

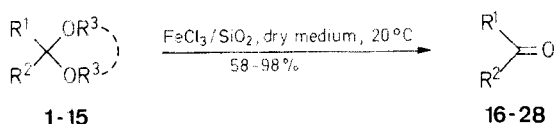
Anhydrous Iron(III) Chloride Dispersed on Silica Gel; III.^{1,2} A Convenient and Mild Reagent for Deacetalization in Dry Medium

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Acetals of various structures are conveniently cleaved under mild conditions by anhydrous iron(III) chloride dispersed on silica gel in the absence of any solvent.

The pale yellow powder obtained by simply stirring anhydrous iron(III) chloride and silica gel in the ratio 8:100 (w/w) in the absence of any solvent at room temperature (24 h) has been reported to induce, in dry medium, the dehydration of tertiary cycloalkanols, specific C₄ → C₅ and C₅ → C₆ ring enlargements, certain formations of spiro compounds and propella- γ -lactones, and the cleavage of *O*-tetrahydropyranyl derivatives.^{1,2} In the present communication, we describe the use of this silica gel-supported reagent for the cleavage of acetals (**1–15**) to carbonyl compounds (**16–28**) under rather mild conditions.



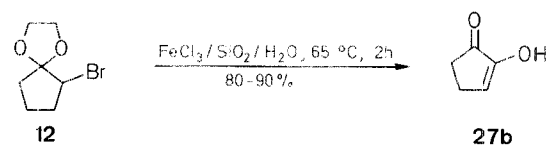
When neat 1,1-dimethoxycyclohexane **1** was added to the FeCl₃–SiO₂ powder at room temperature, complete deacetalization occurred within 5 min as evidenced by TLC monitoring and cyclohexanone (**16**) could be isolated in 97% yield either by simple filtration through Florisil[®] with ether or by vacuum distillation directly from the reaction medium. The corresponding 1,2-ethanediyl acetal (**2**) underwent cleavage more slowly (as shown by GLC): 60 and 70% of cyclohexanone were obtained after 10 and 20 min, respectively, an equilibrium with 73% ketone apparently being reached after 2.5 h. Practically complete hydrolysis (96%) was achieved within 10 min, however, by adding an 35% aqueous formaldehyde solution (0.7 ml for 3 mmol, 2.7 equivalents) to the reaction mixture, to trap the ethylene glycol formed.³ For comparison, the hydrolysis of cyclohexanone 1,2-ethanediyl acetal using wet silica gel required treatment with 15% sulfuric acid for 30 min, neutralization, filtration, evaporation of the solvent, and a second treatment with 15% sulfuric acid followed by the same work-up to give cyclohexanone (**16**) in 82% yield.⁴ In general, deacetalizations are performed by more acidic hydrolysis (*p*-toluenesulfonic acid, pyridinium *p*-toluenesulfonate, mineral acid, boron trifluoride etherate) or transacetalization.^{5,6} Cyclopentanone 1,2-ethanediyl acetal (**3**) is more reactive; thus, addition of aqueous formaldehyde was not necessary to complete the cleavage.

When neat 2-cyclopentenone 1,2-ethanediyl acetal (**4**) was added to the FeCl₃–SiO₂ reagent exothermic polymerization occurred. However, the rate of hydrolysis can be moderated by first mixing the acetal with silica gel and then adding a smaller amount (25%) of the FeCl₃–SiO₂ reagent. In this case, even silica gel alone was effective, but at a much slower rate; thus 2-cyclopentenone 1,2-ethanediyl acetal (**4**) underwent 60% of cleavage on stirring with silica gel for 24 h.

