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Reaction of Trialkyl Orthoformates with the Aluminium Derivatives of Some α-Unsaturated Bromides. Preparation of β-Unsaturated Acetals

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Received November 18, 1985

Reaktion von Trialkylorthoformaten mit den Aluminium-Derivaten einiger α-ungesättigter Bromide. Darstellung von β-ungesättigten Acetalen

Die Aluminium-Derivate **2**, **4** und **7** α-ungesättigter Bromide, dargestellt in Ether, sind sehr reaktionsfähig gegenüber Trialkylorthoformaten. Mit Hilfe dieser Reaktion, durchgeführt bei −80°C, können auf einfache Weise β-ungesättigte Acetale **3**, **5** bzw. **8** dargestellt werden.

It is well known that the reactivity of Grignard reagents towards trialkyl orthoformates is rather low[1-7]: for the formation of an acetal to be successful it is necessary either to reflux the reaction mixture in ether for several hours or to distill the ether from the reaction solution and to cautiously heat the residue until a highly exothermic reaction begins.

It has been shown that by using the mixed orthoformate $C_6H_5O-CH(OC_2H_5)_2$ (**1**) an acetal could be easily prepared from a Grignard reagent at room temperature[8-11].

$$\mathrm{RMgX} + \underset{\mathbf{1}}{\mathrm{C_6H_5O{-}CH(OC_2H_5)_2}} \longrightarrow \mathrm{R{-}CH(OC_2H_5)_2}$$

The increased reactivity of the mixed orthoformate **1** is due to the phenoxy group which is a better leaving group than an ethoxy group.

Some years ago we[11] reported that, when working with the aluminium derivative of an α-unsaturated bromide, the reaction with the orthoformate **1** afforded β-unsaturated acetals at a temperature as low as −80°C.

$$\mathrm{H_2C{=}CH{-}CH_2Br} \xrightarrow[\text{2) }\mathbf{1}]{\text{1) Al/ether}} \mathrm{H_2C{=}CH{-}CH_2{-}CH(OC_2H_5)_2}$$

We now report that the same type of β-unsaturated acetals can be obtained at −80°C from the aluminium derivatives of α-unsaturated bromides and trialkyl orthoformates $HC(OR)_3$ ($R = CH_3$, nC_3H_7).

When substituted α-ethylenic bromides **2** are used, the reaction proceeds with allylic rearrangement (Scheme 1).

Chem. Ber. 119, 1725–1730 (1986)

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Scheme 1

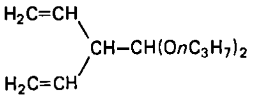
$$\underset{\mathbf{2}}{R^1{-}CH{=}C(R^2){-}CH_2Br} \xrightarrow[\text{2) HC(OR)}_3\text{/–80°C}]{\text{1) Al/ether}} \underset{\mathbf{3}}{H_2C{=}C(R^2){-}CH(R^1){-}CH(OR)_2}$$

3	R^1	R^2	R	Yield %
a	H	H	CH_3	63
b	CH_3	H	CH_3	76
c	nC_4H_9	H	CH_3	80
d	nC_5H_{11}	H	CH_3	73
e	nC_6H_{13}	H	CH_3	67

3	R^1	R^2	R	Yield %
f	C_6H_5	H	CH_3	70
g	CH_3	H	nC_3H_7	90
h	H	CH_3	nC_3H_7	81
i	C_2H_5	H	nC_3H_7	82

However, when we used the diethylenic bromide **4**, we only obtained the unbranched acetal **5** (yield 77%); we were unable to detect the branched isomer **6**.

$$\underset{\mathbf{4}}{H_2C{=}CH{-}CH{=}CH{-}CH_2Br} \xrightarrow[\text{2) HC(O}n\text{C}_3\text{H}_7\text{)}_3\text{/–80°C}]{\text{1) Al/ether}} \underset{\mathbf{5}}{H_2C{=}CH{-}CH{=}CH{-}CH_2{-}CH(OnC_3H_7)_2}$$



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We do not know whether this reaction proceeds without rearrangement or with a double allylic rearrangement; we can only remind here that the reaction between the aluminium derivative of the diethylenic chloride $H_2C=CH-CH=CH-CH_2Cl$ and either a *gem*-amino ether[12,13] or an imonium salt[13] also proceeds mainly to give a β,δ-diethylenic amine, that is without apparent rearrangement.

