IR.-Spektrum (in $cm^{-1}$) von $C_5H_5Co[P(OC_2H_5)_3]_2$, als Film: 3105 *m*, 2988 *ss*, 2938 *ss*, 2904 *ss*, 2762 *w*, 2735 *w*, 2718 *w*, 1735 *w*, 1480 *s*, 1458 *sh*, 1444 *s*, 1387 *ss*, 1363 *m*, 1352 *m*, 1281 *m*, 1268 *m*, 1162 *ss*, 1100 *ss*, 1035 *ss*, 986 *s*, 938 *ss*, 815 *s*, 770 *s*, 725 *s*, 650 *s*, 493 *m*.

IR.-Spektrum (in $cm^{-1}$) von $P(OC_2H_5)_3$, als Film: 2978 *s*, 2928 *s*, 1480 *s*, 1458 *sh*, 1444 *sh*, 1388 *ss*, 1362 *m*, 1290 *m*, 1265 *m*, 1161 *s*, 1098 *ss*, 1042 *ss*, 925 *ss*, 810 *m*, 770 *sh*, 740 *s*.

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# 2. Reduction of 6-Trichloromethyl-2-pyrones with Metal Hydrides and with Zinc

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(22. X. 70)

*Zusammenfassung.* Die vor kurzem beschriebenen 6-Trichlormethyl-2-pyrone wurden mit Zink und mit komplexen Metallhydriden reduziert. 6-Trichlormethylpyron (**15**) und drei an C4 verschieden alkylierte Derivate (**5**, **16** und **17**) ergaben mit Zink in Eisessig die entsprechenden 6-Methyl-2-pyrone **18**, **1**, **19** und **20**. Im Falle des 6-Trichlormethyl-4-(4'-methyl-pent-3'-en-yl)-2-pyrans (**17**) bildete sich auch 3,8,8-Trimethyl-5,6,7,8-tetrahydro-isocumarin (**21**).

Die komplexen Metallhydrid-Reduktionen wurden am Beispiel des 6-Trichlormethyl-4-methyl-2-pyron (**5**) untersucht. Mit Natriumborhydrid in Äthanol entstanden 6-Dichlormethyl-4-methyl-2-pyron (**6**, 14%) und 6,6,6-Trichlor-3-methyl-hex-3-en-1,5-diol (**7**, 37%). Mit Lithiumaluminiumhydrid in Tetrahydrofuran erhielt man 6-Chlor- (**10**, 47%) und 6,6-Dichlor-3-methyl-hexa-3,5-dien-1-ol (**9**, 19%). Für diese Hydridreduktionen wird ein Mechanismus vorgeschlagen, welcher mit den Produkten der Lithiumaluminiumdeuterid-Reduktion nicht in Widerspruch steht.

*Introduction.* The products obtained by reduction of 2-pyrones with complex metal hydrides [1] [2] [3] depend on the hydride used and on the substituents on the pyrone ring. The electrophilic sites in a 2-pyrone ring are positions 2, 4 and 6. *Grignard* reagents attack the ring in position 2 [4], whereas the hydrides usually attack

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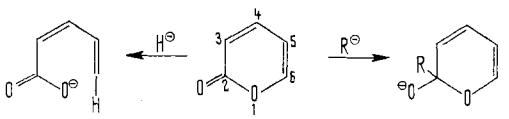
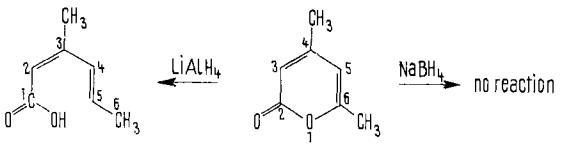
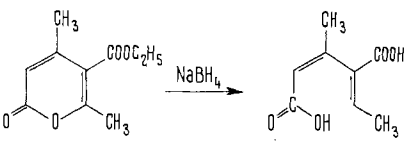
position 6 [2] [3]. In general, electron attracting groups at position 5 facilitate hydride attack at position 6 and thus the reductive ring fissure [2] [3], giving the unsaturated carboxylate, whereas alkyl groups at any position retard this reaction. For example, whereas 4,6-dimethyl-2-pyrone (**1**) (cleaved by lithium aluminium hydride to β-



methyl-sorbic acid (**2**)) is inert to sodium borohydride, the more activated ethyl isodehydroacetate (**3**) is reduced by sodium borohydride to γ-carboxy-β-methyl-sorbic acid (**4**) [3].