Acyclic and benzylic ketone acetals (**5**, **6**) as well as benzaldehyde acetals (**7**) underwent total cleavage upon treatment with FeCl₃–SiO₂ within 5 min, but octanal acetal (**8**) was cleaved more slowly: 69% of octanal (**22**) were formed after 1.5 h and the product underwent degradation on further reaction. However, it was totally cleaved within 10 min in the presence of aqueous formaldehyde. Selective monodeacetalization of 4-oxopentanal bis[1,2-ethanediyl acetal] (**9**) to 4-oxopentanal 1-(1,2-ethanediyl)acetal (**23**) proceeded under our standard conditions. This chemoselectivity must be compared with the recently reported alumina-induced selective acetalization of the formyl group of ketoaldehydes.³

The attempted monoacetalization of 2,2,4,4-tetramethyl-1,3-cyclobutanedione using one equivalent of ethylene glycol in refluxing benzene containing *p*-toluenesulfonic acid as catalyst gave a mixture of monoacetal (**24**; 13%) and diacetal (**10**; 17%) which was difficult to separate. On the other hand, the corresponding diacetal (**10**), which is readily available in high yields from the dione and excess of ethylene glycol under normal conditions, underwent monodeacetalization upon treatment with the FeCl₃–SiO₂ reagent for 2.5 h and gave exclusively 1,1,3,3-tetramethyl-5,6-dioxaspiro[3.4]octan-2-one (**24**). Neither by-products nor dione or bis-acetal were detected by ¹H-NMR in the crude product.

The monoacetals of 1,4-cyclohexanedione are useful starting materials for the synthesis of natural products.⁷ Reactions of the dione with one equivalent of ethylene, propylene, or neopentyl glycols or with propanediol are reported to give statistical mixture of products; reactions with 1,4-butanediol or with 2,2-dimethyl-1,3 propanediol using continuous extraction with hexane gave higher yields of the expected monoacetal.⁷ However, we have achieved the controlled monodeacetalization of 1,4-cyclohexanedione bis-[1,2-ethanediyl acetal] (**11**), readily available from the dione and excess ethylene glycol; 1,4-dioxaspiro[4.5]decan-8-one (**25**) was obtained in 55 or 58% yield upon treatment with FeCl₃–SiO₂ for 2 h, or in the presence of aqueous formaldehyde for 25 min, respectively.⁸ When added to FeCl₃–SiO₂, 2-bromocyclopentanone 1,2-ethanediylacetal⁹ (**12**) underwent 95% deacetalization within 30 min to give 2-bromocyclopentanone (**26a**) containing a small amount of chloroketone (**26b**; ~1%). Further halogen exchange occurred on heating the mixture; thus, 77% of 2-chlorocyclopentanone (**26b**) was formed on heating to 45°C for 2 h.



When neat **12** was treated with FeCl₃–SiO₂ in the presence of 6 equivalents of water (see experimental details) at 65°C for 2 h, 80–90% of 1,2-cyclopentanedione¹⁰ (**27b**) was obtained. Following the same procedure, 1,2-cyclohexanedione¹¹ was obtained in 10% yield, only.

Table. Deacetalization of Various Acetals using Iron(III)Chloride on Silica Gel in Dry Medium

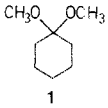
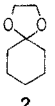


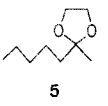
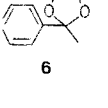
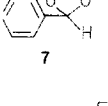
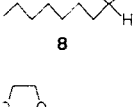
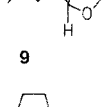
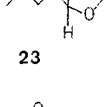
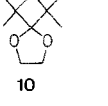
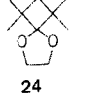
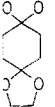
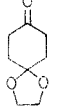
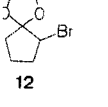
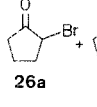
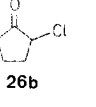
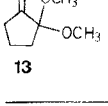
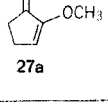