Next, we used the aluminium derivatives of α-acetylenic bromides **7**: the reaction proceeds without rearrangement to give β-acetylenic acetals **8** (Scheme 2).

Scheme 2

$$\underset{\mathbf{7}}{H{-}C{\equiv}C{-}CHBr{-}R^1} \xrightarrow[\text{2) HC(OR)}_3\text{/–80°C}]{\text{1) Al/ether}} H{-}C{\equiv}C{-}CH(R^1){-}CH(OR)_2$$

8	R^1	R	Yield %
a	H	CH_3	73
b	CH_3	CH_3	67
c	C_2H_5	nC_3H_7	82
d	nC_3H_7	nC_3H_7	51

We obtained an untractable mixture from the reaction of the orthoformate $HC(OnC_3H_7)_3$ with the aluminium derivative of the bromide $C_2H_5-C\equiv C-CH_2Br$.

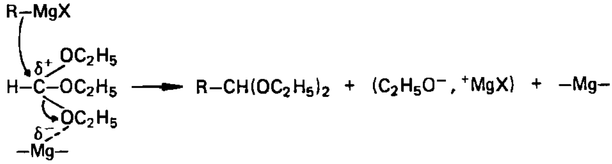
Scheme 3

$$R{-}CH{=}CH{-}CH_2Br \xrightarrow[\text{2) CH}_3\text{C(OCH}_3\text{)}_3\text{/–80°C}]{\text{1) Al/ether}} H_2C{=}CH{-}CH(R){-}C(OCH_3)_2{-}CH_3$$

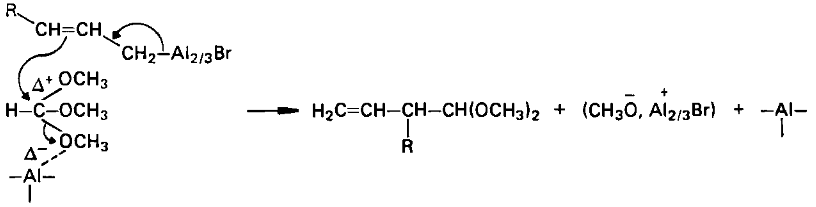
9	R	Yield %
a	H	56
b	CH_3	45

Finally, we extended the same type of reaction to trimethyl orthoacetate: we thus obtained ketals **9** (Scheme 3).

The first step of the reaction of a Grignard reagent with an orthoformate is probably a partial desolvation of one of the various species present in the solution (R_2Mg, RMgX, MgX_2) by one of the orthoformate oxygen atoms to give a polarized complex which is next attacked by the Grignard reagent.



When an α-ethylenic aluminium reagent is used, the same type of complex is produced from the species such as R_3Al, R_2AlBr, $RAlBr_2$, and $AlBr_3$ which are present in solution. The complex thus formed is more polarized than the complex derived from a Grignard reagent since aluminium derivatives are stronger Lewis acids than magnesium derivatives: then, it can react at a temperature as low as −80°C.



In agreement with the proposed mechanism, we observed that, at −80°C, there is no reaction between $H-C(OCH_3)_3$ and the aluminium derivative of $H_2C=CH-CH_2Br$ *prepared in tetrahydrofuran* (THF): here, the oxygen atoms of the orthoformate are not basic enough to take the place of one of the THF molecules which solvate the aluminium species. No polarized complex is formed and no reaction can occur.

We thank Dr. *F. Barbot* (Poitiers) for fruitful discussions.

Experimental Part

^1H NMR spectra: Perkin Elmer 24 A (60 MHz). – $CH_3CH=CHCH_2Br$, $HC(OCH_3)_3$, and $CH_3C(OCH_3)_3$ were commercial products. Bromides $R^1CH=CHCH_2Br$ (R^1 = C_2H_5[14], nC_4H_9[14], nC_5H_{11}[15], nC_6H_{13}[15], $H_2C=CH$[16], C_6H_5[17]), $HC\equiv CCHBr-R^1$ (R^1 = H[18], CH_3[18,19], C_2H_5[19], nC_3H_7[20]), $C_2H_5C\equiv CCH_2Br$[21], and orthoformate $HC(OnC_3H_7)_3$[22] were prepared according to literature procedures.

