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STEREOSELECTIVE SYNTHESIS OF erythro- AND threo-1,2-DIOLS FROM DIKETO SULFIDES VIA cis-3,4-DIHYDROXYTHIOLANES

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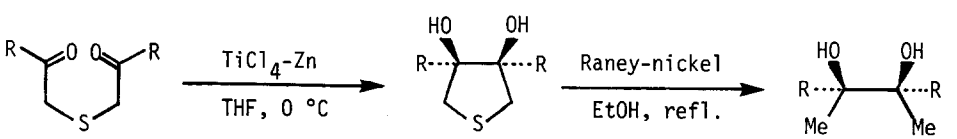
Summary: Intramolecular reductive coupling reaction of a series of diketo sulfides (1) by a low-valent titanium reagent at 0 °C in tetrahydrofuran leads to cis-3,4-dihydroxythiolanes (2) exclusively in 67-89% yields. Desulfurization of 2 by Raney nickel in ethanol affords either erythro- or or threo-1,2-diols (3) in 51-82% yields.

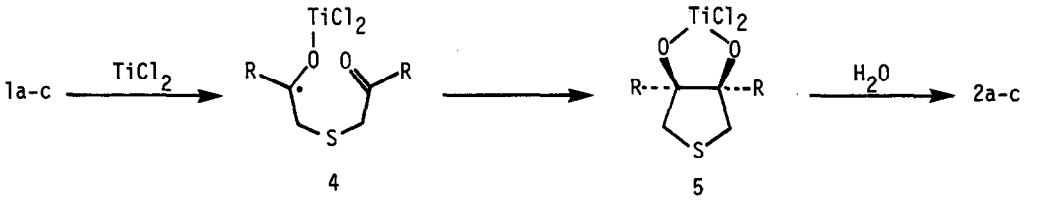
Diketo sulfides (1) are readily accessible compounds. Symmetrically substituted 1 are obtained by reaction of α-haloketones with sodium sulfide and unsymmetrically substituted ones are by reaction of α-haloketones with α-mercaptoketones.[1-4] We previously reported that treatment of 1 at 0 °C or so by a low-valent titanium reagent (prepared from titanium(IV) chloride and zinc powder in tetrahydrofuran)[5] leads to 3,4-dihydroxythiolanes (2).[3] We now found that two hydroxy groups of 2 are in cis-configuration each other in any case and hence desulfurization of 2 by Raney nickel gives rise to either erythro- or threo-1,2-diols (3) depending on the substituents on the thiolane ring.

Thus, intramolecular reductive coupling reaction of diketo sulfides 1a-c by the foregoing low-valent titanium reagent at 0 °C in tetrahydrofuran afforded cis-3,4-diaryl-3,4-dihydroxythiolanes 2a-c[6] exclusively in good yields. Desulfurization of 2a-c by Raney nickel in refluxing ethanol gave the corresponding erythro(meso)-1,2-diols 3a-c[7] in good yields.

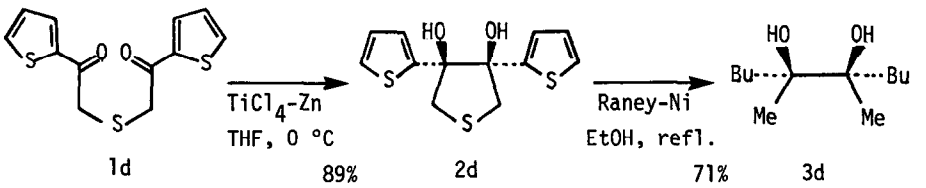


1a : R = C_6H_5	2a : 82%	3a : 75%
b : R = 4-MeC_6H_4	b : 78%	b : 82%
c : R = 4-$MeOC_6H_4$	c : 67%	c : 82%

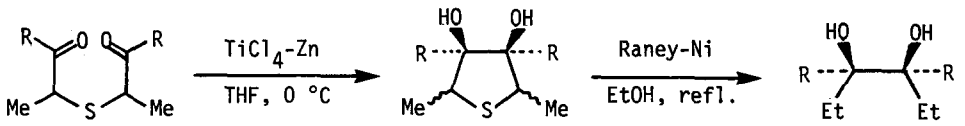
The exclusive formation of cis-3,4-dihydroxythiolanes 2a-c may best be explained as depicted below. Reduction of one of carbonyl groups of 1a-c by titanium(II) chloride, produced by reduction of titanium(IV) chloride with zinc, affords a titanium(III) species (4). Intramolecular cycloaddition of 4 gives rise to a cyclic titanium(IV) derivative (5), which should lead to cis-diols 2a-c after alkaline hydrolysis.[8]



Diketo sulfide 1d also afforded the cis-diol 2d on reductive coupling reaction. Desulfurization of 2d by Raney nickel in refluxing ethanol was accompanied by concomitant reductive desulfurization of the thiophene rings,[9] thus providing erythro-5,6-dihydroxy-5,6-dimethyldecane (3d)[7] in 71% yield.



