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N-IODOSUCCINIMIDE MEDIATED OXIDATIVE CYCLIZATION OF MONO-t-BUTYLDIMETHYLSILYLATED DIOLS

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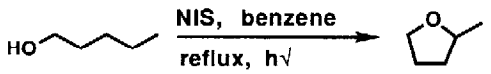
Summary: The oxidation of mono-t-butyldimethylsilylated diols is described. The t-butyldimethylsilyl moiety is useful for controlling both the direction of cyclization and the size of ring being formed.

We have previously shown that treatment of 1-pentanol with N-iodosuccinimide (NIS) in the presence of light leads to the formation of 2-methyltetrahydrofuran.[1] Herein we describe an extension of this

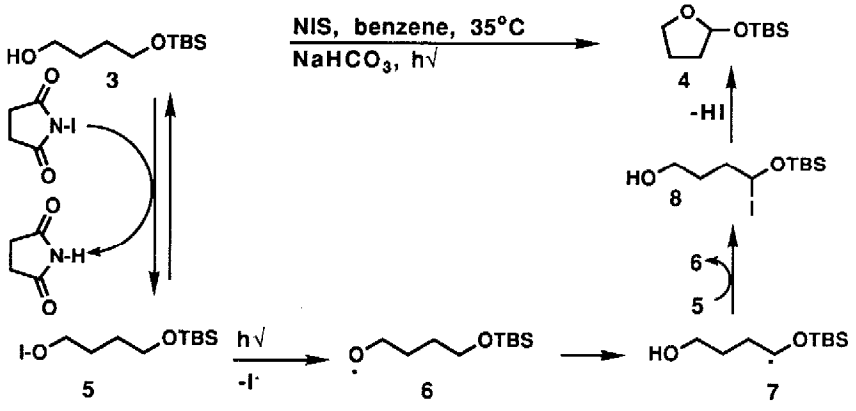


1 2

methodology to the regioselective cyclization of mono-t-butyldimethylsilylated acetals. Symmetrical diols were converted to their mono-t-butyldimethylsilylated diols via their monosodium alkoxides as described by McDougal.[2] Their unsymmetrical counterparts were selectively silylated at the primary hydroxyl group using Chaudary's 4-dimethylaminopyridine catalyzed procedure.[3,4]

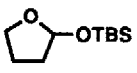
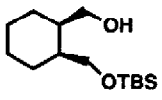
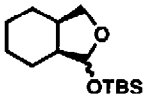
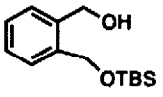
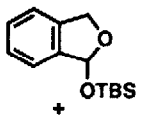
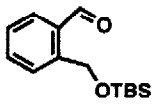
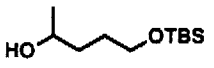
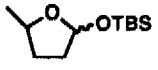
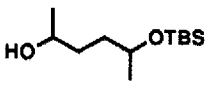
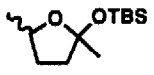
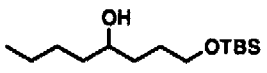
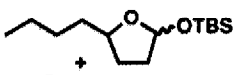
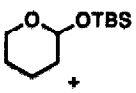
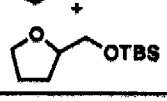
A plausible mechanism for this transformation is shown in Scheme 1.[5] The initially formed hypoiodite **5** is homolytically cleaved to produce an alkoxy radical and an iodine radical. Intramolecular 1,5 hydrogen shift (**6**-->**7**, Barton-type reaction), iodination, and nucleophilic ring closure furnishes the observed t-butyldimethylsilyl acetal **4**.

Scheme 1



The results of our cyclization studies are shown in Table 1.[6] Several aspects of this oxidation are worthy of note. These reactions take place under milder conditions than are required for the corresponding simple aliphatic alcohols. The silylation/oxidation sequence for prim-sec diols constitutes a regioselective oxidation procedure in which the less substituted (and protected) end of the diol gets oxidized. (entries 4 and 6). It is thought that the poor yield of the ketal shown in entry 5