3-Bromo-2-methyl-1-propene (**2h**)[23]: 2-Methyl-2-propen-1-ol (108 g, 1.5 mol) was added to phosphorous tribromide (150 g, 0.55 mol) while the temperature of the solution was maintained at 30°C by intermittent external cooling. The mixture was stirred for 2 h and the flask was next connected to a short column. The bromide was then distilled off (water bath) under reduced pressure: b. p. 70°C/215 Torr. After addition of ether, the raw bromide was washed with iced water (2 × 100 ml), dried ($CaCl_2$), and distilled, b. p. 93–94°C/760 Torr, yield 111 g (55%).

General Procedure for the Reaction of Unsaturated Aluminium Reagents with Orthoesters: The aluminium derivative prepared[18,24] from the α-unsaturated bromide (0.10 mol), alumin-

Table 1. Physicochemical and spectral data of compounds **3**, **5**, **8**, and **9**

	B. p. (°C/Torr)	n_D^{20}	^{1}H NMR (CCl_4/TMS_{int}), δ (ppm)
3a	52/75	1.4057	4.8 – 6.1 (m, 3H, $CH=CH_2$); 4.25 (t, J = 6 Hz, 1H, CH – O); 3.2 (s, 6H, OCH_3); 2.1 – 2.5 (m, 2H, $=CCH_2$)
3b	60 – 61/74	1.4118	4.7 – 6.1 (m, 3H, $CH=CH_2$); 3.95 (d, J = 6 Hz, 1H, CH – O); 3.25 (s, 6H, OCH_3); 2.0 – 2.7 (m, 1H, =CCH)
3c	110 – 112/74	1.4262	4.7 – 5.9 (m, 3H, $CH=CH_2$); 4.0 (d, J = 6 Hz, 1H, CH – O); 3.25 (2 s, 6H, OCH_3); 1.9 – 2.5 (m, 1H, =CCH)
3d	87 – 88/14	1.4305	4.7 – 5.9 (m, 3H, $CH=CH_2$); 4.0 (d, J = 6 Hz, 1H, CH – O); 3.15 – 3.20 (2 s, 6H, OCH_3); 1.9 – 2.5 (m, 1H, =CCH)
3e	60 – 62/0.1	1.4430	4.6 – 6.0 (m, 3H, $CH=CH_2$); 4.0 (d, J = 6 Hz, 1H, CH – O); 3.20, 3.25 (2 s, 6H, OCH_3); 1.9 – 2.5 (m, 1H, =CCH)
3f	110/12	1.5071	7.0 (s, 5H, C_6H_5); 5.7 – 6.4 (m, 1H, CH=); 4.6 – 5.1 (m, 2H, $=CH_2$); 4.35 (d, J = 6 Hz, 1H, CH – O); 3.05, 3.20 (2 s, 6H, OCH_3); 3.2 – 3.8 (m, 1H, =CCH)
3g	68 – 70/12	1.4202	4.7 – 6.1 (m, 3H, $CH=CH_2$); 4.05 (d, J = 6 Hz; 1H, CH – O); 3.1 – 3.7 (m, 4H, CH_2O); 2.0 – 2.6 (m, 1H, =CCH); 1.2 – 1.8 (m, 4H, $CH_3C\mathit{H}_2$)
3h	68 – 69/13	1.4239	4.7 (s, 2H, $=CH_2$); 4.5 (t, J = 6 Hz, 1H, CH – O); 3.1 – 3.7 (m, 4H, CH_2O); 2.2 (d, J = 6 Hz, 2H, $=CCH_2$); 1.75 (s, 3H, $=CCH_3$); 1.2 – 1.8 (m, 4H, $CH_3C\mathit{H}_2$)
3i	82 – 83/11	1.4245	4.7 – 5.9 (m, 3H, $CH=CH_2$); 4.15 (d, J = 6 Hz, 1H, CH – O); 3.0 – 3.7 (m, 4H, CH_2O); 1.8 – 2.4 (m, 1H, =CCH); 1.1 – 1.8 (m, 6H, $CH_3C\mathit{H}_2$)
5	105 – 107/16	1.4521	4.7 – 6.6 (m, 5H, $H_2C=CHCH=CH$); 4.45 (t, J = 6 Hz, 1H, CH – O); 3.1 – 3.7 (m, 4H, CH_2O); 2.3 (dd, $J = J'$ = 6 Hz, 2H, $=CCH_2$); 1.2 – 1.9 (m, 4H, $CH_3C\mathit{H}_2$)
8a	66 – 68/75	1.4215	4.4 (t, J = 6 Hz, 1H, CH – O); 3.25 (s, 6H, OCH_3); 2.4 (dd, J = 6, J' = 3 Hz, 2H, CH_2), 1.85 (t, J' = 3 Hz, 1H, ≡CH)
8b	62 – 64/53	1.4241	4.1 (d, J = 6 Hz, 1H, CH – O); 3.2 (s, 6H, OCH_3); 2.2 – 2.9 (m, 1H, ≡CCH); 1.85 (d, J = 3 Hz, 1H, ≡CH); 1.15 (d, J = 6 Hz, 3H, CCH_3)
8c	96 – 97/16	1.4299	4.25 (d, J = 6 Hz, 1H, CH – O); 3.1 – 3.7 (m, 4H, CH_2O); 2.2 – 2.8 (m, 1H, ≡CCH); 1.9 (d, J = 3 Hz, 1H, ≡CH); 1.2 – 1.8 (m, 6H, $CH_3C\mathit{H}_2$, $CHC\mathit{H}_2$)
8d	108/16	1.4317	4.25 (d, J = 6 Hz, 1H, CH – O); 3.1 – 3.7 (m, 4H, CH_2O); 2.3 – 2.8 (m, 1H, ≡CCH); 1.9 (d, J = 3 Hz, 1H, ≡CH); 1.2 – 1.8 (m, 8H, $CH_3C\mathit{H}_2$, $CHC\mathit{H}_2$)
9a	66/75	1.4170	4.7 – 6.1 (m, 3H, $CH=CH_2$); 3.15 (s, 6H, OCH_3); 2.25 (d, J = 6 Hz, 2H, $=CCH_2$); 1.15 (s, 3H, CH_3)
9b	75 – 77/74	1.4245	4.7 – 6.2 (m, 3H, $CH=CH_2$); 3.15 (s, 6H, OCH_3); 2.3 – 2.8 (m, 1H, =CCH)

