Substituted 1,3-Dichloroisopropanols, Cyclopropanols, and Ethyl Ketones from 1,3-Dichloroacetone

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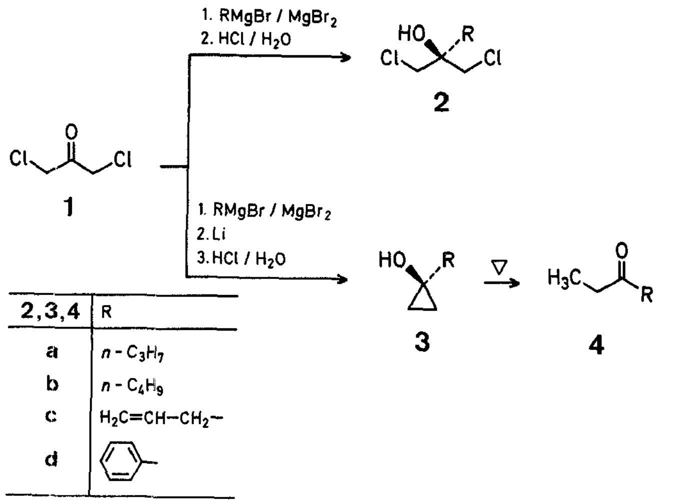
In connection with our investigations on dianionic β- and γ-substituted organoalkaline compounds[1,2] and their decomposition by elimination processes[2,3], we studied the preparation of the corresponding trianionic systems of type **6** by a similar method starting from α,α'-dichloro carbonyl compounds. Compounds of this type **6** were recently prepared by mercury/metal transmetallation from the corresponding substituted organodimercury(II) compounds[4].

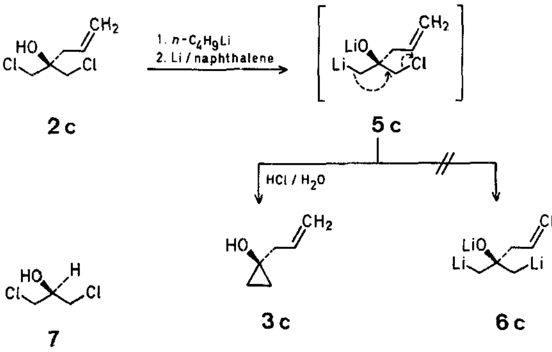
When commercially available 1,3-dichloroacetone (**1**) was allowed to react successively with a mixture of a Grignard reagent, anhydrous magnesium bromide and an excess of lithium powder, the corresponding 1-substituted cyclopropanols **3** were obtained after hydrolysis with aqueous hydrochloric acid. In the absence of magnesium bromide, the yields decrease (e.g. 30% for **2c**). The first step of the reaction is the addition of the organomagnesium compound to the carbonyl group. When the reaction mixture was hydrolyzed after this addition, the corresponding 1,3-dichloroisopropanols **2** were isolated. After the addition of the Grignard reagent to **1**, lithiation leads to an unstable intermediate of type **5**, which by a γ-elimination process yields product **3**. The successive reaction of **2c** with butyllithium[1,3] and an excess of lithium naphthalenide[1] at −78 °C leads to the intermediate **5c** (metallation with lithium powder at low temperature failed). Via a γ-elimination reaction and further acid hydrolysis **5c** is converted into the corresponding 1-allylcyclopropanol **3c** (83%). At −100 °C, the formation of the trianion **6c** was not observed (yield of **3c**: 71%) (Scheme **B**).



Scheme A

The reduced system **7** is formed as a by-product (yield: 13–18%) during the preparation of **2a** or **2b**. Compounds **2a, b** are purified by distillation.

Substituted cyclopropanols **3** can also be prepared from 1,3-dichloroacetone (**1**) by reaction with a Grignard reagent in the presence of iron(III) chloride[5] by a radical mechanism which involves the formation of highly reactive lower valence states of iron[6]. However this method gives only good results for 1-arylcyclopropanes[5,7]. The corresponding 1-alkyl derivatives are obtained in poor yields.



Scheme **B**

When compounds **3** were heated to 160–225 °C (bath temperature; Table 1), ring-opening takes place yielding the corresponding substituted ethyl ketones **4** (Scheme **A**). Ring opening reactions induced by bases or electrophiles leading to **4** were already described[8].