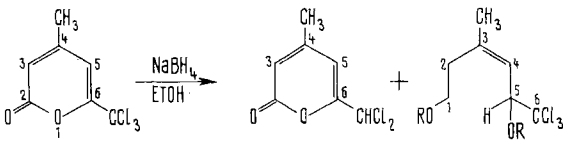


**2** **1**



**3** **4**

**I. Reduction with metal hydrides.** – In the series of recently prepared [5] 4-substituted 6-trichloromethyl-2-pyrones, we have examined the influence of the strongly electronegative, but at the same time bulky, trichloromethyl group at position 6 on the reductive opening of the 2-pyrone ring by complex metal hydrides. Reduction of 6-trichloromethyl-4-methyl-2-pyrone (**5**) (chosen as model) with two mole-equivalents of sodium borohydride in ethanol at 45–50° was exothermic and yielded two main products: 6-dichloromethyl-4-methyl-2-pyrone (**6**) and 6,6,6-trichloro-3-methyl-hex-3-ene-1,5-diol (**7**) (the latter isolated as the diacetate **8**), in 14% and 37% yields respectively, based on unrecovered (86%) starting material.

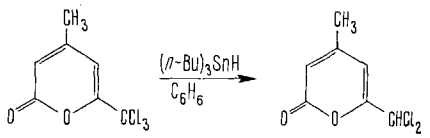


**5** **6** **7**, R = H
**8**, R = $CH_3CO$

The structures of **6**, **7** and **8** were confirmed by their IR., UV., MS. and NMR. data (see exper. part). On electron impact the diacetate **8** splits off acetic acid (most intensive peak: $M^+$–60). The NMR. signals of H–C4 ($\delta$ = 5.62/*bd* ($J$ = 8)) and H–C5 (4.78/*d* ($J$ = 8)) in the diol **7** are readily identified by the (small) allylic coupling of the former. Acetylation (to **8**) shifts the signals of H–C4 to a higher (5.45/*bd* ($J$ = 9)) and

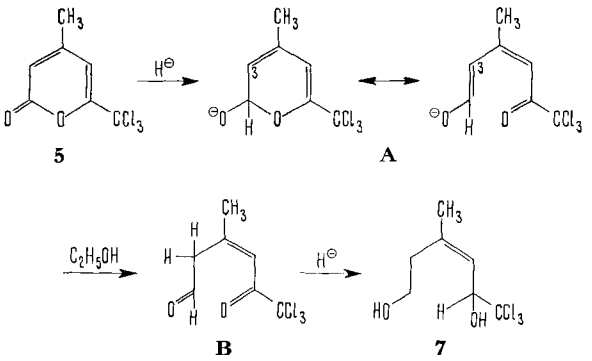
of H–C5 to a considerably lower (6.10/*d* ($J$ = 9)) field. The configuration at the double bond of **7** and **8** is unknown.

Pure **6** was prepared in 57% yield, as the only isolated product, by reduction of **5** with tributyl-tin hydride in benzene; excess reagent did not replace a second chlorine.




**5** **6**

The formation of **7** by sodium borohydride reduction of **5** can be rationalized by assuming that the strongly electronegative trichloromethyl group [6] activates positions 2 and 6 in the 2-pyrone ring but impedes sterically the approach to position 6. Thus the hydride attack is directed to C2 (carbonyl carbon) to give the conjugated



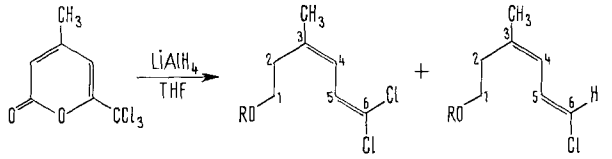

**5** **A** **B** **7**

*Reaction Scheme 1*

(The indicated conformations and configurations are not necessarily significant)

enolate ion (**A**) which, after protonation by ethanol at C3 to **B**, is reduced further at both carbonyl groups to the diol **7** (see reaction scheme 1). The minor product **6** may be formed by the (slower) direct attack of the hydride, replacing one chlorine in **5** by hydrogen.

