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Screening of Various Procedures for the Oxidation of A 1,3-Diol with A 2-Benzylic Position; How to Obtain the 1,3-Diketone?

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SYNTHETIC COMMUNICATIONS, 25(13), 1907-1912 (1995)

SCREENING OF VARIOUS PROCEDURES FOR THE OXIDATION OF A 1,3-DIOL WITH A 2-BENZYLIC POSITION ; HOW TO OBTAIN THE 1,3-DIKETONE ?

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Abstract : Various oxidizing procedures (Swern, Collins, Dess-Martin, Corey (PCC), MnO_2, TEMPO, Jones) have been screened with the aim of oxidizing a 1,3-diol with a 2-benzylic position, into the corresponding β-diketone. Surprisingly, this functional group interconversion has been successfully achieved only by a special version of the Jones procedure .

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In the course of a multistep synthesis, we required a convenient and preparative method for the synthesis of a 1,3-diketone from the corresponding 1,3-diol. The benzylic nature of the central carbon enhanced the difficulty of the required transformation. Surprisingly, there are very few reports describing the oxidation of 1,3-diols or β-hydroxyketones to 1,3-diketones. This is presumably due to the expectation that under oxidation conditions, the intermediary (or starting) β-hydroxyketone derivative would suffer fragmentation (retroaldol process) or undergo β-elimination of water and/or undergo further oxidation of the enolic product . The difficulty of the oxidation of β-hydroxyketones has been

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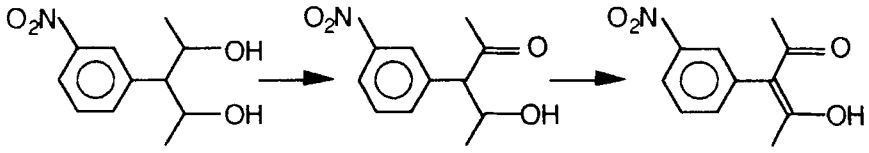
emphasized by Evans[1] who obtained a dichlorinated product when using the Swern reagent ! Starting from 4- hydroxydecan-2-one, Smith[2] has screened various oxidation methods (Collins oxidation, pyridinium chlorochromate and pyridinium dichromate, Jones reagent and two versions of the Swern procedure) ; only Collins oxidation and the oxalyl chloride version of the Swern procedure afforded cleanly the desired 2,4-decanedione. No starting material involving a 2-benzylic position has been studied to our knowledge.

The aim of this work is to find a convenient procedure leading to the 1,3-diketone : (i) starting from a 1,3-diol, (ii) not involving the isolation of the β-hydroxyketone and, (iii) applicable to the case where a 2-benzylic proton is present. The model substrate **1** (meso/d-l mixture : 90/10) was chosen to investigate the reaction.[3]



Taking in account the reactivity of the expected product **3**, **1** was subjected at first to the commonly employed oxidizing agents working in non-acidic media (Table 1) :

- the Swern procedure (dimethyl sulfoxide, oxalyl chloride)[4] which had afforded the best yield in the case of 4-hydroxydecan-2-one[2], gave only the hydroxyketone **2** (85%) beside the unreacted starting material.

- Collins oxidation (CrO_3, pyridine)[5] gave exactly the same result as did the Swern procedure ; when **2** was directly subjected to the reagent (Swern or Collins), it remained unchanged and the formation of **3** was not detected ; another

Table 1 : Screening of oxidizing reagents

Reagent	[Reagent]/[Substrate]	Time	T°C	1	2	3	ArCOCOMe (Ar=$mNO_2C_6H_4$)	m.nitro benzoic acid
Swern	18	45 min	-60	traces	85%	none	none	none
Collins*	3	2.5h	20	traces	76%	none	none	none
MnO_2	4	48 h	40	88%	traces	none	none	none
acetamido TEMPO	4	240 h	20	75%	20%	none	none	none
	0.1 (2 MCPBA)	240 h	20	70%	20%	none	none	none
Dess-Martin	2.5	6 h	20	unidentified products				
Corey	3	10 h	20	none	none	none	65%	traces
Jones	See Table 2							

*the Evans version led only to unidentified products.

version of the Collins procedure, successfully used by Evans[1] (CrO_3, pyridine, Celite), led to a mixture of unidentified products and no formation of **3**.

- tentative oxidation with MnO_2[6] led to trace amounts of **2** ; **1** was quite quantitatively recovered.

- two procedures have been investigated using 4-(acetamido) TEMPO : the first of them implies an excess of the reagent (2 equiv.) in the presence of p-toluenesulfonic acid (2 equiv.)[7] while the second procedure uses catalytic amounts of the nitroxide derivative (0.1 equiv.) in the presence of a stoichiometric amount of m-chloroperbenzoic acid[8] ; after ten days at 20°C, only **2** was detected (20%) and nearly 75 % of **1** recovered, with both procedures.

- Dess-Martin reagent (periodinane)[9] led only to unidentified products.

