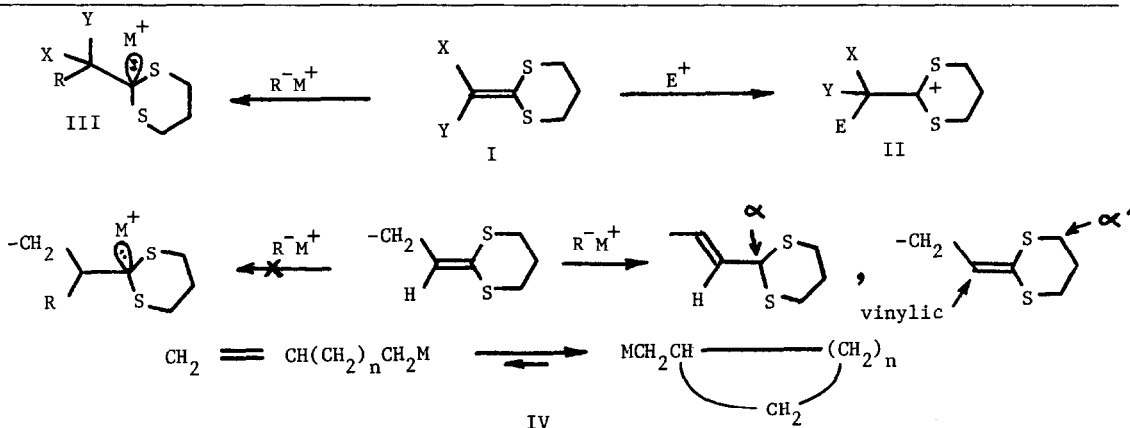


DITHIANE CHEMISTRY. III.¹ THE ADDITION OF GRIGNARD
 REAGENTS TO SUBSTITUTED KETENE DITHIOACETALS.

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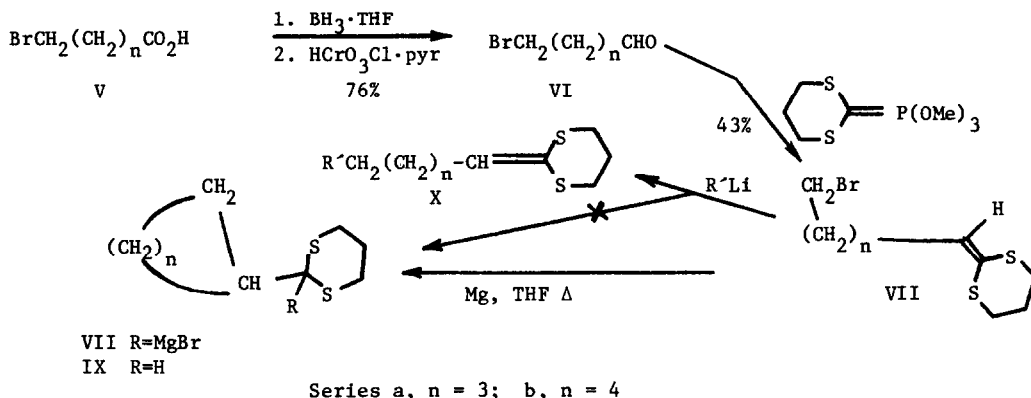
The dithianylidene function (I) is well suited as a trap for anionic, cationic, and radical agents due to the ability of sulfur atoms to stabilize all three classes of carbon provalency.² The use of this function as an internal quench for carbocationic cyclizations, and studies of cyclizations initiated by the formation of dithenium cations (II)^{1a,3} illustrate the electrophilic end of this reaction spectrum. Although the anionic side was recognized essentially from the beginnings of the synthetic exploration of dithiane chemistry,⁴ it has not played a significant role in organic synthesis.⁵ Unlike the ketene dithioacetal monoxides,⁷ the addition of carbanionic agents (RLi,^{6b,8} RMgX, and LiR₂Cu⁸) fails for the substituted compounds (Id,e,f). With alkyl lithium transmetallation occurs giving α -,^{6e,f,8} α' -,^{6f} or vinyl-lithium compounds. We now report that the intramolecular version of this reaction and related addition-elimination sequences (with Ib,c) occur readily, particularly with Grignard reagents.

We were encouraged to try the intramolecular reaction by the reports that ω -unsaturated organometallics cyclize to cycloalkanemethylmetals when $n = 3,4$ (IV).¹⁰



I→III: a) X=Y=H; b) X=Cl, Y=H; c) X=Y=Cl; d) X=Ph, Y=H; e) X= alkyl, Y=H; f) X,Y=alkyl or cycloalkyl; g) X=Cl, Y= alkyl.