Reduction of **5** with two moles of $LiAlH_4$ in tetrahydrofuran (THF) at room temperature gave mainly a mixture of 6,6-dichloro-3-methyl-hexa-3,5-dien-1-ol (**9**) and 6-chloro-3-methyl-hexa-3,5-dien-1-ol (**10**) in a ratio of approximately 1:2. This ratio could be varied; less $LiAlH_4$ yielded more **9** whereas a larger excess of $LiAlH_4$ gave more **10**. The yield of **9** and **10** (60–70%) was determined by NMR. in the crude



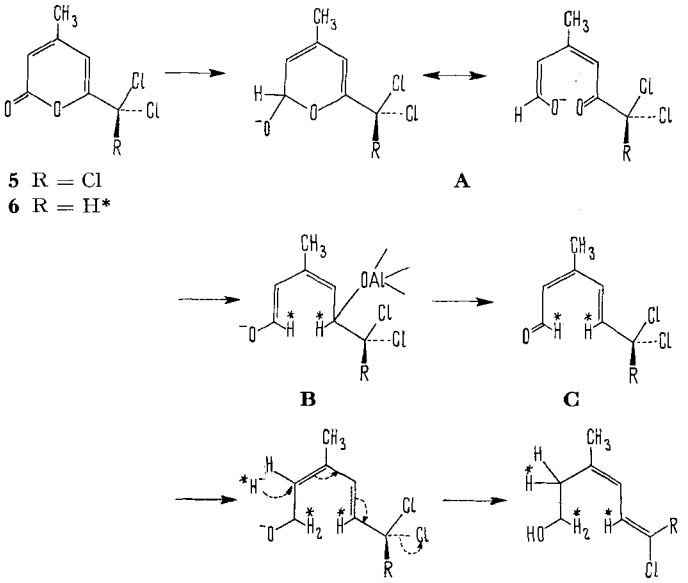

**5** **9** R = H, **11** R = $CH_3CO$ **10** R = H, **12** R = $CH_3CO$

mixture, because extensive decomposition of **9** and **10** (or **11** and **12**) occurred during distillation. The chloroalcohols **9** and **10** were separated by gas-liquid chromatography. The crude mixture of **9** and **10** was also acetylated to a mixture of **11** and **12**, which was then separated in the same way. The structures of **9**, **10**, **11** and **12** were supported by their spectroscopic properties, especially by the NMR. (see table 1) and mass spectra. The latter confirmed also the number of chlorine atoms in **9** and **10** (see exper. part). The configuration at the double bond C3=C4 in **9**, **10**, **11** and **12** is unknown; on the other hand, that at C5=C6 in **10** and **12** is *trans* ($J_{H\text{-}C5/H\text{-}C6} = 13$ Hz).

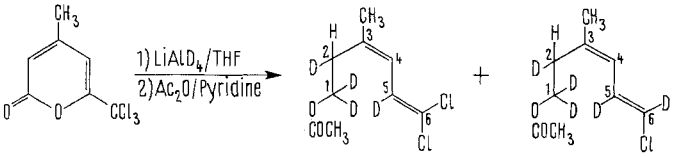
The formation of **9** and **10** can be explained by a mechanism such as that in reaction scheme 2. Just as in the sodium borohydride reduction (see above), the hydride attack at the trichloromethyl carbon of **5** (replacement of chlorine by hydrogen to give **6**) competes with the preferred hydride attack at C2 of the 2-pyrone ring (see also [1]); in one experiment traces of **6** have indeed been isolated. Subsequently reaction of both **5** and **6** follows the same path, resulting in **9** and **10** respectively. The intermediate **A** corresponds to the enolate of a vinylogous $\beta$-dicarbonyl compound. It is presumed to undergo the same eliminative $LiAlH_4$ reduction (via **B** and **C**) directly in the reduction medium as has been observed [7] for simpler enolizable $\beta$-dicarbonyl compounds, to give an allylic alcoholate (in this case **D**). Hydride attack with expulsion of chlorine by an $S_N2''$ mechanism might lead to **9** and/or **10**. Another way to explain the formation of **10** in addition to **9** is to invoke a later replacement of one chlorine by hydrogen, such as in one of the intermediates **A**, **C** or **D**. To confirm the $S_N2''$ step (**D** → **9** or **10**), the reduction of **5** was performed

*Reaction Scheme 2* (H* = H or D)

