Tetrahedron Letters,Vol.22,No.50,pp 5019-5022,1981 0040-4039/81/505019-04$02.00/
Printed in Great Britain

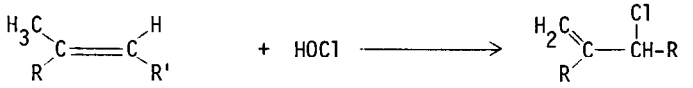
HYPOCHLOROUS ACID. REACTION WITH CONJUGATED KETONES
A SYNTHESIS OF α-CHLORO-β,γ-UNSATURATED KETONES

Shridhar G. Hegde and Joseph Wolinsky*

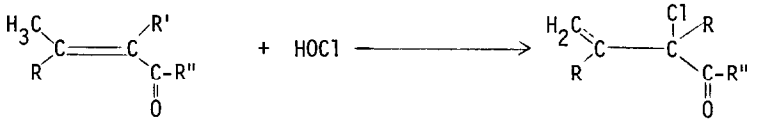
Department of Chemistry, Purdue University, West Lafayette, Indiana 47907

Summary: The two-phase reaction of HOCl with more highly substituted conjugated ketones which can exist in an s-cis conformation yield α-chloro-β,γ-unsaturated ketones in good yield.

In a previous communication[1], we reported that the two-phase reaction of more highly substituted olefins 1 with hypochlorous acid affords allylic chlorides 2 in high yield. Herein we describe the two-phase reaction of hypochlorous acid with various conjugated ketones 3[2] leading to α-chloro-β,γ-unsaturated ketones 4, a class of compound relatively unknown to date.

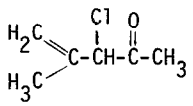


1 2

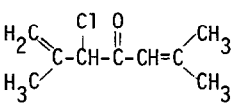


3 4

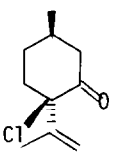
Mesityl oxide[3], phorone and pulegone react cleanly with one equivalent of HOCl[4] to afford α-chloroketones 5, 6 and 7 (a, b) respectively, in high isolated yield. Chloroketone



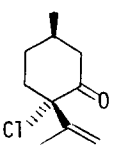
5 (71%)



6 (76%)



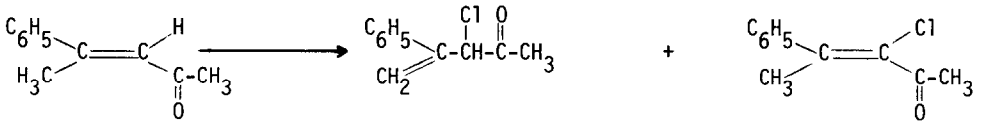
7a (75%)



7b

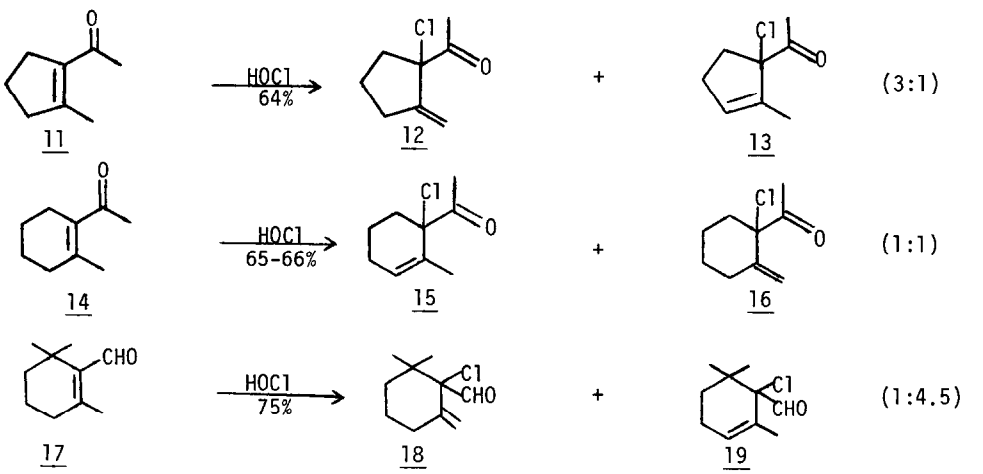
5 [λ_{max} 275 nm, (ε=160); ir 5.8 and 11.0 μ; nmr ($CDCl_3$) δ 1.7 (s, 3H), 2.2 (s, 3H), 4.85 (s, 1H), 5.13 (s, 1H) and 5.25 ppm (s, 1H)] is quite sensitive and even on distillation at temperatures below 100° undergoes decomposition[5] to a mixture of products. Ketone 6 [b.p. 66°/0.05 mm]; λ_{max} 238 nm (ε=11,800); ir 5.9, 6.1 and 10.9 μ; nmr ($CDCl_3$) 1.8 (s, 3H), 1.97 (s, 3H), 2.2 (s, 3H), 4.83 (s, 1H), 5.1 (s, 1H) and 6.3 ppm (s, 1H)] and the isomeric mixture[6] of 7a and 7b [b.p. 80-90°/0.5 mm; λ_{max} 270 nm (ε=171); ir 5.8, 6.1 and 11.0 μ] can be distilled without difficulty.[6a]

2-Phenyl-2-penten-4-one 8, on the other hand, yields a 1:1 mixture of allylic chloride 9 and the vinyl chloride 10 on treatment with HOCl.[7]



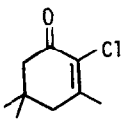
8 9 10

The reaction of conjugated ketones 11[8a] and 14[8b], wherein an addition-elimination process can lead to two different allylic chlorides, yields mixtures of products with varying composition[9] depending on the ring-size and substituents on the ring. The 5-membered ketone yields exocyclic isomer 12 predominantly, whereas the 6-membered ketone affords ca equal amount of the endocyclic 15 and exocyclic 16. The only aldehyde examined to date is β-cyclocitral 17 and it is converted in high yield with HOCl to a mixture of 18 and 19 where the endocyclic isomer predominates.