Table 1

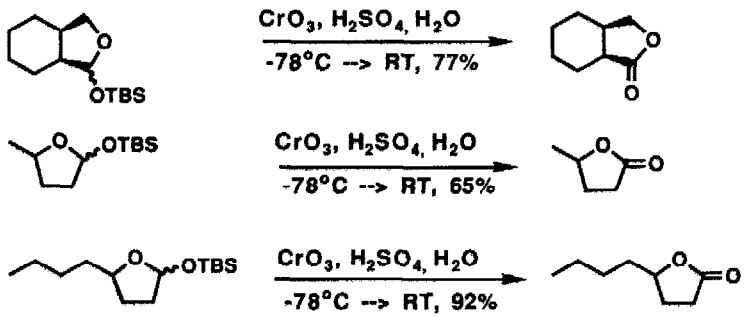
Entry	Alcohol	Eq NIS	Time (h)	Product(s)	Yield [a]
1		1.7	6		72%
2		1.5	12		84%
3		1.5	6	 + 	63% 6%
4		2.3	8		87%
5		1.5	12		11%
6		2.6	12	 + 	77% 12%
7		2.8	34	 + 	60% 7%

[a]All yields are isolated except for entry 7 which were obtained by gas chromatography.

is due to the presence of significant 1,3-syn diaxial interactions in the chair-like transition state for the 1-5 hydrogen shift.[7] It is interesting to note that o-methylbenzyl alcohol furnishes only the aldehyde upon irradiation in the presence of NIS in benzene.[1] The corresponding t-butyldimethylsilyl analogue (entry 3) affords the acetal as the major product upon reaction with NIS. It appears that the t-butyldimethylsiloxy moiety functions as a directing group for the hydrogen shift portion of the mechanism. Entry 6 shows that hydrogen abstraction by the alkoxy radical occurs much more readily when the incipient carbon radical is adjacent to the t-butyldimethylsiloxy group than an alkyl group.[8,9] Entry 7 illustrates the ability of the t-butyldimethylsiloxy group to selectively direct the intramolecular hydrogen abstraction via a seven-membered cyclic transition state rather than the normal six-membered cyclic transition state. The stabilization a t-butyldimethylsiloxy group imparts to an adjacent carbon radical can be viewed as an interaction between the doubly occupied nonbonding molecular orbital of the oxygen and the singly occupied carbon p orbital.[10]

Diastereomeric mixtures of acetals were produced in entries 2, 4, and 6. In these cases further confirmation of the structural assignments was deemed appropriate. These products were thus subjected to Jones oxidation to produce the corresponding known lactones (Scheme 2). In the future we plan to examine Lewis acid mediated substitution processes of t-butyldimethylsilylated acetals.

Scheme 2



Typical Experimental Procedure

To a solution of cis-1-O-t-butyldimethylsilyl-1,2-cyclohexanedimethanol (80 mg, 0.31 mmol, entry 2) in benzene (1.6 mL) was added 105 mg NIS (0.47 mmol) and 51 mg $NaHCO_3$ (0.60 mmol). The heterogenous reaction mixture was irradiated at 35°C for 12 h with a G.E. 150 W, 130 V tungsten lamp. Water (5 mL) and $Na_2S_2O_3 \cdot H_2O$ (0.5 g) were then added to destroy any NIS or hypoiodite containing species. The resultant mixture was extracted with a 50% ether in hexane mixture (4 X 5 mL). The combined organic extracts were then washed with water (5 mL), and the solvent was removed under reduced pressure. The crude residue was chromatographed on a 35 X 1 cm column of silica gel with 1% ethyl acetate in hexane to afford 67 mg (0.26 mmol, 84% yield) of the corresponding cyclic acetal as a colorless oil (1.6 : 1 mixture of diastereomers at the acetal center as determined by integration of the acetal proton ^1H NMR signals). IR (neat) 2940, 2880, 1470, 1460, 1320, cm^{-1}; ^1H NMR (60 MHz, $CDCl_3$) 5.4 (d, J = 2 Hz, 1H, major diastereomer), 5.2 (br s, 1H, minor diastereomer), 3.9 (m, 2H), 2.1 (m, 2H), 1.9-1.2 (m, 8H), 0.9 (s, 9H), 0.1 (s, 6H); MS (CI), m/z (relative intensity) 257 (MH^+, 100), 199 (8), 146 (5), 125 (57).

Acknowledgements

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References and notes

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