(The indicated conformations and double bond configurations were chosen as an aid to visualization and do not necessarily imply that either the products or the intermediates occur as shown)



with lithium aluminium deuteride $LiAlD_4$. The crude reaction mixture was directly acetylated and the acetates, 1-acetoxy-6,6-dichloro-1,1,2,5-tetradeutero-3-methyl-hexa-3,5-diene (**13**) and 1-acetoxy-6-chloro-1,1,2,5,6-pentadeutero-3-methyl-hexa-3,5-diene (**14**), were separated by preparative gas-liquid chromatography. The ratio

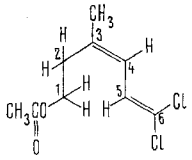
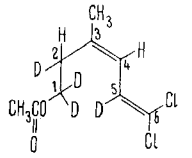
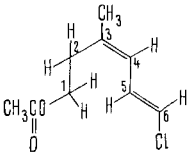
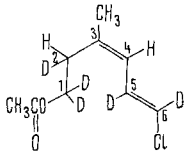



**5** **13** **14**

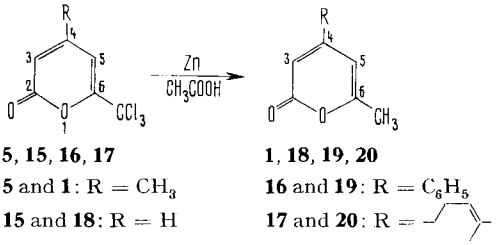
of **13** to **14** was similar to that of their hydrogen analogues **11** and **12**. The structures of **13** and **14** were confirmed by comparison of their NMR. spectra with those of **11** and **12**: The integration showed that **13** and **14** have only one proton at C2. The proton at position 4 is present in both compounds, as seen from the allylic coupling (1 Hz) in the methyl group at C3 (see table 1).

**II. Reduction by zinc in acetic acid.** – In this reduction of 6-trichloromethyl-2-pyrones all three chlorine atoms could easily be replaced by hydrogen in an exo-

Table 1. *Comparison of the NMR. Data of the Products from Reduction of* **5** *with* $LiAlH_4$ *and* $LiAlD_4$

| Product | No. | H–C1 | H–C2 | $CH_3$–C3 | H–C4 | H–C5 | H–C6 | $CH_3C(=O)$–O |
|---|---|---|---|---|---|---|---|---|
|  | **11** | 4.12/*t*<br>*J* = 7<br>2 pr. | 2.40/*t*<br>*J* = 7<br>2 pr. | 1.82/*d*<br>*J* ~ 1<br>3 pr. | 5.95/*d* × *q*<br>*J* = 11<br>& ~ 1<br>1 pr. | 6.52/*d*<br>*J* = 11<br>1 pr. | | 1.98/*s*<br>3 pr. |
|  | **13** | | 2.36/*bs*<br>1 pr. | 1.81/*d*<br>*J* ~ 1<br>3 pr. | 5.94/*bs*<br>1 pr. | | | 1.98/*s*<br>3 pr. |
|  | **12** | 4.14/*t*<br>*J* = 7<br>2 pr. | 2.37/*t*<br>*J* = 7<br>2 pr. | 1.84/*d*<br>*J* ~ 1<br>3 pr. | 5.81/*bd*<br>*J* = 11<br>1 pr. | 6.63/*d* × *d*<br>*J* = 11<br>& 13<br>1 pr. | 6.10/*d*<br>*J* = 13<br>1 pr. | 2.01/*s*<br>3 pr. |
|  | **14** | | 2.30/*bs*<br>1 pr. | 1.79/*d*<br>*J* ~ 1<br>3 pr. | 5.78/*bs*<br>1 pr. | | | 1.97/*s*<br>3 pr. |

thermic reaction. Thus the previously described [5] pyrone synthesis becomes useful for the preparation of 6-methyl-2-pyrones. The results are summarized in table 2.




**5, 15, 16, 17** **1, 18, 19, 20**

**5** and **1**: R = $CH_3$ **16** and **19**: R = $C_6H_5$

**15** and **18**: R = H **17** and **20**: R =

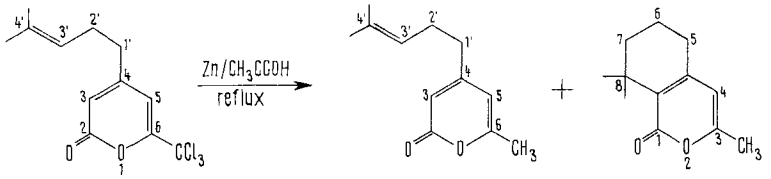
Table 2. *Reduction of 6-Trichloromethyl-2-pyrones with Zinc in Acetic Acid to 6-Methyl-2-pyrones*

| Educt No. | **5** | **15** | **16** | **17** |
|---|---|---|---|---|
| Product No. (yield) [ref.] | **1** (80%) [8] | **18** (75%) [9] | **19** (72%) | **20** (44%) [a] |

[a] Not readily purified by distillation

This reduction does not seem to be selective: with one equivalent of zinc, the product from **5** was shown by gas-liquid chromatography to consist of a mixture of starting material (**5**), 6-dichloromethyl-4-methyl- (**6**), 6-chloromethyl-4-methyl- and 6,4-dimethyl-2-pyrone (**1**).

