21. Skeletal Migrations Observed during the Cob(I)alamin-Catalyzed Reduction of 4*β*-(*tert*-Butyl)-1*β*-(1-methylvinyl)cyclohexanecarbaldehyde[1])

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Dedicated to Professor Dr. *K. Bernauer* on the occasion of his 60th birthday

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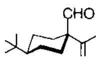
During the cob(I)alamin(**1(I)**)-catalyzed reduction of **3**, intermediate formation of **2** and final generation of **4**–**10** was observed (see *Scheme 1*, *cf. Tables 1* and *2*). Identical products in similar ratios were generated starting from either **2** or **3**. Accepting the intermediate formation of six interconnected cobalt complexes, *i.e.* **A**–**F** *(cf. Scheme 2)*, the generation of all the products observed can be explained.

1. Preparation of 3. – The 4*β*-(*tert*-Butyl)-1*β*-(1-methylvinyl)cyclohexanecarbaldehyde (**3**) was prepared from **2**[2]) by cob(I)alamin-catalyzed isomerization (*cf.* [1a]). Crystalline **3** was accessible after chromatographic purification.



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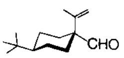

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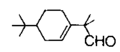

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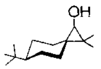

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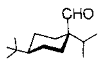

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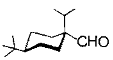

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2. Kinetic Experiments. – The two *β*,*γ*-unsaturated aldehydes **2** and **3** were reduced using catalytic amounts of cob(I)alamin and 10 mol-equiv. of Zn. Aliquots were withdrawn from the reaction mixture after 5, 10, 20, 30, and 60 min and after 2, 2.75, and 5.5 h. Starting from **2** (broken lines), rapid consumption of **2** ($t_{1/2} \approx 22$ min) and intermediate accumulation of **3**, reaching top level (9%) after 20 min, was observed (see *Scheme 1* and *cf.* [1a]). The two cyclopropanols **5** and **6** were gradually formed gaining final concentrations at the time of complete consumption of **2** and **3**. Starting from **3** (dotted lines, $t_{1/2} \approx 13$ min), intermediate formation of **2**, attaining top level (24%) after 20 min, was detected. In the two kinetic experiments, the rate of formation and the

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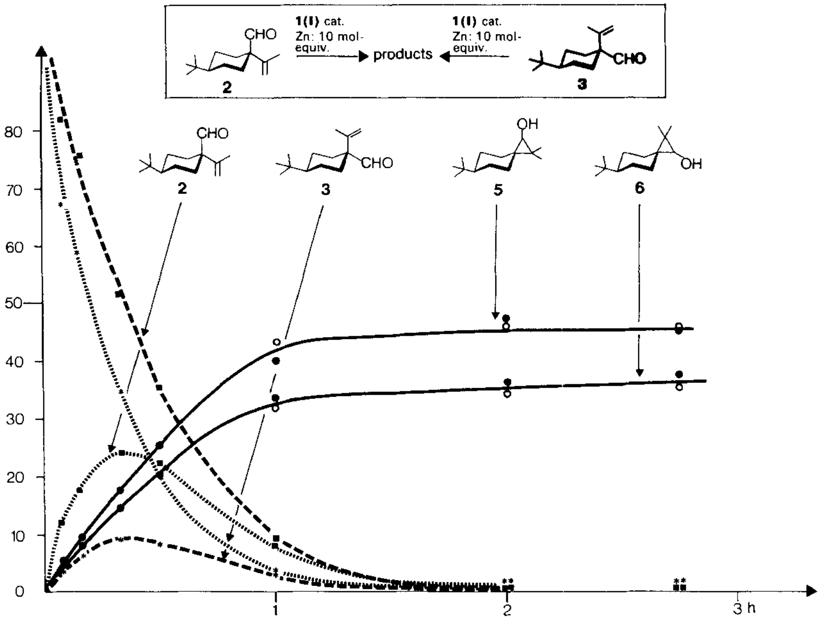
[1]) 15th Communication in the series 'Cob(I)alamin as Catalyst'; for the 14th communication, see [1a]; for the structural formulae of cob(I)- and cob(III)alamin(**1(I)**, **1(III)**), *cf. Scheme 1* in [1b].

