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HIGH-PRESSURE (4+2)CYCLOADDITION OF 1-METHOXY-3-TRIALKYLSILYLOXYBUTA-1,3-DIENES TO BUTYL GLYOXYLATE. ISOLATION OF PRIMARY CYCLOADDUCTS

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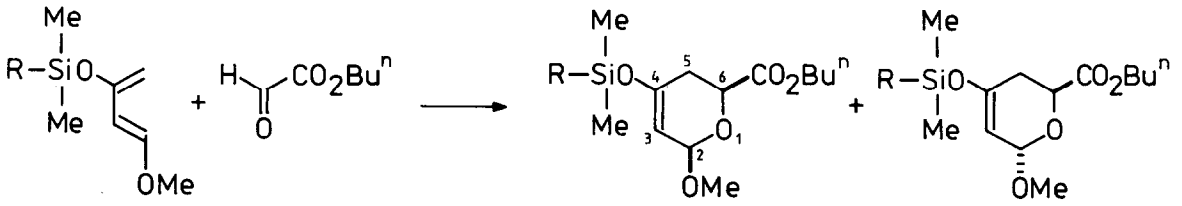
Abstract - High-pressure reactions of 1-methoxy-3-trialkylsilyloxybuta-1,3-dienes (1, 2) with butyl glyoxylate (3) and isolation of the primary cycloadduct 5 as well as its simple chemical transformations are described.

(4+2)Cycloaddition of 1-methoxybuta-1,3-diene to alkyl glyoxylates as dienophiles affords, under thermal conditions, corresponding esters of 2-methoxy-5,6-dihydro-2H-pyran-6-carboxylic acid which are important synthons in total synthesis of monosaccharides.[1] Since the thermal reaction conditions do not provide high yields with various non-activated dienophiles and in addition because the decomposition of the cycloadducts, we decided to apply the high-pressure technique for the synthesis of Diels-Alder adducts.[2]

Several recent papers[3] have shown examples of the use of Danishefsky's diene (1) in thermal or $Eu(fod)_3$ catalyzed (4+2)cycloadditions to various carbonyl compounds. However, due to 3-trimethylsilyloxy function, the primary cycloadducts were very unstable under these conditions. These facts as well as the synthetic importance of the reactions shown in Scheme 1, prompted us to design a convenient preparative route to this type of 2-methoxy-5,6-dihydro-2H-pyran derivatives.[4]

Scheme 1[5]



1: R=Me 2: R=Bu^t 3

4a: R=Me 5a: R=Bu^t 4b: R=Me 5b: R=Bu^t

The source of the instability of diastereoisomeric adducts 4a and 4b emanates from the labile trimethylsilyl protecting group and we have overcome the problem using two different approaches. The first method is to use a more stable trialkylsilyl protecting group,[6] e.g. *tert*-butyldimethylsilyl instead of trimethylsilyl group, and the second approach is to run the reaction under mild temperature conditions and high pressure. The preliminary results of our studies are presented in Table I.

Table 1. The reactions of dienes 1 or 2 with butyl glyoxylate (3)

Diene	Reaction conditions	Adduct	Yield %	Diastereoisomeric ratio 4a:4b
1	benzene, reflux, 1 atm, 20 h	4a+4b	40	1:1
1	ethyl ether, RT, 10 kbar, 24 h	4a+4b	80	5:1
2	benzene, reflux, 1 atm, 15 h	5a+5b	30	4:1
2	ethyl ether, RT, 10 kbar, 24 h	5a+5b	85	10:1
2	ethyl ether, RT, 1 atm, 1% $Eu(fod)_3$, 48 h	5a+5b	75	7:3

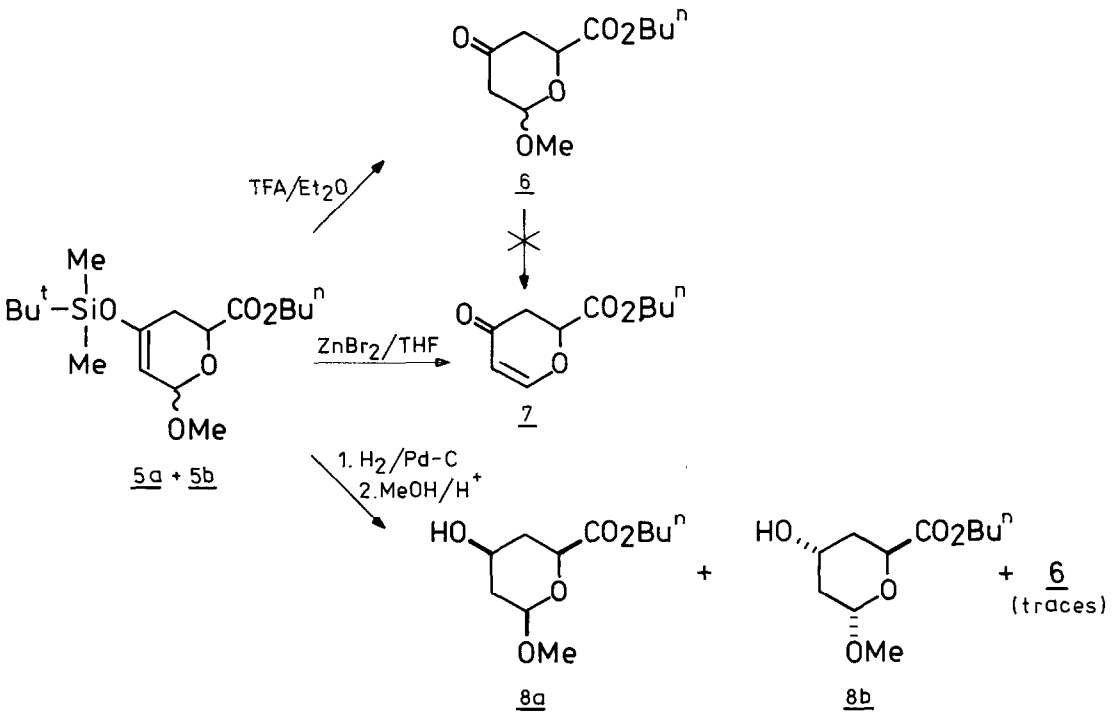
Thermal (4+2) cycloaddition in benzene of both dienes 1 and 2 to dienophile 3 afforded poor yields and low diastereoselectivity in product formation. Much better results were obtained by performing reactions at room temperature, under high pressure, and in ethyl ether. Moreover, the adducts 5a and 5b are stable enough to be isolated using flash chromatography. On the other hand, $Eu(fod)_3$ catalysis also provides a facile reaction between 2 and 3 under atmospheric pressure and ambient temperature and the cis:trans ratio is 7:3. Interestingly, a similar reaction but under high pressure and without catalyst,gives the cis:trans ratio of 10:1.