ium (2.7 g, 0.10 mol), and ether (60 ml) was diluted with ether (300 ml). After cooling to – 80 °C (internal temp.) under nitrogen, the orthoester (0.050 mol), diluted with ether (10 ml), was added within 15 min when using $HC(OCH_3)_3$ or $CH_3C(OCH_3)_3$ and within 45 min when

Table 2. Elemental analysis of compounds **3**, **5**, **8**, and **9**

	Mol. Formula	(Weight)	C		H	
			Calcd.	Found	Calcd.	Found
3a	$C_6H_{12}O_2$	(116.2)	62.04	62.33	10.41	10.42
3b	$C_7H_{14}O_2$	(130.2)	64.58	64.85	10.84	10.75
3c	$C_{10}H_{20}O_2$	(172.3)	69.72	69.95	11.70	11.55
3d	$C_{11}H_{22}O_2$	(186.3)	70.92	70.90	11.90	11.88
3e	$C_{12}H_{24}O_2$	(200.3)	71.95	72.05	12.08	11.95
3f	$C_{12}H_{16}O_2$	(192.3)	74.97	74.86	8.39	8.40
3g	$C_{11}H_{22}O_2$	(186.3)	70.92	71.01	11.90	11.75
3h	$C_{11}H_{22}O_2$	(186.3)	70.92	71.15	11.90	11.72
3i	$C_{12}H_{24}O_2$	(200.3)	71.95	72.21	12.08	11.85
5	$C_{12}H_{22}O_2$	(198.3)	72.68	72.70	11.18	11.97
8a	$C_6H_{10}O_2$	(114.1)	63.14	63.20	8.83	8.58
8b	$C_7H_{12}O_2$	(128.2)	65.60	65.81	9.44	9.51
8c	$C_{12}H_{22}O_2$	(198.3)	72.68	72.75	11.18	11.05
8d	$C_{13}H_{24}O_2$	(212.3)	73.54	73.50	11.39	11.10
9a	$C_7H_{14}O_2$	(130.2)	64.58	64.50	10.84	10.80
9b	$C_8H_{16}O_2$	(144.2)	66.63	66.78	11.18	10.97

using $HC(OnC_3H_7)_3$. The temperature was maintained for either 15 min at −80°C ($HC(OCH_3)_3$ and $CH_3C(OCH_3)_3$) or 45 min at −80°C ($HC(OnC_3H_7)_3$). The mixture was cooled at −100°C and water was added (75 ml). After 2 h of stirring at room temp., the liquid mixture was decanted, the aqueous phase was extracted with ether (3 × 40 ml), and the combined phases were washed with NaOH (5 M, 70 ml) and water (2 × 70 ml). After drying (K_2CO_3), the acetal was distilled (Tables 1, 2).