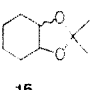

Acetal	Carbonyl Compound ^a or Other Products	Method ^b	Reaction Time	Conversion ^c (%)	Yield ^d (%)	m. p. (°C) or b. p. (°C)/torr	
						found	reported
	cyclohexanone 16	A	5 min	100	97		
	cyclohexanone 16	A	10 min	60	94		
		A	20 min	70			
		A	2.5 h	73			
		B	10 min	96			
	cyclopentanone 17	A	10 min	99.5	90		
		B	5 min	99.7	90		
	2-cyclopentenone 18	1. SiO ₂ ; 2. A with ratio 4: reagent = 1:4 (w/w) SiO ₂ alone	10 min	99	87	62/21	69/23 ⁹
			24 h	60			
	2-heptanone 19	A	5 min	100	98	149/760	150/760
	acetophenone 20	A	5 min	98	83	201/760	202/760
	benzaldehyde 21	A	5 min	99.5	85		
	octanal 22	A	1.5 h	69	55	171/760	171/760
		B	10 min	100	80		
		A	10 min	92	78 ^e		
		A	2.5 h	100	89	46.7	C ₁₀ H ₁₆ O ₃ (184.2)
		A	2 h		55 ^f	73	73–74 ⁷
		B	25 min	95	55 ^g		
	 + 	A A at 45°C	30 min 2 h	(Br : Cl = 99 : 1) (Br : Cl = 23 : 77)	90 95		
		A	1 h	97	71		112–114/16 ¹⁰

Table. (Continued)

Acetal	Carbonyl Compound ^a or Other Products	Method ^b	Reaction Time	Conversion ^c (%)	Yield ^d (%)	m. p. (°C) or b. p. (°C), torr	
						found	reported
		A	20 min	100	90		
		A	5 min	95	84	73	72.5–75

^a All products were characterized by their physical data, and their mass, IR, and NMR spectra. The purity of the products was >98% as determined by GLC and NMR.

^b Method A: Acetal (1 mmol) stirred with the 8% FeCl₃-SiO₂ reagent (1.2 g) at 20°C; Method B: Acetal (1 mmol) stirred with the 8% FeCl₃-SiO₂ reagent (1.2 g) and 35% aqueous formaldehyde solution (0.23 ml, 0.9 mmol) at 20°C.

^c Determined by GLC analysis of the reaction mixture.

^d Yield of product isolated by distillation or column chromatography.

^e The product of complete hydrolysis, 4-oxopentanal, was also formed in 8% yield, as determined by GLC.

^f 1,4-Cyclohexanedione was formed in 16% yield, as determined by GLC.

^g 1,4-Cyclohexanedione was formed in 22% yield, as determined by GLC.

2,2-Dimethoxycyclopentanone (**13**) gave 2-methoxycyclopenten-2-one (**27a**) in 71% yield upon treatment with FeCl₃/SiO₂ for 1 h at 20°C. Further stirring (5 days) or heating to 40°C did not give completely deacetalized 1,2-cyclopentanedione although 1-methoxycyclopentene (cyclopentanone enol methyl ether) **14** was totally cleaved with FeCl₃-SiO₂ at room temperature within 20 min. 1,2-Cyclohexanediol (**28**) was recovered in 84% yield when the corresponding acetone (**15**) was stirred with FeCl₃-SiO₂ at room temperature for 5 min.

Finally, an enantioselective α -alkylation of amino acid based on the diastereoselective alkylation and hydrolysis of 1,3-oxazolidin-5-ones has recently been achieved in high yield (95%) and high optical purity (>98% ee) by FeCl₃-SiO₂ induced cleavage of the *N,O*-acetals of pivalaldehyde indicating that no racemization occurs in the process.¹²

The anhydrous FeCl₃-SiO₂ reagent is prepared according to Lit.¹.

Cleavage of Acetals with Iron(III) Chloride on Silica Gel; General Procedures:

Method A, in Dry Medium: The neat acetal (3 mmol) is added to the anhydrous FeCl₃/SiO₂ reagent (3.6 g) placed in a 25 ml flask containing a magnetic stirring bar. The flask is stoppered with a cork and the mixture is then stirred at room temperature, the progress of the reaction being monitored by TLC or GLC of an aliquot (prepared from a small spatular of the mixture and 5 drops of ether). When the reaction is complete the product is either directly distilled under vacuum from the dry reaction medium (volatile compounds) or chromatographed with ether through a short column packed with Florisil® (~6 g). After removal of solvent on a rotary evaporator, the product is obtained practically pure or purified by flash chromatography¹³ if necessary.