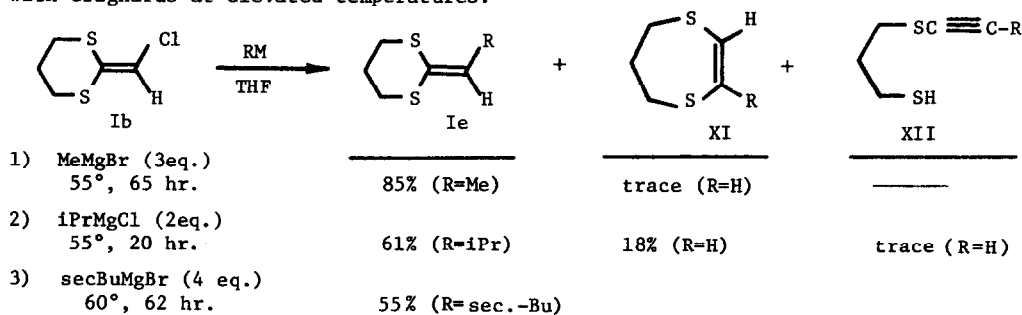
*Camille and Henry Dreyfus Teacher-Scholar, 1974-1979. Support from this source and a PHS grant is gratefully acknowledged.



For these studies the essentially neutral phosphite dithianylid reagent of Corey and Markl¹¹ was used (VI-VII) rather than the usual Peterson olefination sequence. The aldehydes¹² were obtained from the known acids as shown. The dithianylids VII ($\text{S}_2\text{C}=\text{CHR}$ ν 3010, 1585-1595 cm^{-1} , vinyl-H trip. 5.85 ppm) were obtained in moderate yield and were reacted immediately due to their decomposition on storage (-20° , under nitrogen). With $n\text{BuLi}$ (-20° , THF) ketene dithioacetal VIIa affords only recovered starting material and the ω -alkylation product (50%, Xa, $\text{R}' = n\text{Bu}$). With $t\text{-BuLi}$ (-78° or -20° , 1-3 days, THF-toluene) acetal VII is recovered (60-80%) with the only reaction being a slow vinylic transmetalation.

The desired cyclization of VIIa could be effected (90% conv., 74% yield) with excess Mg turnings (50° , 5 hr, THF) using dibromoethane to initiate the reaction. The cyclopentane product (IXa) was characterized by spectral comparison with authentic material and hydrolysis to the aldehyde (2,4-DNP, mp and mixed mp 156-157°). The cyclization of VIIb proceeded more slowly under the same conditions (40% yield after 20 hr) affording, on aqueous work-up, 2-cyclohexyl-1,3-dithiane (mp 51-52°, lit.^{4b} mp 51.6-52.4°).

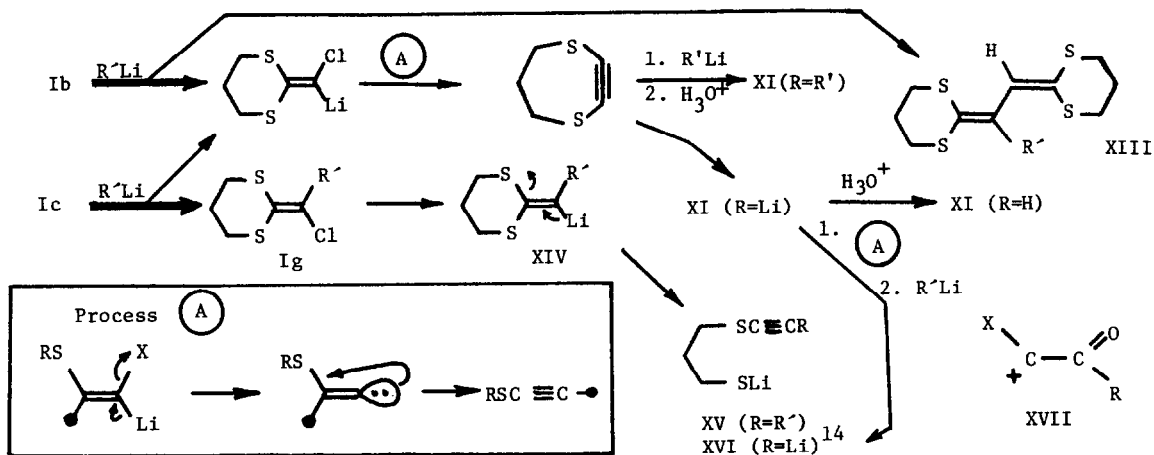
With this success we turned to the chloroketene acetals (Ib,c).⁹ We reasoned that intermediate III (X and/or Y = Cl) would undergo rapid loss of chloride affording alkyl substituted dithioacetals which would be stable to the reaction conditions. The monochloro compound (Ib) was examined first. As with VII, relatively uncomplicated addition-elimination occurs only with Grignards at elevated temperatures.^{12b}



