CHEMISTRY LETTERS, pp. 1173-1176, 1985.

EFFICIENT PREPARATION OF POLYSUBSTITUTED 1,3-DIENES FROM α,α'-DIKETO SULFIDES

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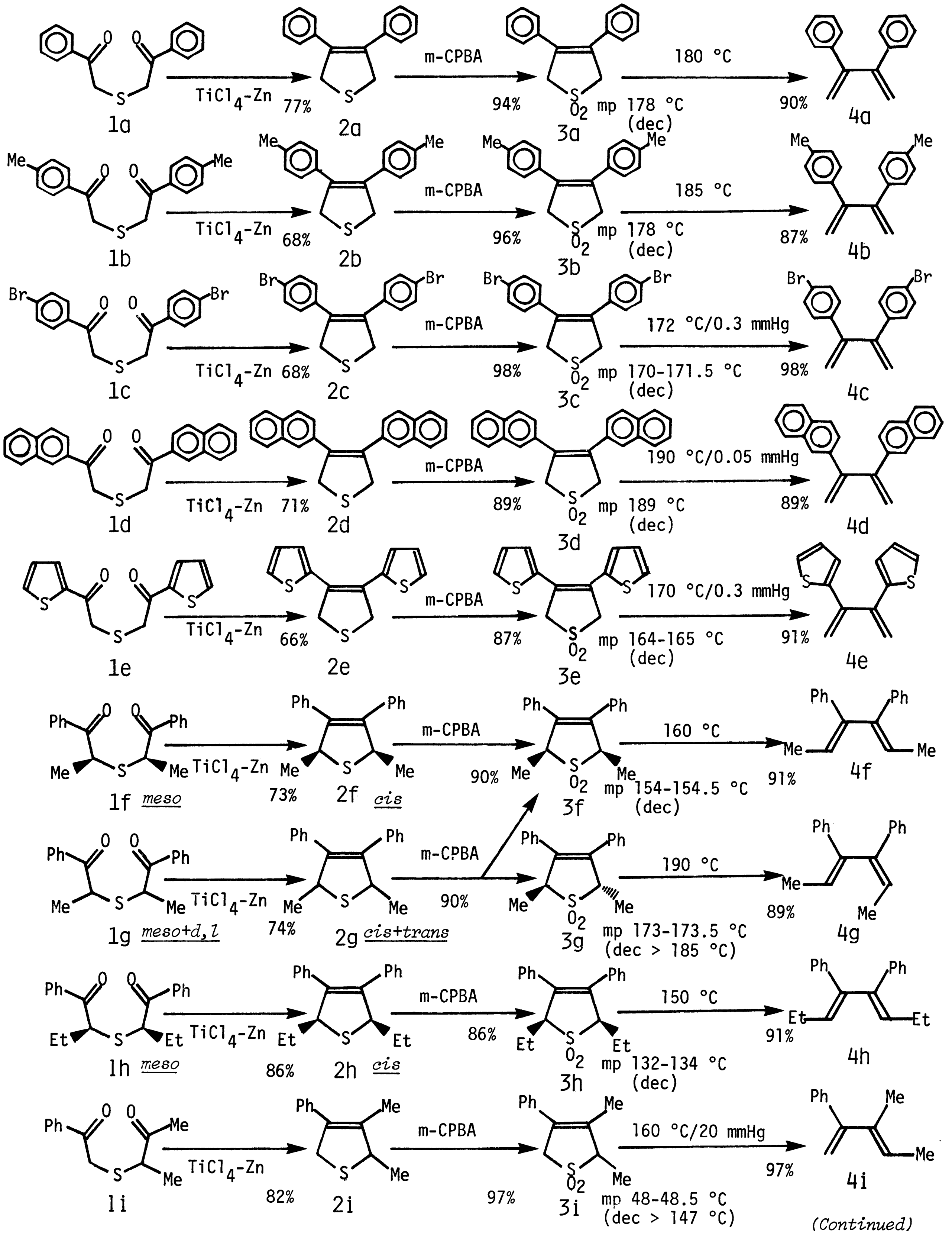
A series of polysubstituted 1,3-dienes were prepared in good overall yields in three steps starting from readily accessible α,α'-diketo sulfides.

α,α'-Diketo sulfides (**1**) are readily accessible compounds in which three functional groups [carbonyl, active methylene (methine), and sulfide moieties] are suitably arranged for various intra- and intermolecular chemical transformations. However, synthesis with **1** has not been fully explored. As a part of our synthetic study with **1**, we reported the preparation of 2,5-dihydrothiophenes (**2**) by intramolecular reductive coupling reaction of **1** using a low-valent titanium reagent prepared from titanium(IV) chloride and zinc powder.1,2) 2,5-Dihydrothiophene 1,1-dioxides (**3**) are known to undergo the thermal extrusion of sulfur dioxide to form 1,3-dienes in a stereospecific disrotatory manner.3-5) Herein we report that the combination of this reaction with our 2,5-dihydrothiophene synthesis provides an efficient method for preparation of polysubstituted 1,3-dienes which are otherwise difficult to prepare.