Method B, in the Presence of Aqueous Formaldehyde: The neat acetal (3 mmol) is added to the anhydrous FeCl₃-SiO₂ reagent (3.6 g) in a 25 ml flask containing a magnetic stirring bar. To this is added 35% aqueous formaldehyde solution (0.7 ml, 2.7 equiv) and then, Method A is followed for performance and work-up.

Cleavage of 2-Cyclopentanone 1,2-Ethanedyl Acetal (1,4-Dioxaspiro[4.4]non-6-ene, **4**):

Neat 2-cyclopentanone 1,2-ethanedyl acetal (**4**; 378 mg, 3 mmol) is added to silica gel (2.7 g). This mixture is stirred, the FeCl₃/SiO₂ reagent (0.9 g) is slowly added, and stirring is continued for 10 min. The reaction is now complete according to GLC. The product is column-chromatographed on Florisil® using ether as eluent as in Method A; yield of 2-cyclopentanone (**18**): 215 mg (87%); b. p. 62°C/21 torr.

2,2,4,4-Tetramethyl-1,3-cyclobutanedione Mono[1,2-ethanedyl Acetal] (1,1,3,3-Tetramethyl-5,8-dioxaspiro[3.4]octan-2-one, **24**):

A mixture of 2,2,4,4-tetramethyl-1,3-cyclobutanedione bis[1,2-ethanedylacetal] (**10**; 674 mg, 3 mmol) and the FeCl₃-SiO₂ reagent (3.6 g) is stirred at room temperature for 2.5 h as in Method A to give, after flash chromatography¹³ (ether/hexane 1:9) product **24** as a colorless oil which solidifies on standing; yield: 490 mg (89%); m. p. 46.7°C.

C₁₀H₁₆O₃ calc. C 65.19 H 8.75
(184.2) found 64.90 8.46

MS: *m/e* = 115 (8%), 114 [M⁺ - (CH₃)₂C=C=O, 100], 113 (13), 99 [M⁺ - (CH₃)₂C=C=O - CH₃], 70 (8), 55 (5), 42 (14), 41 (27).

IR (CCl₄): ν = 2980 (m), 1785 (s), 1460 (m), 1382 (m), 1130 (s), 1050 (m), 1035 (m), 1020 (m) cm⁻¹.

¹H-NMR (CCl₄): δ = 3.95 (s, 4 H, 2 CH₂); 1.14 ppm (s, 12 H, 4 CH₃).

2-Bromocyclopentanone (**26a**):

2-Bromocyclopentanone 1,2-ethanedyl acetal (**12**; 414 mg, 2 mmol) and the FeCl₃-SiO₂ reagent (2.4 g) are stirred at room temperature for 30 min (95% conversion according to GLC) as in Method A. The mixture is column-chromatographed on Florisil® (4 g) using ether as eluent to give product **26a** containing ~1% 2-chlorocyclopentanone (**26b**) (as shown by GLC); yield: 295 mg (90%).

When the same mixture of **12** and reagent is stirred at room temperature for 18 h products **26a** and **26b** are obtained in a 64:36 ratio. When the same mixture is stirred at 45°C for 2 h the color turns from yellow to brownish-orange. Chromatography (Florisil, ether) then affords a 1:3.8 mixture of products **26a** and **26b**; yield: 200 mg (80%).

1,2-Cyclopentanedione (**27b**):

A mixture of 2-bromocyclopentanone 1,2-ethanedyl acetal (**12**; 1.03 g, 5 mmol), the FeCl₃-SiO₂ reagent (5 g) [prepared from anhydrous iron(III) chloride (20 g) and silica gel (100 g)], and water (0.54 ml, 30 mmol) is stirred at 65°C for 2 h. The color of the mixture at first turns to deep orange and then to deep-green. The mixture is then chromatographed over a short column of Florisil® (10 g) using ethyl acetate or chloroform as eluent to give enolized 1,2-cyclopentanedione (**27b**); yield: 420 mg (86%); m. p. 101–102°C (Lit.¹¹, m. p. 103°C). The spectral data of product **27b** thus obtained were identical with the reported^{10,11} data.

Received: 27 January 1986
(Revised form: 16 April 1986)

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