6,6-Dipropoxy-1,3-hexadiene (**5**): Owing to the very high tendancy of 5-bromo-1,3-pentadiene to give a Wurtz reaction when reacted with a metal, the preparation of the corresponding aluminium derivative requires special conditions[25]: a pinch of $HgCl_2$ was added under nitrogen to a stirred suspension of aluminium (3.5 g, 0.13 mol) in ether (10 ml). The mixture was heated under reflux for 30 min. The heating was stopped and some pure bromide (5 drops) was rapidly added. The reaction started immediatly (the ether boiled again). The remaining bromide (total amount 14.7 g, 0.10 mol) in ether (100 ml) was slowly (8 h) added at such a rate that the temp. maintained at 17−18°C exactly: since the reaction is exothermic, it was necessary, from time to time, to cool the flask with fresh water. When the addition was over, the mixture was stirred for 1 h at room temperature. The solution thus obtained was decanted off the excess aluminium into another flask and next reacted at −80°C with $HC(OnC_3H_7)_3$ (5.7 g, 0.03 mol) diluted with ether (6 ml) according to the general procedure (Tables 1, 2). Yield 4.6 g (77%).

CAS Registry Numbers

2a: 106-95-6 / **2b**: 106-94-5 / **2c**: 34686-77-6 / **2d**: 25466-54-0 / **2e**: 76853-14-0 / **2f**: 4392-24-9 / **2h**: 1458-98-6 / **2i**: 16400-32-1 / **3a**: 72380-56-4 / **3b**: 100514-44-1 / **3c**: 87745-56-0 / **3d**: 100514-48-5 / **3e**: 100514-49-6 / **3f**: 81505-22-8 / **3g**: 100514-46-3 / **3h**: 100514-47-4 / **3i**: 100514-50-9 / **4**: 1001-93-0 / **5**: 100514-51-0 / **7a**: 106-96-7 / **7b**: 18668-72-9 / **7c**: 24480-13-5 / **7d**: 49769-87-1 / **8a**: 33639-45-1 / **8b**: 100514-52-1 / **8c**: 100514-53-2 / **8d**: 100514-54-3 / **9a**: 98429-28-8 / **9b**: 100514-45-2 / $HC(OMe)_3$: 149-73-5 / $HC(OPr)_3$: 621-76-1 / $CH_3C(OMe)_3$: 1445-45-0 / $H_2C{=}CMeCH_2OH$: 513-42-8 / $EtC{\equiv}CCH_2CH(OPr)_2$: 100570-87-4 / $(H_2C{=}CHCH_2)_3Al_2Br_3$: 67702-85-6 / $(CH_3CH{=}CHCH_2)_3Al_2Br_3$: 12354-30-2 /

$(H_2C=CMeCH_2)_3Al_2Br_3$: 70688-45-8 / $(BuCH=CHCH_2)_3Al_2Br_3$: 70688-44-7 / $((CH_3(CH_2)_4CH=CHCH_2)_3Al_2Br_3$: 100514-37-2 / $(CH_3(CH_2)_5CH=CHCH_2)_3Al_2Br_3$: 95313-92-1 / $(PhCH=CHCH_2)_3Al_2Br_3$: 100514-38-3 / $(EtCH=CHCH_2)_3Al_2Br_3$: 70688-43-6 / $(H_2C=CHCH=CHCH_2)_3Al_2Br_3$:100514-39-4 /$(HC\equiv CCH_2)_3Al_2Br_3$:61781-91-7 /$(HC\equiv CCHMe)_3Al_2Br_3$: 100514-40-7 / $(HC\equiv CCHEt)_3Al_2Br_3$: 100514-41-8 / $(HC\equiv CCHPr)_3Al_2Br_3$: 100514-42-9 / $(EtC\equiv CCH_2)_3Al_2Br_3$: 100514-43-0

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