When external heat was used in the reduction of 6-trichloromethyl-4-(4'-methyl-pent-3'-en-yl)-2-pyrone (**17**), the direct reduction product (**20**, 13% yield) was accompanied by a *Friedel-Crafts* cyclization product, namely 3,8,8-trimethyl-5,6,7,8-tetrahydro-isocoumarin (**21**) in 26% yield. The two products **20** and **21** were separated by preparative thin-layer chromatography.




**17** **20** **21**

The structures of the 6-methyl-2-pyrones **1**, **18**, **19**, **20** and **21** were supported by their spectroscopic properties (especially UV. and NMR. [5] [10]).

This work was supported by the *Schweizerischer Nationalfonds zur Förderung der wissenschaftlichen Forschung*. We are also grateful to *Sandoz AG*, Basle, for a research grant.

## Experimental Part

**General.** – The purity of all new compounds was checked by gas-liquid chromatography and thin-layer chromatography, and confirmed by their spectroscopic properties. M. p.'s were determined in a *Büchi* apparatus (system Dr. *Tottoli*) and are uncorrected. All compounds except those preparatively separated by gas chromatography gave correct elemental analyses.

The *NMR. spectra* were recorded on a *Varian* A-60 or HA-100 spectrometer and are reported in $\delta$ units, ppm/multiplicity (coupling constant in Hz), number of protons pr. (assignment[2]). The $\delta$ units correspond to tetramethylsilane ($\delta = 0$) as internal standard. Peak shapes are denoted as follows: *s* = singlet, *d* = doublet, *t* = triplet, *q* = quartet, *m* = multiplet, *b* = broad.

*Gas-liquid chromatography (GC.).* – *GC.-A:* Analytical, 1520-B (*Aerograph*) flame ionization detector, oven temperature 130°, column: 5 feet × 1/8 inch, loaded with 5% silicone SE-30 on chromosorb W-AW/DMCS, 20 ml/min nitrogen. – *GC.-B:* The same as GC.-A, but loaded with 6% polyphenyl ether (6-ring) and oven temperature 225°. – *GC.-C:* The same as GC.-A, but loaded with 5% emulphor and oven temperature 160°. – *GC.-D:* Preparative, *Aerograph* Autoprep. Model 700, thermal conductivity detector, oven temperature 220°, column 6 feet × 3/8 inch, loaded with 20% silicone SE-30 on chromosorb W, 180 ml/min helium.

*Thin-layer chromatography (TLC.):* For analytical purposes *Polygram Sil* N-HR/$UV_{254}$ 5 × 20 cm plates were used, and for preparative separations 20 × 20 cm glass plates were prepared directly before use. Each plate was covered homogeneously with a mixture of 20 g Kieselgel $PF_{254}$ containing $CaSO_4$ (*Merck*) and 40 ml distilled water, then dried for about 3 h at 120–130° and cooled to room temperature. – *TLC.-A:* Preparative, developing with hexane: acetone 4:1. – *TLC.-B:* Analytical, developing with the same solvent mixture.

**Reduction of 6-trichloromethyl-4-methyl-2-pyrone (5) [5] with sodium borohydride.** – To a magnetically stirred solution of 4.54 g (20 mmoles) **5** in 50 ml ethanol, 1.52 g (40 mmoles) of sodium borohydride were added during approximately 5 min, the mixture resulting from the exothermic reaction being kept at 45–50° with a cold water-bath; it was then stirred for 15 min at room temperature, while a white precipitate accumulated gradually. The mixture was acidified by careful addition of ice and concentrated hydrochloric acid.

