atom, a rearrangement occurs in which the beta lactone 1 expands to a butyrolactone 4 with the concommitant migration of a hydrogen or carbon atom into the lactone ring.2 If the oxygen is bonded to a tertiary carbon, an ionization/elimination sequence ensues, producing a 1,2-unsaturated carboxylic acid 5.3
This behavior is predictable based on initial lactone ionization to a carboxylate/cation intermediate such as 2 followed by either rearrangement to another secondary carbocation 3 followed by carboxylate attack (to give 4) or via loss of an adjacent proton in lieu of an unfavorable tertiary-to-secondary cation shift (to give 5). In search of additional confirmation of this mechanism, we decided to examine the behavior of a series of 3,3-dichloro beta lactones (3,3-dichloro oxetan-2-ones) when exposed to Lewis acid catalysts. We felt that the presence of the chlorine atoms adjacent to the incipient tertiary carbocation might raise its energy close enough to a secondary cation that a ring expansion might occur. The ready availability of the dichloro beta lactones, via reaction of a ketone with dichloroketene or dilithiodichloroacetate (followed by dehydration of the obtained beta hydroxy acid), increased the attractiveness of the test system. If the chlorine atoms indeed enabled a lactone ring expansion rather than ionization, they could be subsequently removed via any of a number of known processes.

In the event, 3-pentanone was treated with dichloroketene, generated via the dehalogenation of trichloroacetyl chloride, to produce the expected beta lactone 6 in 25% yield following chromatographic purification. Treatment of this compound with anhydrous magnesium bromide etherate in dichloromethane for 12 hours afforded, as the predominant product (64%), the quite unexpected 3-chloro butenolide 7.
A predominant spectral feature was the indication of an ethyl group in the proton NMR (500 MHz) whose methylene protons were well-resolved and diastereotopic, as a consequence of their proximity to the asymmetric carbon atom at C-5. Other spectral data were in full accord with the assigned structure. The minor products proved to be the less-surprising dichloro butyrolactone 8 (17% yield) and the unsaturated acid 9 (6% yield). Employing freshly-prepared magnesium bromide as the catalyst increased the yield of 7 to 86%, totally suppressing the formation of the other products, and enabled the use of diethyl ether as the reaction solvent. Additionally, use of the dianion/dehydration route afforded beta lactones in much higher yield (approximately 75% overall) than dichloroketene cycloaddition.

The rearrangement/dehydrohalogenation reaction has proven to be general for acyclic ketones. The substrates examined and yield data are compiled in the Table. Not surprisingly, beta lactones derived from unsymmetrical ketones (e.g., R₁ = R₂ = Me) always rearranged toward the more highly substituted carbon atom. The reaction has also been tested on cyclohexanone and cycloheptanone, but at this point is not as clean as in the acyclic cases and thus is not currently useful from a synthetic standpoint. We are continuing our pursuit of this area, however, since successful development of the reaction on cyclic ketones would constitute a very simple and rapid butenolide annulation sequence.
The mechanism for formation of the chloro butenolides is intriguing. An obvious possibility was dehydrohalogenation of dichloro lactones such as 8 under the reaction conditions. Exposure of 8 to the reaction conditions for several days, however, caused no such reaction and the material was recovered quantitatively. Another possibility is that dichloro acids such as 9 are intermediates, which then undergo an intramolecular S_N2' process. This point is currently being addressed experimentally.

3-Halo butenolides have been studied extensively in the recent past, both as target compounds^{11} and as synthetic intermediates. Chloro butenolides are facile Michael acceptors^{12}, vinyl anion precursors^{13}, and have served as key intermediates in the preparation of tetronic...
acid\textsuperscript{14} and other\textsuperscript{15} molecules. The operational simplicity and brevity of this sequence should provide an attractive alternative to the currently-available synthetic methods for these compounds. We are actively pursuing extensions of this method to more highly-substituted butenolides.

Acknowledgement: We wish to thank the donors of the Petroleum Research Fund, administered by the American Chemical Society, along with the Research Corporation, for support of this research.

REFERENCES

4. This type of rearrangement was originally thought to be an example of an organic dyotropic process (Mulzer, J.; Bruntrup, G. \textit{Angew. Chem., Int. Ed. Engl.} 1979, \textit{18}, 793); however, subsequent work is more consistent with a carbocation intermediate.
8. This method was far superior to generation of dichloroketene via amine-mediated dehydrochlorination of dichloroacetyl chloride.
9. FT-IR (neat): 2982.2, 2941.2, 1767.8, 1651.2, 1463.2, 1383.8, 1323.2, 1172.6, 1108.4, 1026.0 cm⁻¹;¹ H-NMR (500 MHz, CDCl₃): δ = 4.97 (q, J = 6.7 Hz, 1H), 2.53 (sextet, J = 7.5 Hz, 1H), 2.29 (sextet, J = 7.3 Hz, 1H), 1.39 (d, J = 6.7 Hz, 3H), 1.11 (t, J = 7.6 Hz, 3H);¹³C-NMR (500 MHz, CDCl₃): δ = 167.97, 165.30, 118.61, 78.73, 20.08, 18.16, 11.14 ppm. TLC (CH₂Cl₂): Rᵢ = 0.51.

10. Prepared via the reaction of 1,2-dibromoethane with magnesium.


(Received in USA 23 July, 1990)