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Table 2 : Jones reagent

[Reagent] / [Substrate]	Time	T°C	1	2	3	ArCOCOMe	m.nitro benzoic acid
4*	40 h	20	none	traces	none	85%	traces
20	19 h	20	none	none	10%	traces	73%
1	5 min	20	18%	27%	47%	none	traces
2	3.5 h	-20	none	15%	57%	none	traces
2	5.5 h	-20	none	5%	70%	none	5%
2	6.5 h	-20	none	traces	65%	none	10%

*biphasic medium (CH_2Cl_2/H_2O)

After these failures, we tried the reactions of the commonly employed oxidizing reagents working in acidic media :

- the Corey procedure (pyridinium chlorochromate)[10] led only to the α-diketone m-$NO_2C_6H_4COCOCH_3$, putatively from the oxidative cleavage of the C-C double bond of the enolic form of **2** or **3**, and trace amounts of nitrobenzoic acid.
- various procedures using the Jones reagent (CrO_3, H_2SO_4)[11] have been investigated (see Table 2), leading in one case to the desired **3** in an acceptable yield.

Reactions with the Jones reagent :

With the aim of limiting the contact between the oxidizing reagent and the reaction product, we have used biphasic water-dichloromethane media ; unfortunately, we have obtained the same result (with various time periods) as with the Corey reagent. The progress of the reaction in biphasic medium has been

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followed by TLC and ^1H NMR : the oxidative cleavage of **2** (and not **3**) is evidenced by the detection of transient m-$NO_2C_6H_4COCHOHCH_3$.

The classical Jones procedure (in acetone) applied for a long time (19 h) led to nitrobenzoic acid as the main product ; applied for a short time (5 min), the reaction afforded a mixture containing **1** (18%), **2** (27%), the target product **3** (47%) and trace amounts of nitrobenzoic acid. The presence of both nitrobenzoic acid and **1** evidences that the oxidative degradation of **2** and **3** is faster than the oxidation of **1**.

Finally, we investigated the classical Jones procedure (in acetone) at a lower temperature (- 20°C) for various reaction times. The main results are depicted in Table 2. In the best case, the target product **3** has been isolated with a 70% yield. The experimental procedure for this assay is given herein.

Experimental procedure : 1 mmol (225 mg) of **1** was dissolved in 15 ml of acetone. To the chilled solution (- 20°C), 2 mmol of the Jones reagent (CrO_3, H_2SO_4, H_2O) were added. The solution was kept at -20°C under stirring for 5.5 hours. After addition of 4 ml of propan-2-ol, the solution was rised to room temperature and then made homogenous with addition of water. EDTA tetrasodium salt was added in excess and the solution stirred for 2 hours. After extraction with dichloromethane, drying on Na_2SO_4 and evaporation of the solvent, a yellow oil was obtained. Chromatography (silicagel, hexane/ethyl acetate) gave 154 mg (0.7 mmol) of pure **3** as a yellow solid (yield : 70%) identified by comparaison with an authentic sample.[3] TLC (hexane / ethyl acetate =7/3): R_f= 0.63.

References and notes

1. Dow R.L., Evans D.A., Shih T., Takacs J.M., Zahler R.S., *J. Am. Chem. Soc.* **1990**, *112*, 5290.

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2. Smith A.B., Levenberg P.A., *Synthesis* **1981**, 567.

3. An authentic sample of **3** was synthesized according to the procedure of Dell'Erba et al[12] ; the diol **1** was prepared from this sample by reduction with sodium borohydride: a 90/10 meso/d-l mixture was obtained. Data for the meso isomer : 200 MHz ^{1}H NMR ($CDCl_3$) δ = 1.03 (6 H, d, J=6.3 Hz), 2.54 (1 H, t, J=3.6 Hz), 3.16 (2 H (hydroxyl), s), 4.30-4.50 (2 H, m), 7.41-7.75 (2H, m), 8.05-8.28 (2H, m) ; 50 MHz ^{13}C NMR ($CDCl_3$) δ= 21.8 (6 C (CH_3)), 57.2 (1C, (benzylic)), 70.8 (2 C (CHOH)), 121.8-125.5-128.6-137.3 (4 C, (aromatic)), 139.3 (1C, (C-$C_{benzylic}$)), 147.9 (1C, (C-NO_2)).
Data for **2** : TLC (hexane / ethyl acetate=7/3) : R_f =0.33 ; 200 MHz ^{1}H NMR ($CDCl_3$) δ = 1.05 (3H, d), 2.27 (3H, s), 2.60 (1H, m), 4.45 (1H, m), 7.45-7.60 (2H, m), 8.06-8.14 (2H, m).

4. Mancuso A.J., Huang S.L., Swern D., *J. Org. Chem.* **1978**, *43*, 2480.

5. Collins J.C., Hess W.W., Frank F.J., *Tetrahedron Lett.* **1968**, 3363.

6. Mancera O., Rosenkranz G., Sondheimer F., *J. Chem. Soc.* **1953**, 2189.

7. Ma Z., Bobbitt J.M., *J. Org. Chem.* **1991**, *56*, 6110.

8. Cella J.A., Kelley J., Kenehan E.F., *J. Org. Chem.* **1975**, *40*, 1860.

9. Dess D.B., Martin J.C., *J. Org. Chem.* **1983**, *48*, 4155.

10. Corey E.J., Suggs J.W., *Tetrahedron Lett.* **1975**, 2647.

11. Braude E.A., Jones E.R.H., Sondheimer F., Toogood J.B., *J. Chem. Soc.* **1949**, 607.

12. Dell'Erba C., Novi M., Petrillo G., Tavani C., Bellandi P., *Tetrahedron* **1991**, *47*, 333.

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