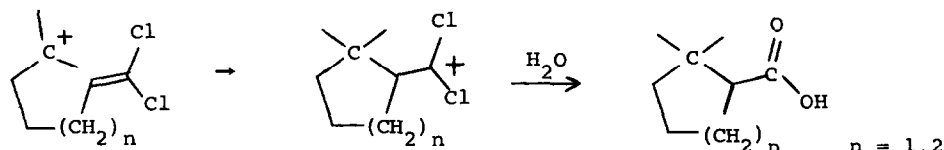


CYCLOALKANECARBOXYLIC ACID SYNTHESIS BY  
INTRAMOLECULAR CHLORO OLEFIN ANNELETION

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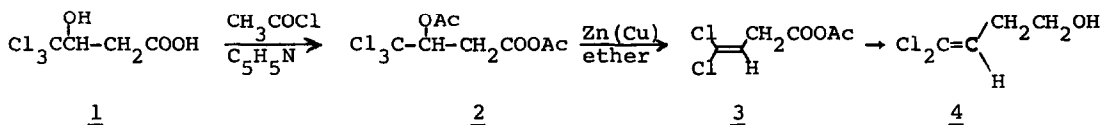
(Received in USA 2 January 1973; received in UK for publication 20 March 1973)

Chloro olefin annelation has been shown to have great utility in the construction of cycloalkanone and acylcycloalkane rings, using terminal and internal chloroalkene moieties, respectively, as sites for electrophilic closure.<sup>1</sup> In addition, we have investigated substrates bearing 1,1-dichloro-1-ene side chains, since cationic attack can lead directly to cycloalkanecarboxylic acids<sup>2</sup>, e.g.

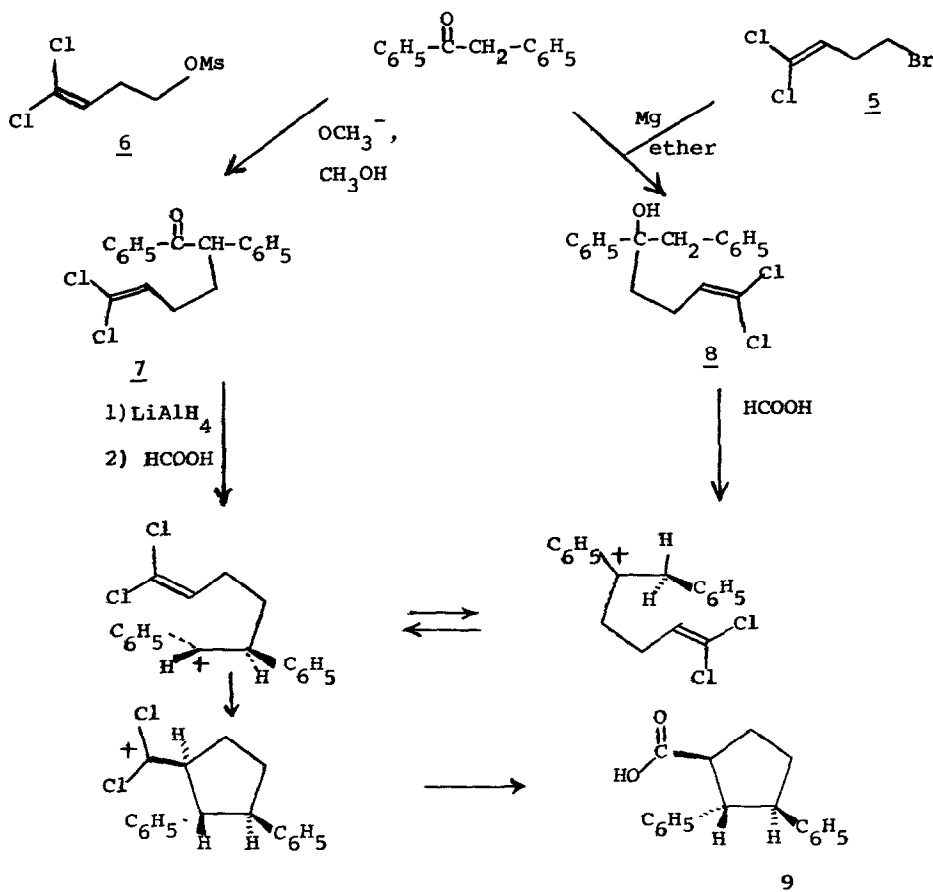


This note reports typical five- and six-membered ring syntheses which culminate in closure of the above type, and which illustrate the use of two easily preparable and generally useful alkylating agents