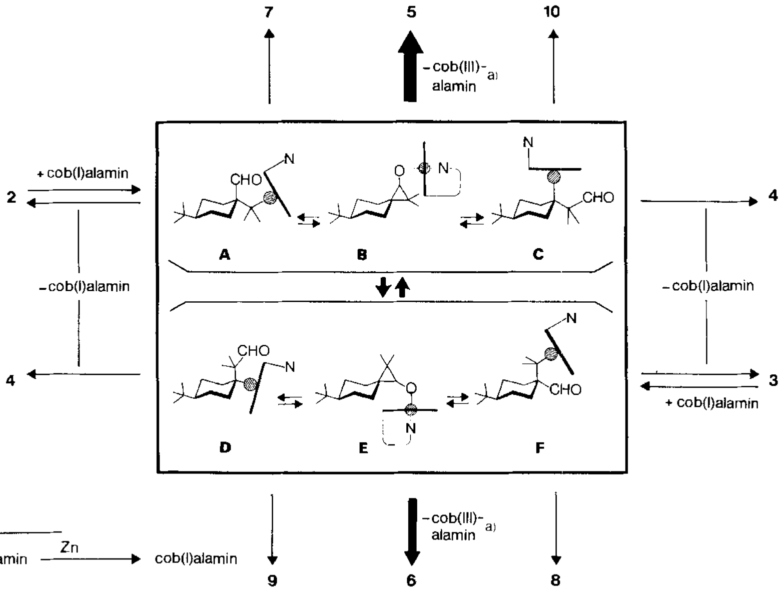
[2]) For the preparation and data of **2**, *cf.* [1c].

Scheme 1



final level of the two main products, *i.e.* **5** (45.4% from **2**, 46.1% from **3**) and **6** (38.2% from **2**, 35.3% from **3**), was very similar. Detailed data are compiled in *Tables 1* and *2* (see *Exper. Part*).

Scheme 2



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a) cob(III)alamin $\xrightarrow{Zn}$ cob(I)alamin

3. Discussion. – The cob(I)alamin-catalyzed transformation of **2** has been published [1a]. The formation of the products generated by this skeletal migration was explained *via* intermediate formation of the tertiary alkylcobalamin **A** *(cf. Scheme 2)*. This alkylcobalamin was assumed to be in equilibrium with the alkylcobalamins **C**, **D**, and **F** and with the (cyclopropanolo)cobalamins **B** and **E** (*cf.* also [1b]). Accepting these six intermediates, the formation of all the products observed could be explained.

Based on the same mechanism, we assume **F** to be initially formed starting from **3**. From **F**, the five cobalt complexes **A** to **E** should be accessible by the equilibrium cited above. Identical products in similar relations should therefore be generated starting from **2** as well as from **3**. The experimental data show this to be the case.

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Experimental Part

General. See [1c]. The cob(I)alamin catalyst was prepared according to the procedure in [1d].

*4β-(*tert*-Butyl)-1β-(1-methylvinyl)cyclohexanecarbaldehyde* (**3**). Cyanocob(III)alamin (745 mg, 0.1 mol-equiv.) was transformed to the catalyst according to [1d]. The red residue was dissolved in AcOH (16 ml), and activated metallic Zn (1.08 g, 3 mol-equiv.) was added. The suspension was stirred at r.t. in the dark under Ar. After 10 min, the colour turned to green. To this suspension, **2** (1.15 g) in AcOH (2 ml) was added in 1 portion. The mixture was stirred in the dark at r.t. under Ar for 18 min. After a rapid dilution with Et_2O (200 ml), aq. workup, and chromatography (SiO_2, hexane), **3** (127 mg, 11%) was isolated and crystallized from hexane at −80°, m.p. 15–16°. ^{13}C-NMR (100.6 MHz): 20.48 (*q*, $CH_2{=}C{-}CH_3$); 22.34 (2*t*); 27.49 (3*q*, $(CH_3)_3C$); 28.81 (2*t*); 32.42 (*s*, $(CH_3)_3C$); 48.03 (*d*, C(4)); 56.04 (*s*, C(1)); 117.02 (*t*, $C{=}CH_2$); 140.23 (*s*, $C{=}CH_2$); 202.01 (*d*, CHO). For R_f, t_R, IR, ^{1}H-NMR and MS, *cf.* [1b].

