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HETEROLYTIC FRAGMENTATION OF 1, 3-DITHIANYL TOSYLATES

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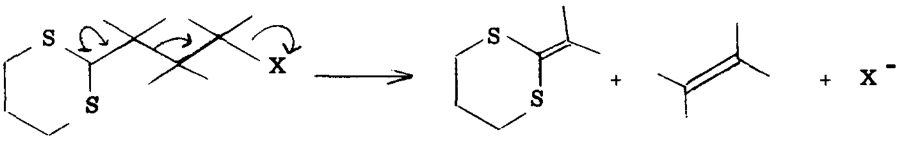
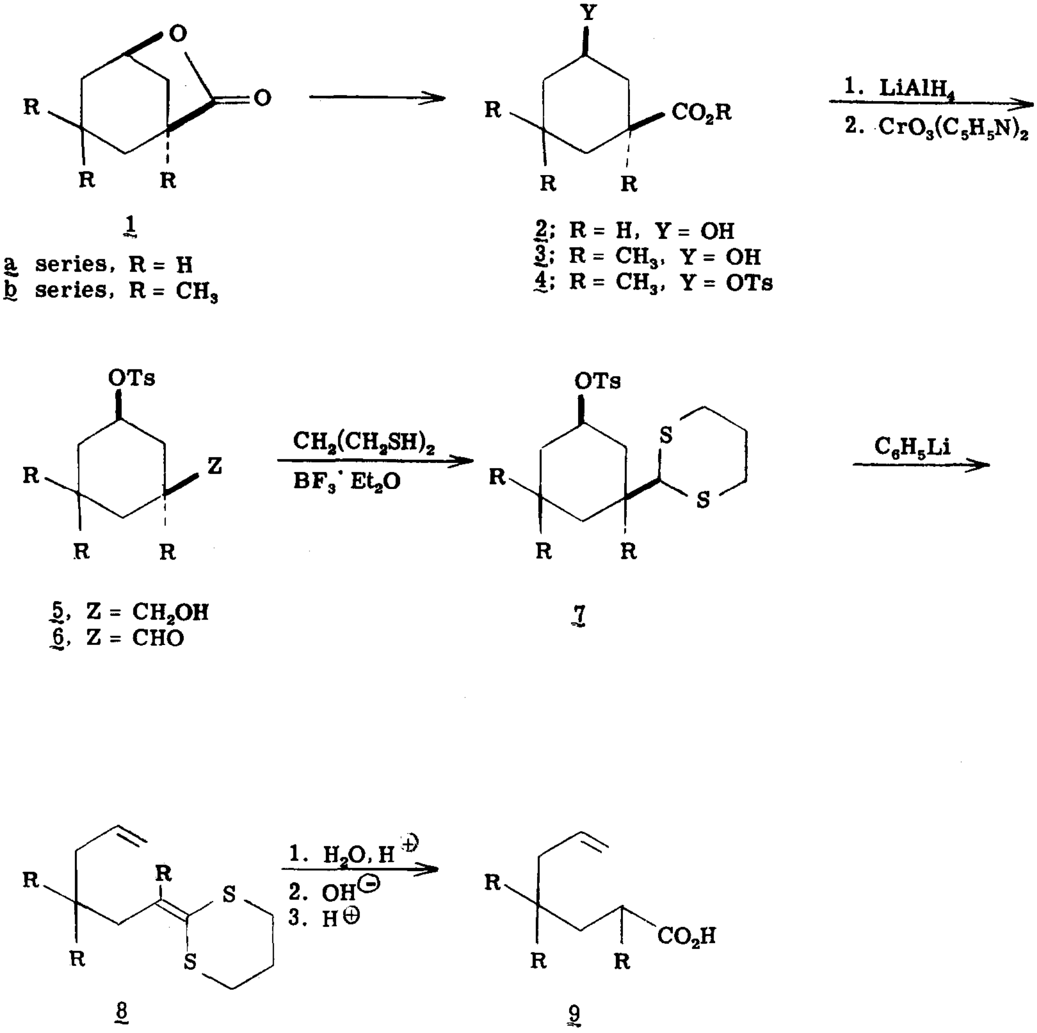
The class of organic reactions known as heterolytic fragmentations[2] has figured prominently in multistep synthesis over the past several years.[3] We report herein a new member of this class in which, at least formally, a 1, 3-dithiane anion[4] serves as part of the electrofugal group[2] in the fragmentation reaction. Although our work has thus far dealt only with cyclohexyl systems, we expect this reaction to apply to a variety of cyclic and acyclic systems according to the following expression:



In the case of cyclic systems (e.g. 7 8)the substituted ketene thioacetal products can be made to undergo a number of synthetically useful transformations,[5] thus enhancing the value of the above fragmentation scheme.