	Ie	XI	XII
4) nBuMgI (2 eq.), 65°, 72 hr.	30% (R=nBu)	—	trace (R=H)
b) 25°, Cu(OAc) ₂ cat., 24 hr.	40% (R=nBu) 5% (R=H)		
5) nBuLi (2 eq.)			
a) -78°, 3 min.	20% (R=Bu)	20% (R=Bu)	10% (R=H and Bu)
b) -20°, 78 hr.	10% (R=Bu) 5% (R=H)	20% (R=H) 15% (R=Bu)	trace (R=H)

Transmetalation both initially and subsequently to introduction of the alkyl group are minor, but significant pathways with Grignards, as seen in the isolation of dihydro-dithiepin XI (R=H) - δ 5.87 (2H, s), 3.50 (4H, trip., 6), and 2.16 ppm (2H, quint., 6 Hz); m/e 131.9986 (C₅H₈S₂); ν 3020, 1545 cm⁻¹ (SCH=CHS). With alkylolithiums reactions with Ib are extremely rapid at -78°. Even after only 3 min., the addition-elimination product (Ia) accounts for only a 20% yield. The isomer XI (R=Bu) - δ 5.70 (1H, bs) and 3.45 (4H, two trip., $\Delta\nu = 4$, J = 6 Hz) - occurs in equal yield together with coupling products resulting from later transmetalation. The major (\sim 40% yield) coupling product was XIII (R'=Bu) - m/e 318.0550 (C₁₄H₂₂S₄), δ 6.25 (1H, s), and 2.80 ppm (4H, \sim quart., α -H to S).

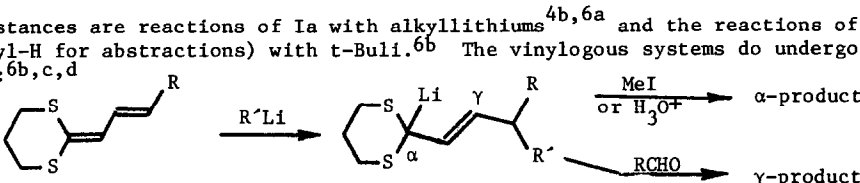
Dichloroketene dithioacetal Ic proved less reactive with Grignards, only 10-20% incorporation of the alkyl group (as Ig)¹³ occurs under conditions 1) \rightarrow 4) above. After three weeks at room temperature with excess iPrMgCl, Ig (Y=iPr)¹³ is isolated in 50% yield. However, with nBuLi (THF, -78°, 30 min.), addition-elimination takes precedence over initial transmetalation: Ig (Y=nBu)¹³ is isolated in 78% yield. Prolonged reaction with excess nBuLi affords, in addition, dialkylated product (If, X=Y=nBu)¹³ as well as XI (R=Bu)¹³ and XII (R=H and Bu)¹³. A scheme rationalizing the results in both the mono- and dichloro-series appears below.



The formation of compounds of the 7-membered ring series and XII can be viewed as sequential vinylcarbenoid insertions (Process A).¹⁵ Apparently the intermediate cyclic acetylene undergoes either alkylmetal addition (\rightarrow XI, R=R') or reduction (\rightarrow XI, R=Li). For the fragmented acetylenic products, β -elimination (as in XIV \rightarrow XV) is an alternative route.¹⁵

Studies of the use of Ib and Ic as the equivalent of XVII in total synthesis are in progress.¹⁶

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- The chloroketene dithioacetals are conveniently prepared (90+%) from 2-dichloromethyl (mp. 39.5-40.5°) and 2-trichloromethyl-1,3-dithiane (mp. 107°) on stirring with excess methanolic sodium methoxide (25°, 15 min.): Ib - ν 3095, 1540 cm^{-1} ($\text{S}_2\text{C}=\text{CHCl}$), δ 6.23 ppm (vinyl-H, s); and Ic - ν 1530 cm^{-1} ($\text{S}_2\text{C}=\text{CCl}_2$). Both were characterized by high resolution ms after molecular distillation (80-100°, 0.1-0.3 torr). Ib was used within a week of preparation. Ic can be stored for months at -20°C under argon.
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- Aldehydes VIa,b were characterized by NMR and high resolution ms; VIa (bp 84°, 14 torr; DNP mp. 106.5-107.5°), VIb (bp 51°, 0.15 torr; DNP mp. 95.5-96.5°).
- As suggested by the Cu(I) catalysis observed (entry 4b), chloroketene thioacetal Ib reacts more rapidly with cuprates (LiCuMe_2 ; 25°C, 8 hr., > 80% completion). We view this as a coupling, rather than an addition-elimination, reaction.
- The structures of all compounds mentioned are supported by a full complement of spectral data, including high resolution ms.
- The presence of XVI is supported by quenches with MeI which produces the S-Me, methyl acetylene.
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