The *precipitate* was filtered off, dissolved in methylene chloride, washed with water, and dried over $MgSO_4$. The solvent was removed *in vacuo*, yielding 1 g of a solid residue which was found to be (GC.-A) a mixture of two compounds in an approximate ratio of 1:1. Separation was achieved by TLC.-A. The faster moving component was the starting material (**5**, identified by its Rf value in TLC.-B and by the NMR. spectrum of the mixture). The second component was pure *6-dichloromethyl-4-methyl-2-pyrone* (**6**), m.p. 121–122° (cyclohexane); yield 0.5 g (14% (GC.-A), based on unrecovered **5**). – UV. ($C_2H_5OH$): Max. 289 (7200) nm ($\varepsilon$). – IR. ($CH_2Cl_2$): C=O 1740; C=C 1655 $cm^{-1}$. – NMR. ($CDCl_3$): 6.38/*d* (*J* = ~1), 1 pr. (H—C5)[2]); 6.32/*s*, 1 pr. (CH—C6); 6.14/*q* (*J* = ~1), 1 pr. (H—C3); 2.22/*d* (*J* = ~1), 3 pr. ($CH_3$—C4); $\delta$ (Hz).

The *aqueous filtrate* from the acidified reaction mixture was saturated with $NH_4Cl$ and extracted with 3 × 20 ml of ether, the combined extracts were washed with a saturated solution of $NaHCO_3$ and dried over $MgSO_4$. After removal of the solvent *in vacuo*, the residue (2.5 g) was distilled at 110–115°/0.03 Torr, yielding 0.9–1.4 g (20–30%) of approximately 80% pure (according to NMR.) *6,6,6-trichloro-3-methyl-hex-3-ene-1,5 diol* (**7**). Small amounts of starting material **5** were always present. – NMR. ($CDCl_3$): 5.61/*bd* (*J* = 8), 1 pr. (H—C4)[2]); 4.77/*d* (*J* = 8), 1 pr. (H—C5); 4.35/*bs*, 2 pr. (OH); 3.75/*m*, 2 pr. (2 × H—C1); 2.24/*m*, 2 pr. (2 × H—C2); 1.83/*d* (*J* = ~1), 3 pr. ($CH_3$—C3); $\delta$ (Hz).

*Acetylation of* **7**: The crude diol **7**, prepared by reduction of **5**, as described above, was dissolved in 10 ml of dry pyridine and 6 ml of acetic anhydride. The mixture was left overnight at room temperature, poured on ice and acidified with conc. hydrochloric acid. The diacetate was extracted with several portions of methylene chloride, the extract washed with saturated $NaHCO_3$ solution, dried over $MgSO_4$, and evaporated *in vacuo*. The residue (3 g) consisted mainly of one compound (GC.-B). Distillation at 93–94°/0.01 Torr gave 2.1 g (37%) of *1,5-diacetoxy-6,6,6-trichloro-3-methyl-hex-3-ene* (**8**). – IR. (neat): C=O 1740 $cm^{-1}$. – NMR. ($CDCl_3$): 6.10/*d* (*J* = 9), 1 pr. (H—C5)[2]); 5.45/*bd* (*J* = 9), 1 pr. (H—C4); 4.20/*t* (*J* = 7), 2 pr. (2 × H—C1); 2.62/*t* (*J* = 7), 2 pr. (2 × H—C2); 2.12/*s*, 3 pr. ($CH_3COO$—C5); 2.03/*s*, 3 pr. ($CH_3$—COO—C1); 1.86/*d* (*J* = ~1), 3 pr. ($CH_3$—C3); $\delta$ (Hz). – MS.: $M^+$ absent, highest peak ($M^+ - 60$) ($CH_3COOH$) 256, 258 and 260 *m/e*.

**Reduction of 6-trichloromethyl-4-methyl-2-pyrone (5) [5] with tri-(*n*-butyl)-tin hydride.** – A mixture of 5.7 g (25 mmoles) **5** and 15 g (51,5 mmoles) tri-(*n*-butyl)-tin hydride [11]

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[2]) For numbering of carbon atoms see formula in the general part.

in 70 ml of dry benzene was stirred magnetically for 16 h at room temperature, after which time GC.-A showed only one product. The mixture was then stirred with 50 ml of 10% sulfuric acid for 30 min, the organic layer was separated, washed with water, and dried over $MgSO_4$. After removal of the benzene *in vacuo*, a solid product precipitated from the oily residue; it was filtered and washed with hexane, yielding 2.8 g (57%) of *6-dichloromethyl-4-methyl-2-pyrone* (**6**), m.p. 117–120°. The NMR. spectrum of this sample was identical with that of **6** described in the preceding experiment.