The known γ-lactone 1a[6] upon basic methanolysis followed by treatment with p-toluenesulfonyl chloride in pyridine afforded the diester 4a [m.p. 85-86°, λ^{KBr}_{max} 5.80, 7.41, 8.42, 8.53 and 10.70μm; $\delta^{CDCl_3}_{TMS}$ 7.53 (aromatic AB, J = 9 Hz, $\Delta\nu_{AB}$ = 28 Hz), 3.64 (OCH_3), and 2.44 p.p.m. (CH_3)]. Reduction with lithium aluminum hydride in tetrahydrofuran at -30° and subsequent oxidation with Collins' reagent[7] yielded the aldehyde 6a [89% yield based on diester



1: a series, $R = H$; b series, $R = CH_3$

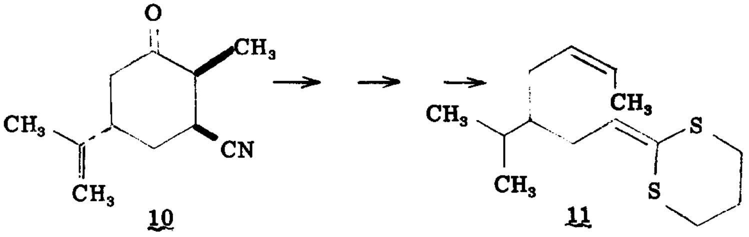
2; $R = H$, $Y = OH$
3; $R = CH_3$, $Y = OH$
4; $R = CH_3$, $Y = OTs$

5, $Z = CH_2OH$
6, $Z = CHO$

4: λ_{max}^{film} 5.80, 7.41, 8.43, 8.53 and 10.70μm; $\delta_{TMS}^{CCl_4}$ 9.38 (aldehyde CH), 7.44 (aromatic AB, J = 8 Hz, $\Delta\nu_{AB}$ = 27 Hz) and 2.45 p.p.m. (CH_3)]. Conversion to the 1,3-thiane derivative **7a** [92% yield: $\delta_{TMS}^{CCl_4}$ 7.50 (aromatic AB, J = 8.5 Hz, $\Delta\nu_{AB}$ = 28 Hz), 3.95 (CH doublet, J = 3.5 Hz), and 2.42 p.p.m. (CH_3)] followed by treatment with phenyllithium in tetrahydrofuran at room temperature for 10 hr afforded the ketene thioacetal **8a** [52% yield of 75% purity according to gas chromatography: λ_{max}^{film} 6.11, 10.15 and 11.0μm; $\delta_{TMS}^{CDCl_3}$ 6.1-4.8 (vinyl multiplet) and 5.90 p.p.m. (vinyl H triplet, J = 7 Hz)]. Hydrolysis of this substance was accomplished by stirring with methanolic aqueous p-toluenesulfonic acid which gave the thiol ester derivative of acid **9a**. Basic hydrolysis of this substance yielded the acid **9a** [48% yield from **8a**: λ_{max}^{film} 5.85, 6.13, 10.15 and 11.0μm] identified through its hydrogenation product, heptanoic acid.

Similarly, hydroxy acid **2b** (prepared by hydrocyanation[8] of isophorone, sodium borohydride reduction of the resulting keto nitrile and basic hydrolysis) (m.p. 140-141°: λ_{max}^{KBr} 2.93, 5.85, 7.88 and 9.73μm) was converted to the dithiane tosylate **7b** (69% overall yield) via the ester **3b**, the diester **4b** [m.p. 61-62°: λ_{max}^{KBr} 5.80, 7.42, 8.51 and 10.75μm; $\delta_{TMS}^{CDCl_3}$ 7.58 (aromatic AB, J = 8 Hz, $\Delta\nu_{AB}$ = 29 Hz), 3.64 (OCH_3), 1.23 and 0.98 p.p.m. (CH_3)], the alcohol **5b** [m.p. 111-112.5°: λ_{max}^{KBr} 2.98, 7.42, 8.58, and 10.90μm; $\delta_{TMS}^{CDCl_3}$ 7.54 (aromatic AB, J = 8 Hz, $\Delta\nu_{AB}$ = 29 Hz), 3.14 (CH_2OH), 2.43 (aromatic CH_3), 0.91, 0.90, and 0.89 p.p.m. (CH_3)], and the aldehyde **6b** [m.p. 71-72°: λ_{max}^{KBr} 5.80, 7.45, 8.60 and 11.10μm; $\delta_{TMS}^{CCl_4}$ 11.0 (aldehyde CH), 7.51 (aromatic AB, J = 8 Hz, $\Delta\nu_{AB}$ = 27 Hz), 1.01, 0.96 and 0.95 p.p.m. (CH_3)]. The dithiane tosylate **7b** [m.p. 117-118°: λ_{max}^{KBr} 7.41, 8.48, 8.58 and 10.85μm; $\delta_{TMS}^{CDCl_3}$ 7.55 (aromatic AB, J = 8 Hz, $\Delta\nu_{AB}$ = 28 Hz), 3.86 (CH), 1.16 and 0.95 p.p.m. (CH_3)] was treated with phenyllithium in tetrahydrofuran to give the ketene thioacetal **8b** [73% yield of 91% purity according to gas chromatography: λ_{max}^{film} 6.10, 10.09 and 10.99μm; $\delta_{TMS}^{CCl_4}$ 6.15-4.75 (vinyl multiplet), 2.37 (vinyl CH_3) and 0.90 p.p.m. (CH_3)]. The acid **9b** [58% yield: λ_{max}^{film} 2.9-3.7, 5.86, 8.18, 10.1 and 11.0μm: $\delta_{TMS}^{CDCl_3}$ 11.55 (COOH), 4.8-6.1 (vinyl multiplet), 1.10 (CH_3 doublet, J = 7 Hz), and 0.91 p.p.m. (CH_3)] was obtained by the two-step hydrolysis method described above.

In a like manner, the hydrocyanation product 10 of carvone[8] was converted to the ketene thioacetal 11.



Further applications of the 1,3-dithiane fragmentation scheme are currently under investigation.

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