Diketo sulfides 1e and 1f are obtained as a mixture of meso- and d,l-isomers. Reduction of a mixture of meso- and d,l-isomers of 1e and 1f affords 2e and 2f which are a mixture of three geometrical isomers (note that there exist three isomers in 2e and 2f even if two hydroxy groups are cis each other).[10] However, desulfurization of these isomeric mixtures gave only erythro-isomers 3e and 3f,[7] although it required prolonged refluxing in ethanol and the use of a large excess of Raney nickel probably because of steric reason.[11]

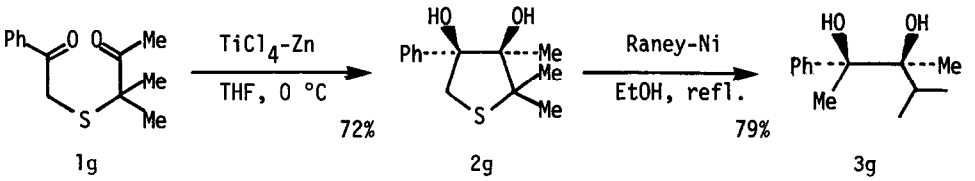


1e : R = Ph
f : R = Me

2e : 82%
f : 71%

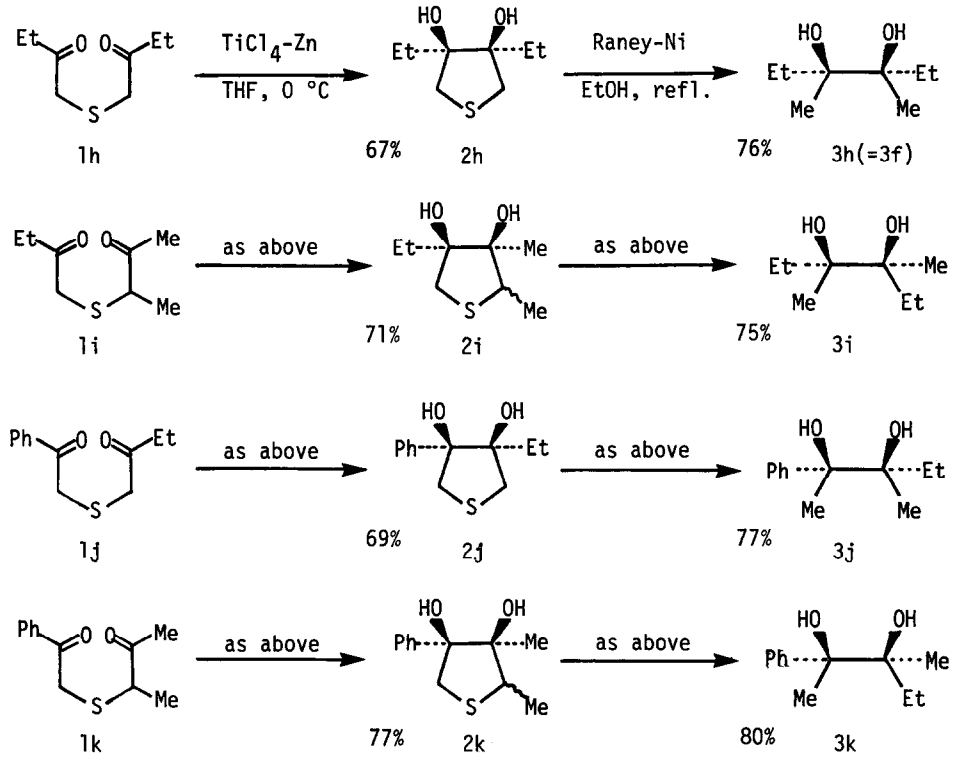
3e : 51%
f : 81%

Although only erythro-isomers were synthesized in the foregoing instances, preparation of threo-isomers is also possible. Thus, starting from unsymmetrically substituted diketo sulfide 1g, highly substituted threo-1,2-diol 3g[7] was satisfactorily synthesized.



1g 2g 3g

Finally effort was made to elaborate both erythro- and threo-isomers starting from different diketo sulfides. Thus, starting from sulfides 1h and 1j, erythro-1,2-diols 3h (=3f) and 3j[7] were satisfactorily synthesized, while the corresponding threo-isomers 3i and 3k[7] were cleanly prepared from sulfides 1i and 1k, respectively.