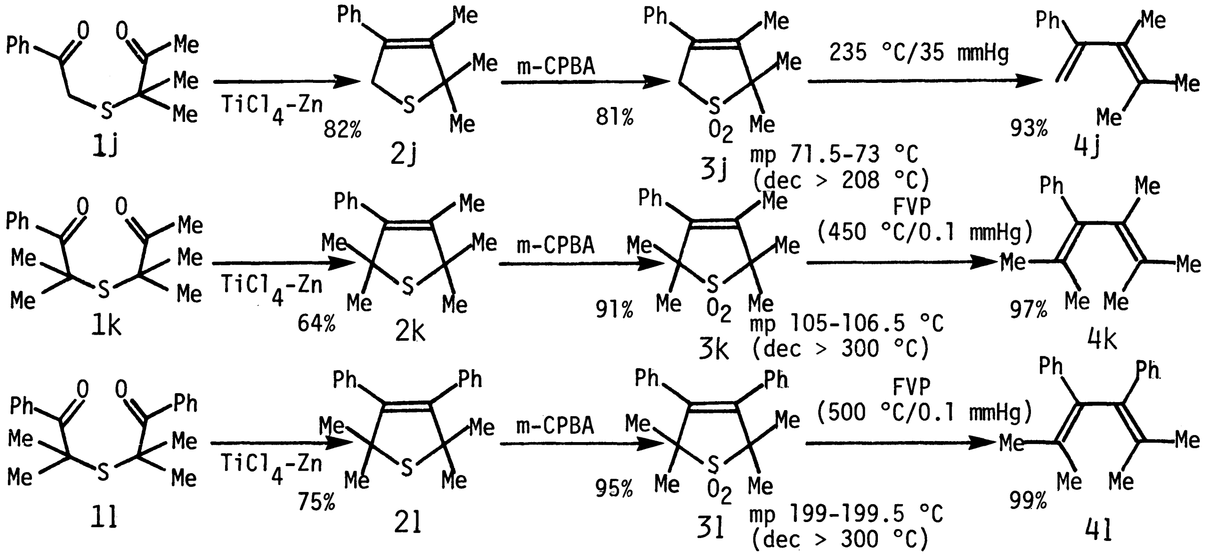
Our results are summarized in Scheme 1. 2,5-Dihydrothiophenes **2** are obtained in good yields from easily accessible **1**.1) Of great importance here is that the reductive coupling reaction of meso-diketo sulfides leads to cis-2,5-disubstituted 2,5-dihydrothiophenes exclusively (see conversions, **1f**,**h** → **2f**,**h**). meso-Diketo sulfides are easily obtained in a pure form by recrystallizing mixtures of meso- and d,l-isomers. The reduction of a mixture of meso- and d,l-isomers affords a mixture of cis- and trans-isomers (see conversion, **1g** → **2g**).

2,5-Dihydrothiophene 1,1-dioxides **3** were obtained in excellent yields by oxidation of **2** with *m*-chloroperoxybenzoic acid (m-CPBA) in chloroform at room temperature. Since the double bond of **2** resists the epoxidation with m-CPBA,6) this conversion can be done without any difficulty. The oxidation of a mixture of cis- and trans-isomers affords the corresponding sulfone as a mixture of cis- and trans-isomers, which are separable by fractional recrystallization (see conversion, **2g** → **3f**+**3g**).

Thermolyses of the sulfones **3** to the corresponding 1,3-dienes (**4**) were done by three methods. Most sulfones decompose at their melting points. This is a good measure for setting the temperature of the thermolysis. First, the thermolysis was done by heating the sulfones slightly higher than their decomposition


1a
TiCl4-Zn 77%
2a
m-CPBA 94%
3a mp 178 °C (dec)
180 °C 90%
4a
1b
TiCl4-Zn 68%
2b
m-CPBA 96%
3b mp 178 °C (dec)
185 °C 87%
4b
1c
TiCl4-Zn 68%
2c
m-CPBA 98%
3c mp 170-171.5 °C (dec)
172 °C/0.3 mmHg 98%
4c
1d
TiCl4-Zn 71%
2d
m-CPBA 89%
3d mp 189 °C (dec)
190 °C/0.05 mmHg 89%
4d
1e
TiCl4-Zn 66%
2e
m-CPBA 87%
3e mp 164-165 °C (dec)
170 °C/0.3 mmHg 91%
4e
1f meso
TiCl4-Zn 73%
2f cis
m-CPBA 90%
3f mp 154-154.5 °C (dec)
160 °C 91%
4f
1g meso+d,l
TiCl4-Zn 74%
2g cis+trans
m-CPBA 90%
3g mp 173-173.5 °C (dec > 185 °C)
190 °C 89%
4g
1h meso
TiCl4-Zn 86%
2h cis
m-CPBA 86%
3h mp 132-134 °C (dec)
150 °C 91%
4h
1i
TiCl4-Zn 82%
2i
m-CPBA 97%
3i mp 48-48.5 °C (dec > 147 °C)
160 °C/20 mmHg 97%
4i

(Continued)



Scheme 1.

