gem-Dichlorocyclopropanes as Masked Esters: A Novel Synthesis of β-Methoxycarbonyl Aldehydes and Ketones

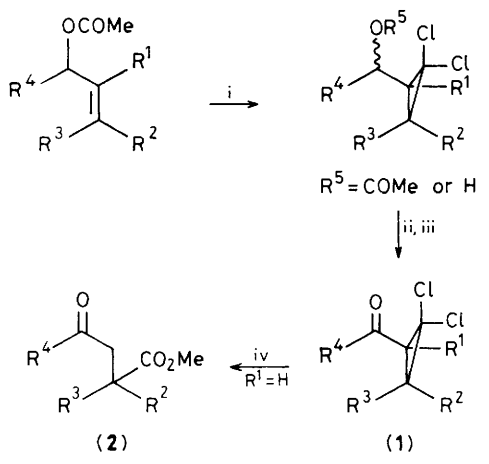
Martin G. Banwell

Department of Chemistry, The University of Auckland, Private Bag, Auckland, New Zealand

The carbonyl conjugated *gem*-dichlorocyclopropanes (**1**) react with sodium methoxide in methanol affording β-methoxycarbonyl aldehydes and ketones in high yield.

The ring-opening reactions of carbonyl conjugated cyclopropanes have been studied extensively.[1] By comparison, little is known about the chemistry of the corresponding *gem*-dihalogenocyclopropanes.[2] Herein, we report that both ring-fused and open-chain *gem*-dichlorocyclopropyl ketones or aldehydes of the type (**1**) undergo a novel ring cleavage reaction affording β-methoxycarbonyl ketones or aldehydes and thereby providing an expeditious route to these synthetically useful[3] 1,4-dicarbonyl compounds.

Thus the cyclopropanes (**1a**)—(**1f**) (readily available in multigram quantities and high yield *via* the route illustrated in Scheme 1) afford the methoxycarbonylated products (**2a**)—(**2f**)† on treatment with sodium methoxide in methanol. The simplicity of the procedure is illustrated by the preparation of the keto-ester (**2a**) from the cyclopropane (**1a**): a stirred solution of (**1a**) (1 equiv.) in a small volume of anhydrous methanol was treated in one portion with 1.0 M sodium methoxide (10 equiv.) in methanol and stirring continued at 18 °C for 1.0 h. After this time, chromatographic analysis indicated no starting material remained. Dilution of the reaction mixture with water followed by standard work-up procedures (CH_2Cl_2 extraction) and subsequent distillation afforded (**2a**) (b.p. 140—142 °C at 30 mmHg; lit.,[4] 131—131.3 °C at 18 mmHg) with spectroscopic properties identical to those reported for authentic material.



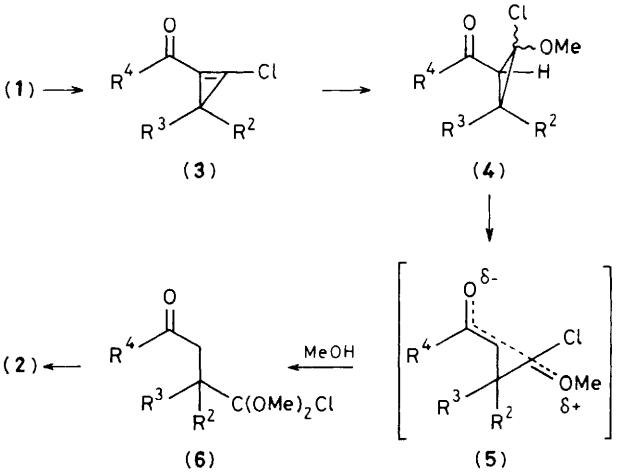
a; $R^1 = R^2 = H$, $R^3, R^4 = -[CH_2]_3-$
b; $R^1 = H$, $R^2 = Me$, $R^3, R^4 = -[CH_2]_3-$
c; $R^1 = R^2 = H$, $R^3, R^4 = -[CH_2]_4-$
d; $R^1 = R^2 = H$, $R^3, R^4 = -[CH_2]_5-$
e; $R^1 = H$, $R^2 = R^3 = R^4 = Me$
f; $R^1 = R^4 = H$, $R^2, R^3 = -[CH_2]_5-$
g; $R^1 = Me$, $R^2 = H$, $R^3, R^4 = -[CH_2]_3-$
h; $R^1 = R^2 = H$, $R^3, R^4 = -[CH_2]_2-$

Scheme 1. *Reagents and conditions:* i, 50% aqueous NaOH, $CHCl_3$, $PhCH_2NEt_3Cl$, 18 °C, 40 h; ii, NaOH, 1.3 equiv., MeOH, 18 °C, 12 h; iii, pyridinium chlorochromate, 1.7 equiv., CH_2Cl_2, 18 °C, 3 h; iv, NaOMe, MeOH.