**Reduction of 6-trichloromethyl-4-methyl-2-pyrone (5) [5] with $LiAlH_4$.** – To a magnetically stirred, ice cooled solution of 2.27 g (10 mmoles) **5** in 15 ml dry tetrahydrofuran was added dropwise a solution of 0.75 g (20 mmoles) $LiAlH_4$ in 20 ml of the same solvent. The mixture was stirred for 4 h at room temperature while the colour turned green at the beginning and changed to yellow green at the end. Decomposition was achieved by careful addition of ice and acidification with dilute hydrochloric acid. Most of the tetrahydrofuran was removed *in vacuo* and the residue was extracted with $3\times25$ ml ether, the extract washed with $NaHCO_3$ solution, and dried over $MgSO_4$. The ether was removed *in vacuo* giving 1.4 g (88%) of a brown residue which according to NMR. and GC.-C contained 60–70% of a mixture of **9** and **10** in an approximate ratio of 1:2. The yield of material, distilled in a bulb tube ('Kugelrohr') at 70–85°/0.02 Torr, was only 20–30%, due to extensive decomposition during distillation.

The alcohols **9** and **10** were separated by GC.-D and could then be distilled in a small bulb tube at 50–60°/0.01 Torr. The first product eluted from the GC. was *6-chloro-3-methyl-hexa-3,5-dien-1-ol* (**10**). – UV. ($C_2H_5OH$): Max. 242 (14600) nm ($\varepsilon$). – IR. ($CCl_4$): OH 3450 (broad) $cm^{-1}$. – NMR. ($CCl_4$): 6.55/*d*×*d* (*J* = 13 & 11), 1 pr. (H–C5)[2]; 6.01/*d* (*J* = 13), 1 pr. (H–C6); 5.75/*bd* (*J* = 11), 1 pr. (H–C4); 3.60/*t* (*J* = 6.5), 2 pr. (2×H–C1); 2.52/*bs*, 1 pr. (OH); 2.21/*t* (*J* = 6.5), 2 pr. (2×H–C2); 1.76/*d* (*J* = ~1), 3 pr. ($CH_3$–C3); $\delta$ (Hz). – MS: $M^+$ 146, 148 *m/e*.

The second product eluted from the GC. was *6,6-dichloro-3-methyl-hexa-3,5-dien-1-ol* (**9**). – UV. ($C_2H_5OH$): Max. 253 (9500) nm ($\varepsilon$). – IR. ($CCl_4$): OH 3370 (broad) $cm^{-1}$. – NMR. ($CCl_4$): 6.50/*d* (*J* = 11), 1 pr. (H–C5)[2]; 5.92/*bd* (*J* = 11), 1 pr. (H–C4); 3.64/*t* (*J* = 7), 2 pr. (2×H–C1); 2.91/*bs*, 1 pr. (OH), 2.28/*t* (*J* = 7), 2 pr. (2×H–C2); 1.76/*d* (*J* = ~1), 3 pr. ($CH_3$–C3); $\delta$ (Hz). – MS.: $M^+$ 180, 182, 184 *m/e*.

*Acetylation of* **9** *and* **10**. A part (0.4 g) of the crude mixture of **9** and **10**, acetylated with 2 ml of dry pyridine and 1 ml of acetic anhydride as described above, yielded 0.38 g (~60%) of the crude acetate mixture **11** and **12**. The two compounds were separated by GC.-D and found, by NMR., to be purer than the alcohols **9** and **10**. Distillation of the acetate mixture was, as in the case of the alcohols, accompanied by decomposition.

**12**: NMR. ($CCl_4$): 6.63/*d*×*d* (*J* = 13 & 11), 1 pr. (H–C5)[2]; 6.10/*d* (*J* = 13), 1 pr. (H–C6); 5.81/*bd* (*J* = 11), 1 pr. (H–C4); 4.14/*t* (*J* = 7), 2 pr. (2×H–C1); 2.37/*t* (*J* = 7), 2 pr. (2×H–C2); 2.01/*s*, 3 pr. ($CH_3COO$–); 1.84/*d* (*J* = ~1), 3 pr. ($CH_3$–C3); $\delta$ (Hz).