1h 2h 3h(=3f)

1i 2i 3i

1j 2j 3j

1k 2k 3k

One of general methods for the preparation of 1,2-diols involves pinacolic reduction of carbonyl compounds.[12] This method, however, leads to a mixture of erythro- and threo-isomers, when applied to aldehydes and unsymmetrically substituted ketones, and usually cannot be applied to the preparation of constitutionally unsymmetrical 1,2-diols (cross-coupling reaction between different carbonyl compounds). Diketo sulfides 1 are prepared from ketones as starting material. The net result of the present conversion, therefore, implies that stereospecific pinacolic reduction, not only between same carbonyl compounds but also between different carbonyl compounds, could be attained. In summary, the method developed here provides a novel selective synthesis of both erythro- and threo-1,2-diols, whose preparation hitherto required pure E- or Z-olefins.[12]

References and Notes

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3. (a) J. Nakayama, H. Machida, R. Saito, and M. Hoshino, *Tetrahedron Lett.*, 26, 1983 (1985).
   (b) J. Nakayama, H. Machida, and M. Hoshino, *Tetrahedron Lett.*, 26, 1981 (1985).
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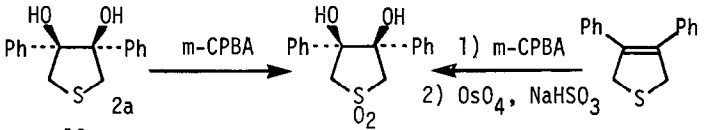
6. cis-Configuration of 2a is also established by the following chemical conversions.



7. mp and ^{1}H-NMR (^{13}C-NMR) data ($CDCl_3$ as solvent) of 1,2-diols 3a-k are as follows. 3a: mp 117.5-118.5 °C (lit., mp 120 °C); ^{1}H-NMR δ 1.56 (6H, s, Me), 2.24 (2H, s, OH), 7.15 (10H, s, Ph). 3b: mp 136-137 °C (lit., mp 134-135 °C); ^{1}H-NMR δ 1.51 (6H, s, Me), 2.15 (2H, s, OH), 2.29 (6H, s, Me), 6.9-7.3 (8H, m, benzene rings). 3c: mp 169-171 °C (lit., mp 168-169 °C); ^{1}H-NMR δ 1.53 (6H, s, Me), 2.24 (2H, broad s, OH), 3.76 (6H, s, OMe), 6.6-7.2 (8H, m, benzene rings). 3d: viscous oil; ^{1}H-NMR δ 0.92 (6H, t, Me), 1.16 (6H, s, Me), 1.1-1.9 (12H, m, methylene), 2.0 (2H, broad s, OH). 3e: mp 138-139 °C (lit., mp 138 °C); ^{1}H-NMR δ 0.60 (6H, t, Me), 1.2-2.6 (4H, double quartet, methylene), 2.12 (2H, s, OH), 7.21 (10H, s, Ph). 3f (=3h): mp 49.5-51 °C; ^{1}H-NMR δ 0.96 (6H, t, Me), 1.14 (6H, s, Me), ca. 1.3-1.7 (4H, m, methylene), 2.06 (2H, s, OH); ^{13}C-NMR δ 7.8, 20.3, 28.0, 76.8. 3g: mp 58-59 °C; ^{1}H-NMR δ 0.85 (3H, d, Me), 0.92 (3H, d, Me), 1.07 (3H, s, Me), 1.66 (3H, s, Me), 1.79 (1H, broad s, OH), 1.5-2.1 (1H, m, methine), 2.52 (1H, broad s, OH), 7.1-7.6 (5H, m, Ph). 3i: mp 51-52 °C (lit., mp 52 °C); ^{1}H-NMR δ 0.96 (6H, t, Me), 1.12 (3H, s, Me), 1.13 (3H, s, Me), ca. 1.2-1.9 (4H, m, methylene), 1.83 (2H, broad s, OH); ^{13}C-NMR δ 7.7, 19.8, 28.4, 76.8. 3j: mp 76-76.5 °C; ^{1}H-NMR δ 0.80 (3H, t, Me), 1.19 (3H, s, Me), ca. 1.2-2.0 (2H, m, methylene), 1.63 (3H, s, Me), 1.83 (1H, broad s, OH), 2.65 (1H, broad s, OH), 7.1-7.6 (5H, m, Ph). 3k: mp 94.5 °C; ^{1}H-NMR δ 0.93 (3H, t, Me), 0.98 (3H, s, Me), 1.59 (3H, s, Me), ca. 1.1-1,9 (2H, m, methylene), 1.81 (1H, broad s, OH), 2.62 (1H, broad s, OH), 7.2-7.5 (5H, m, Ph).
8. E. J. Corey, R. L. Danheiser, and S. Chandrasekaran, *J. Org. Chem.*, 41, 260 (1976).
9. Selective desulfurization of only thiolane ring could not be attained.
10. Two isomers are formed from meso-sulfides and one isomer from d,l-sulfides.
11. More sterically crowded 2,5-diethyl-3,4-dihydroxy-3,4-diphenylthiolane resisted desulfurization. The desulfurization under forced conditions gave a complex mixture.
12. S. G. Wilkinson in "Comprehensive Organic Chemistry," Vol. 1, J. F. Stoddart Ed., Pergamon Press, Oxford, 1979, p. 666.

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