In view of relatively facile synthesis of our cycloadducts, we then studied the removal reactions for the *tert*-butyldimethylsilyl protecting group and to retain the stereoselectivity found in the Diels-Alder reaction (Scheme 2).

The treatment of 5a and 5b with trifluoroacetic acid according to Danishefsky's procedure[8] affords the ketone 6. However, when this mixture is treated with zinc bromide in wet tetrahydrofuran, the unsaturated ketone 7 is formed. A more interesting method for removal of the *tert*-butyldimethylsilyl protecting group is the hydrogenation of 5a + 5b in the presence of palladium-on-charcoal followed by methanolysis. In the first step, the double bond is stereoselectively hydrogenated, and in the second one, the protecting group is cleaved to afford a mixture of compounds 8a and 8b[9] in the same ratio as the starting diastereoisomeric mixture of 5a and 5b. The stereochemical course of the double bond hydrogenation is strictly controlled by the configuration of the methoxy group at position 2 in the dihydropyran ring. This hydrogenolysisreaction provides a ready access to 2,4-dideoxysugars.[10]

The high-pressure reaction reported in the present Communication offers a stereocontrolled synthesis of relatively unstable silyloxyderivatives of the 5,6-dihydro-2H-pyran system which have considerable potential applications in the synthesis of natural products.

Scheme 2[5]



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References and Notes

1. A. Konował, J. Jurczak, and A. Zamojski, Roczniki Chem., 42, 2045 (1968); A. Konował, J. Jurczak, and A. Zamojski, Tetrahedron, 32, 2976 (1976).

2. J. Jurczak, M. Chmielewski, and S. Filipek, Synthesis, 1979, 41; J. Jurczak, T. Bauer, S. Filipek, M. Tkacz, and K. Zygo, J. Chem. Soc., Chem. Commun., 1983, 540.

3. J. F. W. Keana and P. E. Eckler, J. Org. Chem., 41, 2850 (1976); M. E. Jung, K. Shishido, L. Light, and L. Davis, Tetrahedron Lett., 22, 4607 (1981); R. W. Aben and J. W. Scheeren, Synthesis, 1982, 779; J. Bélanger, N. L. Landry, J. R. J. Paré, and K. Jankowski, J. Org. Chem., 47, 3649 (1982); M. Bednarski and S. J. Danishefsky, J. Am. Chem. Soc., 105, 6968 (1983); S. J. Danishefsky, E. Larson, D. Askin, and N. Kato, J. Am. Chem. Soc., 107, 1246 (1985).

4. Preservation of the trialkylsilyloxy group offers several interesting possibilities of functionalization of prochiral centres C-3 and C-4, cf. the recent review on silyl enol ethers in synthesis: P. Brownbridge, Synthesis, 1983, 1, 85.

5. For the sake of simplicity we represent all compounds as enantiomers, when in fact they are racemic modifications.

6. B. Fraser-Reid, H. A. Rahman, D. R. Kelly, and R. M. Srivastava, J. Org. Chem., 49, 1835 (1984); S. J. Danishefsky, Biing Jium Uang, and G. Quallich, J. Am. Chem. Soc., 106, 2453 (1984).

7. The stereochemistry of the methoxy group plays an important role in the control of the functionalization of prochiral centres C-3 and C-4, cf. Ref. 4.

8. S. J. Danishefsky, J. F. Kervin, Jr., and S. Kobayashi, J. Am. Chem. Soc., 104, 358 (1982).

9. Selected ^{1}H NMR (360 MHz, δ, ppm) data: 8a, 4.38 (m, 1H, H-6), 3.97 (pd, J_1 = 11.5 Hz, J_2 = 1.8 Hz, 1H, H-2), 3.90 (m, 1H, H-4), 3.53 (s, 3H, OMe); 8b, 5.00 (bs, 1H, H-2), 4.62 (m, 1H, H-6), 4.14 (m, 1H, H-4), 3.44 (s, 3H, OMe).

10. The same products 8a and 8b can be obtained by reduction of ketone 6 using lithium tri--*tert*-butoxyaluminohydride. However, the reaction carried out in diethyl ether at -10°C gave besides the desired alcohols 8a and 8b, two other diastereoisomers derived from the lower stereoselectivity of the reduction.

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