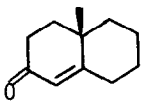


11 12 13 14 15 16 17 18 19

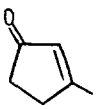
The two phase reaction of HOCl with conjugated carbonyl compounds only appears to succeed in cases where the compound can exist in an s-cis conformation. Thus enforced s-trans compounds like isophorone yield 20 and other yet unidentified products, whereas santonin[10] and ketones 21 and 22 do not react even with the use of excess HOCl.



20

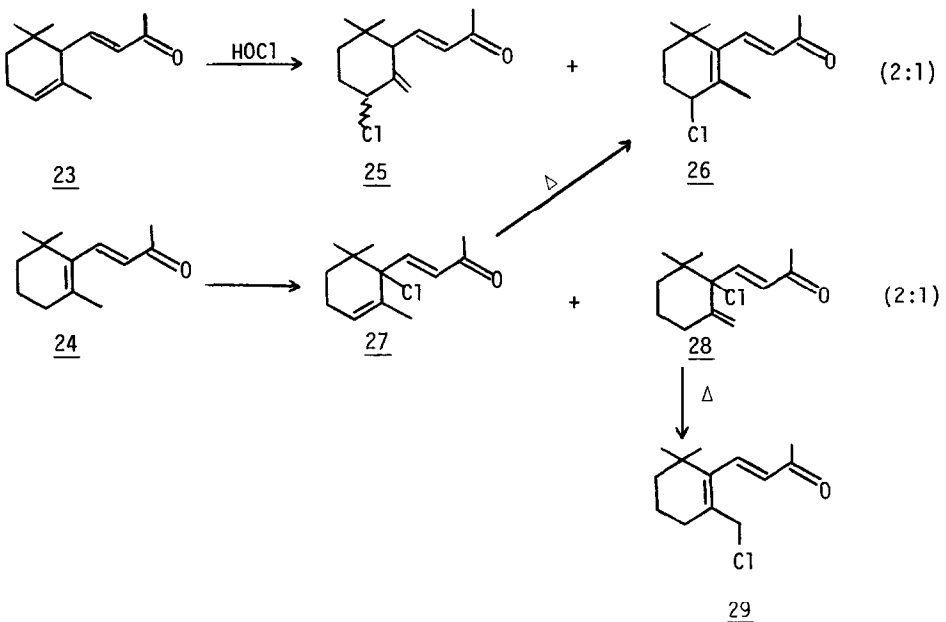


21



22

Finally, the more highly unsaturated α- and β-ionones (23 and 24) give mixtures of allylic chlorides with HOCl. The allylic chlorides 27 and 28 are found to undergo facile thermal isomerization to the more highly conjugated compounds 26 and 29 respectively, during distillation.

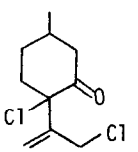


23 25 26 24 27 28 29

The utility of α-chloro-β,γ-unsaturated compounds in organic synthesis is under investigation.

References and Notes

1. S. G. Hegde, M. K. Vogel, J. Saddler, T. Hrinyo, N. Rockwell, R. Haynes, M. Oliver and J. Wolinsky, Tetrahedron Lett., 441 (1980).
2. The reaction is easily performed by simply adding ca 40 g of dry ice slowly over a period of 3-4 hrs. to a mixture of 4.1 g of "70%" calcium hypochlorite, 20 ml of water, 40 mmol of conjugated ketone and 200 ml of dichloromethane. The insoluble salts are removed by filtration, the organic layer is separated and the CH_2Cl_2 removed to yield the crude chloro compound.
3. For the production of chlorohydrins in the reaction of hypochlorous acid with mesityloxide, pulegone and related compounds see: (a) M. Pastureau and H. Bernard, Bull. Soc. Chim. Fr., 33, 1440 (1923); (b) G. Cauquil and P. Mion, ibid., 659 (1940); (c) S. Marmor, J. Org. Chem., 30, 3556 (1965); (d) Z. Jedlinski and J. Majnusz, CA 73, 44840 k (1970).
4. With two equivalents of HOCl, pulegone is converted to a dichloride 30, which is undoubtedly a mixture of stereoisomers and has not yet been separated into its pure components.



30

5. Chloroketone 5 is best purified by evaporative distillation at room temperature (1.0 mm)
6. NMR analysis indicated a 3:2 ratio for the mixture of 7a and 7b (based on the relative integration of signals due to methyl group on the double bond at 1.8 δ and 1.9 δ). Work is in progress to determine whether the major product is 7a or 7b

6a. New compounds had satisfactory microanalytical data and/or spectroscopic properties.

7. Vinyl formation competing with the production of allyl chloride is also observed in the reaction of HOCl with other olefinic substrates containing a conjugating substituent such as a phenyl group (α-methylstyrene) or a vinyl group (isoprene). In these cases vinyl chlorides predominate by a factor of a least two.
8. (a) I. Tabushi, K. Fujita and R. Oda, Tetrahedron Lett., 4247 (1968); (b) R. B. Turner and D. M. Voitle, J. Am. Chem. Soc., 73, 1403 (1951).
9. The composition is determined by the relative integration of olefinic signals in the nmr spectra of these allylic chloride mixtures.
10. E. Wedekind and A. Koch, Ber., 38, 429, 1848 (1905).

(Received in USA 13 August 1981)