1-Chloro-2-chloromethyl-2-pentanol (2a); Typical Procedure:

1,3-Dichloroacetone (**1**; 1.91 g, 15 mmol) in ether (30 ml) is treated with magnesium bromide etherate (4.64 g, 18 mmol). The mixture is cooled to −20 °C (bath temperature), then ~1.5 normal propylmagnesium bromide in ether (~12 ml, 18 mmol) is added, the mixture is stirred overnight (23 h), and allowed to warm up slowly to 20 °C. The mixture is hydrolyzed with aqueous hydrochloric acid till neutral pH,

Table 1. Preparation of Products **2**, **3**, and **4**

Product	Reaction conditions Temperature [°C][a]	Time [h]	Yield [%][b]	b.p./torr [°C]	Molecular formula[c] or Lit. b.p./torr [°C]	
2b	−20 to 20°	9	32	43–45°/0.1	$C_7H_{14}Cl_2O$	(185.1)
2c	−70 to −30°	4	78	87–89°/15	$C_6H_{10}Cl_2O$	(169.05)
2d	−20 to 20°	7	81	88–90°/0.1	$C_9H_{10}Cl_2O$	(205.1)
3b	−20 to 20°[c,d]	4.5/15[e]	48	64–66°/15	$C_7H_{14}O$	(114.2)
3c	−20 to 20°[c,d]	2.5/22[e]	67	44–46°/15	$C_6H_{10}O$	(98.15)
3d	−20 to 20°[c,d]	5/17[e]	56	102–104°/15	106–107°/20[7]	
4b	170 to 180°	2	53[f]	52–54°/15	147°/765[9]	
4c	160 to 170°	5.5	78[f]	43–45°/15	126–127°/760[10]	
4d	220 to 225°	12.5	70[f]	—[g]	217–218°/760[9]	

[a] Bath temperature.
[b] Isolated yields based on starting compound **1**.
[c] Satisfactory microanalyses obtained: C ±0.24, H ±0.13. Purity >95% from G.L.C. analysis (Chromosorb OV-101).
[d] The reaction temperature for the reaction with the Grignard reagent and for the lithiation was the same.
[e] Reaction time for the reaction with the Grignard reagent/for the lithiation.
[f] Based on compound **3**.
[g] Product **4d** was condensed trap to trap at 0.1 torr (bath temperature: 50–60 °C).

Table 2. Spectral Data for Products **2**, **3**, and **4**[a]

Product	I.R. (film)[b] ν [cm⁻¹]	¹H-N.M.R. (CCl_4/TMS)[c] δ [ppm]	¹³C-N.M.R. (CCl_4)[c] δ [ppm][d]
2b	3440 (OH)	0.95 (m, 3H); 1.2–1.7 (m, 6H); 2.4 (s, 1H, OH); 3.50, 3.55 (2s, 4H)	13.9, 23.0, 24.8, 34.7 (n-C_4H_9); 48.3 (CH_2Cl); 73.8 (C—O)
2c	3420 (OH); 3060, 1645 (C═CH)	2.40 (d, J=8 Hz, 2H); 2.75 (s, 1H, OH); 3.55 (s, 4H); 4.95–5.3 (m, 2H); 5.55–6.1 (m, 1H)	39.4, 119.65, 131.45 (allyl); 48.15 (CH_2Cl); 73.4 (C—O)
2d	3500 (OH); 3020, 1500, 1455, 730, 705 (C_6H_5)	3.15 (s, 1H, OH); 3.7 (s, 4H); 7.0–7.4 (m, 5H, C_6H_5)	50.7 (CH_2Cl); 75.5 (C—O); 125.8, 128.2, 128.4, 140.15 (C_6H_5)
3b	3310 (OH); 3060 (CH-ring)	0.4, 0.7 (2m, 4H); 1.0 (m, 3H); 1.2–1.6 (m, 6H); 4.3 (br. s, 1H, OH)	12.6 (CH_2-ring); 13.7, 22.6, 28.0, 37.9 (n-C_4H_9); 54.5 (C—O)
3c	3320 (OH); 3060 (CH-ring and ═CH); 1645 (C═C)	0.4, 0.7 (2m, 4H); 2.3 (d, J=8 Hz, 2H); 3.95 (s, 1H, OH); 4.9–5.2 (m, 2H); 5.55–6.1 (m, 1H)	12.0 (CH_2 ring); 42.3, 116.7, 135.0 (allyl); 54.3 (C—O)
3d	3340 (OH); 3060, (CH-ring); 3020, 1600, 1490, 750, 690 (C_6H_5)	—[11]	17.5 (CH_2-ring); 55.7 (C—O); 124.3, 125.85, 127.9, 144.2 (C_6H_5)
4b	—[12]	—[13]	7.4, 13.6, 22.2, 25.8, 35.2, 41.5 (C_2H_5 and n-C_4H_9); 188.5 (C═O)
4c	1695 (C═O); 1630 (C═C)	0.90 (t, J=8 Hz, 3H); 1.80 (d, J=8 Hz, 2H); 2.35 (t, J=8 Hz, 2H); 5.75–6.1 (m, 2H); 6.4–6.95 (m, 1H)	7.4, 17.3 (C_2H_5); 32.3, 131.4, 141.0 (allyl); 198.3 (C═O)
4d	—[12]	—[13]	—[14]