For the data of **2** see [1c].

Kinetic Experiments. From cyanocob(III)alamin (64 mg, 0.1 mol-equiv.) the catalyst was prepared according to [1d]. To this catalyst in AcOH (7 ml) and activated granular Zn (305 mg, 10 mol-equiv.) were added 99 mg of **2** or **3** in AcOH (2 ml). The green[3]) suspension was stirred in the dark at r.t. under Ar. From this mixture were removed 0.75-ml aliquots during intervals of 5, 10, 20, 30, and 60 min and 2, 2.75, and finally 5.5 h. Each aliquot was diluted in Et_2O (25 ml), filtered, and then neutralized with aq. $NaHCO_3$ soln. The aliquots were analyzed by GC for product and reactant content. Data in *Table 1* and *2*. For anal. and spectroscopical data of **2**, **4**, **7**, **9**, and **10**, see [1c], and of **5**, **6**, and **8**, see [1e].

Table 1. *Product Distributions after Treatment of* **2** *with* **1**(I) *in the Presence of Zn/AcOH*

	Time								
Yield [%]	0	5 min	10 min	20 min	30 min	1 h	2 h	2.75 h	5.5 h
2	97.9	82.1	76.3	52.5	35.9	9.1	0.6	0.8	0.5
3	–	3.3	6.0	9.0	8.1	3.1	0.2	0.2	< 0.1
4	–	0.2	0.3	0.5	0.8	1.2	1.1	1.2	1.2
5	–	4.4	8.4	17.0	25.2	39.2	46.9	44.5	45.4
6	–	5.6	7.7	14.4	20.5	33.4	36.4	36.9	38.2
7	1.1	1.3	1.5	1.7	2.2	2.9	3.2	3.5	3.3
8	–	< 0.1	< 0.1	0.1	0.3	0.35	0.35	0.4	0.4
9/10	–	0.7	0.6	0.95	1.3	1.7	1.5	2.0	1.7

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[3]) After 5–10 min stirring under Ar, the colour turned to green.

Table 2. *Product Distributions after Treatment of* **3** *with* **1(I)** *in the Presence of Zn/AcOH*

	Time								
Yield [%]	0	5 min	10 min	20 min	30 min	1 h	2 h	2.75 h	5.5 h
2	0.7	11.3	17.4	23.9	21.9	8.2	0.8	0.8	1.0
3	98.3	66.8	58.3	34.3	19.6	3.8	0.3	0.3	0.2
4	0.4	0.8	0.8	1.0	1.4	1.6	1.9	1.5	1.8
5	–	5.4	9.5	17.6	25.2	43.1	45.1	45.7	46.1
6	–	6.4	8.5	14.3	20.1	31.8	34.4	34.6	35.3
7	–	0.1	0.4	0.7	0.9	1.5	2.3	2.2	2.3
8	–	0.1	0.3	0.3	0.3	1.3	0.7	0.7	0.7
9/10	–	1.1	0.9	1.3	1.8	1.6	1.8	1.9	1.9

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[1] a) T.S. Wan, A. Fischli, *Helv. Chim. Acta* **1984,** *67,* 1883; b) T.S. Wan, A. Fischli, *ibid.* **1984,** *67,* 1461; c) P. Schönholzer, D. Süss, T.S. Wan, A. Fischli, *ibid.* **1984,** *67,* 669; d) A. Fischli, D. Süss, *ibid.* **1979,** *62,* 48; e) P. Schönholzer, T.S. Wan, A. Fischli, *ibid.* **1984,** *67,* 684.