The condensation product 1, derived from chloral and malonic acid<sup>3</sup>, when successively acetylated, treated with zinc to effect dechloroacetoxylation (2→3), and reduced with lithium aluminum hydride, all without isolation of intermediates provides pure 4,4-dichloro-3-buten-1-ol<sup>4</sup> (4), bp 80-81.5°/10mm, in ca. 30% yield (not optimized).



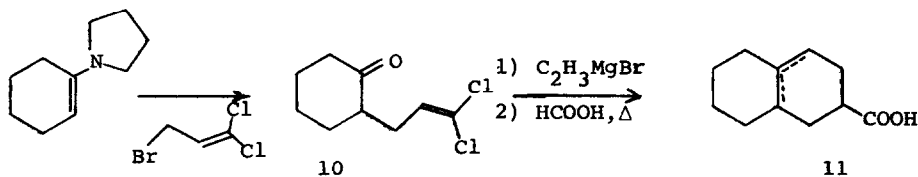
Conversion of 4 to its bromide<sup>5</sup> 5 and mesylate<sup>5</sup> 6 by phosphorous tribromide and methanesulfonyl chloride, respectively, allows introduction of the annelating agent into a bifunctional substrate such as desoxybenzoïn either electrophilically ( $\rightarrow$ 7) or nucleophilically ( $\rightarrow$ 8).



When ketone<sup>5</sup> 7 is reduced and the resulting carbinol<sup>5</sup> refluxed overnight in 97% formic acid, cyclization occurs in the same manner as with 8<sup>5</sup> to afford trans, trans-2,3-diphenylcyclopentanecarboxylic acid (9), mp 150.5–152°, in ca. 50% yield by either route. Thus, prior carbonium ion rearrangement before the non-nucleophilic dichlorobutenyl side chain cyclizes provides a single product as planned.<sup>1</sup> The trans, trans configuration of 9 is assigned by analogy with a similar cyclization which produced trans-3,4-diphenylcyclopentanone and by the absence of epimerization on heating<sup>7</sup>, which verifies the trans relationships of the

carboxyl group and adjacent phenyl ring.

Six-membered ring formation is exemplified by the sequence below, commencing with the alkylation of cyclohexanone pyrrolidine enamine by 1,1-dichloro-3-bromopropene<sup>5</sup>. The latter was readily acquired by benzoyl peroxide-initiated N-bromosuccinimide reaction with 1,1-dichloropropene in carbon tetrachloride, affording 66% yield of the expected bromide, bp 65-66.5/17mm. Ketone 10 (semicarbazone<sup>4</sup>: mp 169-170°) was reacted with ethereal vinylmagnesium bromide and the resultant carbinol<sup>5</sup> formolyzed.



The isomeric octalin carboxylic acids<sup>5</sup> (11), formed in ca. 40% yield, were hydrogenated (Pt catalyst in acetic acid) to a mixture of cis,cis- and cis,trans-decahydro-2-naphthoic acids, whose identities were established by comparison with authentic samples<sup>8</sup>.

Not surprisingly, these "intramolecular Bott reactions" proceed in more satisfactory yields than were noted in intermolecular combination of hindered 1-methylcycloalkyl cations with 1,1-dichloroethylene<sup>2</sup> and may have utility in generating the carbocyclic framework of terpenes and of picrotaxane alkaloids such as dendrobine<sup>9</sup>. We also wish to point out that the three- and four-carbon annelating agents used to assemble 7, 8, and 11 can be easily homologated and thus extend the possibilities for cycloalkanecarboxylic acid synthesis to rings larger than six-membered.

#### References

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Acknowledgment: We are grateful to the National Science Foundation for financial support of this research.