[a] Spectral data for the described products **3d** and **4** were identical with those reported[11–14].
[b] Recorded in a Pye Unicam SP-1000 I.R. spectrometer.
[c] Recorded in a Varian FT-80 spectrometer with a D_2O capillary.
[d] Referred to the solvent CCl_4. Assignments were made by off resonance experiments.

extracted with ether (25 ml), and the ether layer is dried with anhydrous sodium sulfate. The ether is evaporated (15 torr) and the residue is distilled at the same pressure to give pure **2a**; yield: 1.05 g (41%); b.p. 80–84 °C/15 torr.

$C_6H_{12}Cl_2O$	calc.	C 42.13	H 7.07
(171.1)	found	42.05	7.20

I.R. (film): ν = 3400 cm^{-1} (OH).

^{1}H-N.M.R. (CCl_4/TMS): δ = 0.8–1.1 (m, 3 H); 1.4–1.7 (m, 4 H); 3.15 (s, 1 H); 3.55 ppm (s, 4 H).

^{13}C-N.M.R. (CCl_4): δ = 14.2, 15.9, 37.1 (n-C_3H_7); 48.1 (CH_2Cl); 73.8 ppm (C—O).

1-Propylcyclopropanol (3a); Typical Procedure:

To a suspension of magnesium bromide etherate (4.64 g, 18 mmol) in 1,3-dichloroacetone **1** (1.91 g, 15 mmol) and ether (30 ml), ~1.5 normal propylmagnesium bromide in ether (~12 ml, 18 mmol) is added at −20 °C. The mixture is stirred for 9 h allowing the temperature to rise to 20 °C. The resulting suspension is cooled to −20 °C and lithium powder (0.44 g, 63 mmol) is added. The mixture is stirred overnight (16 h) and the temperature is allowed to rise to 20 °C. Then, the suspension is hydrolyzed with aqueous hydrochloric acid till neutral pH, extracted with ether (25 ml), and the organic layer is dried with anhydrous sodium sulfate. Ether is removed by distillation and the residue is distilled under reduced pressure (15 torr) to give pure **3a**; yield: 0.65 g (43%); b.p. 42–43 °C/15 torr.

$C_6H_{12}O$	calc.	C 71.95	H 12.08
(100.2)	found	71.78	12.16

I.R. (film): ν = 3350 (OH), 3060 cm^{-1} (CH-ring).

^{1}H-N.M.R. (CCl_4/TMS): δ = 0.3, 0.6 (2m, 4 H); 0.8–1.3 (m, 5 H); 1.6 (m, 2 H); 4.80 ppm (s, 1 H).

^{13}C-N.M.R. (CCl_4): δ = 12.7 (CH_2-ring); 14.0, 19.0, 40.5 (n-C_3H_7); 54.4 ppm (C—O).

3-Hexanone (4a); Typical Procedure:

1-Propylcyclopropanol (**3a**; 1.0 g, 10 mmol) is heated to 160–170 °C (bath temperature) for 2 h. Then, the resulting liquid is distilled under reduced pressure (15 torr) to give pure **4a**; yield: 0.85 g (85%); b.p. 42–45 °C/15 torr (Ref.[9], b.p. 125 °C/760 torr); I.R. and ^{1}H-N.M.R. spectra identical with those reported in Refs.[12,13].

^{13}C-N.M.R. (CCl_4): δ = 9.1, 13.7, 17.0, 35.4, 43.8 (C_2H_5 and n-C_3H_7); 212.7 ppm (C=O).

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