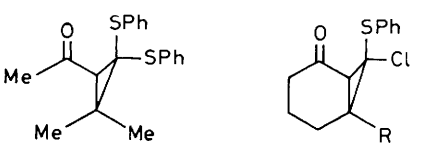
† Yields (**2a**)—(**2d**) 100%, (**2e**) 83%, and (**2f**) 75%. No reaction was observed with substrate (**1g**) while (**1h**) gave a complex mixture of products.

The mechanism (Scheme 2) by which we envisage the conversion (**1**)→(**2**) occurring involves initial 1,2-elimination[5] of the elements of hydrogen chloride from (**1**) delivering the cyclopropenone (**3**). Conjugate addition of methoxide ion to this strained enone[6] and subsequent protonation would produce a chloro-ether (**4**). (Such a sequence must be favoured over direct nucleophilic substitution at the cyclopropyl carbon given the reluctance of halogenocyclopropanes to engage in these reactions).[7] Solvolytic ring-fission of (**4**) would yield the chloro-acetal (**6**) which hydrolyses to (**2**) on aqueous work-up. Presumably both the ease and regiochemistry of ring-cleavage in (**4**) are determined by the stabilisation of developing charge as shown in (**5**).

A number of observations are consistent with these mechanistic proposals. The conjugated cyclopropyl compound (**1g**), a substrate incapable of undergoing initial 1,2-elimination, is inert towards sodium methoxide. Furthermore, treatment of compound (**1e**) with sodium benzenethiolate (4 equiv.) in methanolic sodium methoxide affords the cyclopropyl ketone (**7**) (98%). The formation of this disubstituted product is possible because an *anti-periplanar* relationship (for elimination) between either chlorine atom and the cyclopropyl hydrogen in (**1e**) can be achieved *via* epimerization of the acetyl moiety. In contrast, treatment of the ring-fused



Scheme 2



compound (**1a**) under similar conditions affords a single monosubstituted product (85%) which is resistant to further reaction on treatment with sodium methoxide. On this basis, we have assigned this latter product as the *exo*-chloro-compound (**8**). Compound (**1b**) behaves similarly affording the monochlorocyclopropane (**9**) (80%). These results suggest that ring cleavage during the conversion of (**1**) into (**2**) occurs after monosubstitution by methoxide ion, and that cyclopropanone acetals (products of disubstitution) are not involved in the reaction.

The methodology described in this paper permits the construction of quaternary carbon centres[8] incorporating a methoxycarbonyl group, structures not available *via* conjugate addition of ester anion equivalents to tertiary carbon centres.[4] In addition, formal nucleophilic substitution of halogen atoms in *gem*-dichlorocyclopropanes which are 'activated' by conjugation with a carbonyl moiety has been shown to proceed in high yield and stereospecifically in certain cases.

I thank Dr. R. A. J. Smith (University of Otago) for providing spectroscopic data on authentic (**2a**) and Professors B. R. Davis and D. J. McLennan (University of Auckland) for helpful discussions.

Received, 5th September 1983; Com. 1188

References

1 R. K. Dieter and S. Pounds, *J. Org. Chem.*, 1982, **47**, 3174 and references therein.
2 I. G. Tischenko, O. G. Kulinkovich, and Yu. V. Glazkov, *J. Org. Chem. USSR (Engl. Transl.)*, 1975, **11**, 579.
3 M. Miyashita, T. Kumazawa, and A. Yoshikoshi, *Chem. Lett.*, 1980, 1043.
4 A-R. B. Manas and R. A. J. Smith, *J. Chem. Soc., Chem. Commun.*, 1975, 216.
5 M. G. Banwell and C. Papamihail, *J. Chem. Soc., Chem. Commun.*, 1981, 1182.
6 H. O. House, R. F. Sieloff, T. V. Lee, and M. B. Detar, *J. Org. Chem.*, 1980, **45**, 1800.
7 L. A. M. Turkenburg, W. H. de Wolf, F. Bickelhaupt, C. H. Stam, and M. Konijn, *J. Am. Chem. Soc.*, 1982, **104**, 3471.
8 S. F. Martin, *Tetrahedron*, 1980, **36**, 419.