points for a short period (see preparation of 4a,b,f,g,h). However, in certain cases the polymerization of the resulting 1,3-dienes occurred appreciably (thermolysis of 3c-e). In such cases the thermolysis was satisfactorily achieved by using a bulb-to-bulb distillation apparatus (Kugelrohl); the resulting 1,3-dienes were immediately removed by distillation to minimize the polymerization (see preparation of 4c-e,i,j). In cases where the sulfones are thermally very stable and cannot be thermolyzed by the above methods, flash vacuum pyrolysis (FVP) was applied (see preparation of 4k,l). In this way all of the sulfones were converted to the corresponding 1,3-dienes 4 in excellent yields without any exceptions.[7)]

As for the stereochemistry of the thermolysis, the followings are worthy of mention. The thermolysis of 3f-h proceeded in a stereospecific disrotatory manner to produce the corresponding isomerically pure 1,3-dienes. No Z,Z-isomers were formed in the thermolysis of 3f,h because the disrotatory ring-opening reaction occurs in a manner to avoid the steric repulsion between the hydrogen and alkyl group. The higher temperature required for the thermolysis of 3g compared with that of 3f can be explained as the result of the inevitable repulsion between the hydrogen and methyl group in the transition state of the thermolysis of 3g. The exclusive formation of the single isomer 4i from the sulfone 3i can be explained in a similar way. Extreme case that the steric repulsion between alkyl substituents makes sulfones thermally very stable is found in the sulfones 3k,l. No report has appeared on the thermolysis of such heavily substituted sulfones. The present results show, however, that even such highly substituted sulfones can be converted to the corresponding 1,3-dienes by using an FVP technique.

In conclusion the 1,3-diene synthesis developed here starting from easily accessible α,α'-diketo sulfides is particularly useful for the preparation of highly substituted 1,3-dienes which are otherwise difficult to obtain.

References

1) J. Nakayama, H. Machida, and M. Hoshino, Tetrahedron Lett., **26**, 1981 (1985).

2) T. Mukaiyama, T. Sato, and J. Hanna, Chem. Lett., **1973**, 1041.

3) W. L. Mock, J. Am. Chem. Soc., **88**, 2857 (1966); S. D. McGregor and D. M. Lemal, ibid., **88**, 2858 (1966); A. I. Meyers, "Heterocycles in Organic Synthesis," Wiley, New York (1973), p. 68; E. Block, "Reactions of Organosulfur Compounds," Academic Press, New York (1978), p. 268.

4) Synthetic utility of this reaction unfortunately suffers from the lack of availability of the starting sulfones **3**. Sulfones **3** are often prepared by the reaction of the corresponding dienes with sulfur dioxide.

5) For recent modification of this reaction, see R. Block, C. Benecou, and E. Guibe-Jampel, Tetrahedron Lett., **26**, 1301 (1985) and references cited therein.

6) Epoxidation of 3,4-diphenyl-2,5-dihydrothiophene 1,1-dioxide (**3f**) with m-CPBA does not occur in refluxing chloroform.

7) Melting points and ^{1}HNMR data (CCl_4 as solvent) of the 1,3-dienes **4a**-**l** are given below. **4a**: mp 46-47 °C; δ 5.22 (2H, d), 5.43 (2H, d), 7.0-7.3 (10H, m). **4b**: mp 33-35 °C; δ 2.23 (6H, s), 5.10 (2H, d), 5.33 (2H, d), 6.7-7.1 (8H, m). **4c**: mp 83-84 °C; δ 5.23 (2H, d), 5.43 (2H, d), 7.0-7.4 (8H, m). **4d**: mp 146-148 °C; δ 5.37 (2H, d), 5.63 (2H, d), 7.2-7.8 (14H, m). **4e**: viscous oil; δ 5.13 (2H, d), 5.48 (2H, d), 6.7-7.1 (6H, m). **4f**: mp 105-105.5 °C; δ 1.43 (6H, d), 5.17 (2H, q), 6.9-7.3 (10H, m). **4g**: viscous oil; δ 1.87 (3H, d), 1.90 (3H, d), 5.67 (1H, q), 5.93 (1H, q), 6.9-7.3 (10H, m). **4h**: mp 71.5-72.5 °C; δ 0.80 (6H, t), 1.80 (4H, quintet), 5.07 (2H, t), 6.9-7.4 (10H, m). **4i**: viscous oil; δ 1.69 (3H, d), 1.80 (3H, m), 4.93 (1H, d), 5.10 (1H, d), 5.39 (1H, q), 7.17 (5H, s). **4j**: viscous oil; δ 1.68 (6H, s), 1.77 (3H, s), 4.81 (1H, d), 5.37 (1H, d), 6.9-7.3 (5H, m). **4k**: viscous oil; δ 1.54 (3H, broad s), 1.67 (6H, s), 1.69 (3H, s), 1.71 (3H, s), 6.9-7.2 (5H, m). **4l**: mp 37-38 °C; δ 1.70 (6H, s), 1.90 (6H, s), 6.7-7.2 (10H, m).

(Received May 30, 1985)