**11**: NMR. ($CCl_4$): 6.52/*d* (*J* = 11), 1 pr. (H–C5)[2]; 5.95/*d*×*d* (*J* = 11 & ~1), 1 pr. (H–C4); 4.12/*t* (*J* = 7), 2 pr. (2×H–C1); 2.40/*t* (*J* = 7), 2 pr. (2×H–C2); 1.98/*s*, 3 pr. ($CH_3COO$–); 1.82/*d* (*J* = ~1), 3 pr. ($CH_3$–C3); $\delta$ (Hz).

The *ratio of* **9** *and* **10**, as determined by GC.-C, could be varied by changing the reaction conditions and using different amounts of $LiAlH_4$ in the reduction of **5**; a) When 1 mole-equivalent of **5** was reduced with 1 mole-equivalent of $LiAlH_4$ for only one hour at room temperature, the ratio of **9**:**10** was approximately 4:1; b) When 1 mole-equivalent of **5** was reduced with 4 mole-equivalents of $LiAlH_4$ for 5 h at 55°, the ratio of **9**:**10** was approximately 1:4.

*Reduction of* **5** *[5] with* $LiAlD_4$. Reduction of 1.14 g (5 mmoles) **5** with 0.40 g (10 mmoles) $LiAlD_4$ was performed as described for the reduction of **5** with $LiAlH_4$. The crude reaction products were acetylated with 3 ml of acetic anhydride and 6 ml of dry pyridine, yielding 0.85 g (~70%) of a crude mixture of **13** and **14**. The two acetates were separated by GC.-D and their NMR. spectra recorded.

a) *1-Acetoxy-6-chloro-1,1,2,5,6-pentadeutero-3-methyl-hexa-3,5-diene* (**14**): NMR. ($CCl_4$): 5.78/*bs*, 1 pr. (H–C4)[2]; 2.30/*bs*, 1 pr. (H–C2); 1.97/*s*, 3 pr. ($CH_3COO$); 1.79/*d* (*J* = ~1), 3 pr. ($CH_3$–C3); $\delta$ (Hz).

b) *1-Acetoxy-6,6-dichloro-1,1,2,5-tetradeutero-3-methyl-hexa-3,5-diene* (**13**): NMR. ($CCl_4$): 5.94/*bs*, 1 pr. (H–C4)[2]; 2.36/*bs*, 1 pr. (H–C2); 1.98/*s*, 3 pr. ($CH_3COO$); 1.81/*d* (*J* = ~1), 3 pr. ($CH_3$–C3); $\delta$ (Hz).

**Reduction of 6-trichloromethyl-2-pyrones [5] with zinc in acetic acid.** – a) *Reduction of 6-trichloromethyl-4-methyl-2-pyrone* (**5**). To a solution of 1.14 g (5 mmoles) **5** in 25 ml of acetic acid were added portionwise 2 g (~30 mmoles) of zinc powder. The mixture became hot and was subsequently stirred magnetically for 2 h at room temperature. The precipitated zinc chloride and the excess zinc were filtered off and most of the acetic acid was removed *in vacuo*. To the residue 20 ml of water were added and the product was extracted with 3×15 ml of ether, the extract washed with $NaHCO_3$ solution and dried over $MgSO_4$. The ether was removed *in vacuo* and the residue distilled at 60–70°/0.05 Torr in a bulb tube, yielding 0.5 g (80%) of *4,6-dimethyl-2-pyrone* (**1**), m.p. 47–48° (hexane) (lit. [8]: m.p. 48–49°). – NMR. ($CDCl_3$): 5.88/*bs*, 2 pr. (H—C3, H—C5)[2]); 2.21/*d* (*J* = ~1), 3 pr. ($CH_3$—C6); 2.13/*d* (*J* = ~1), 3 pr. ($CH_3$—C4); $\delta$ (Hz).

b) *Reduction of 6-trichloromethyl-2-pyrone* (**15**). The reduction of 1.07 g (5 mmoles) **15** with 2 g (~30 mmoles) of zinc, as described above, gave 0.41 g (75%) of *6-methyl-2-pyrone* (**18**) b.p. 80–85°/20 Torr (bulb tube). – UV. ($C_2H_5OH$): Max. 297 (5700) nm ($\varepsilon$). – IR. (neat): C=O 1730; C=C 1640 $cm^{-1}$. – NMR. ($CCl_4$): 7.17/*d*×*d* (*J* = 10 & 6), 1 pr. (H—C4)[2]); 5.95/*bd* (*J* = 10), 1 pr. (H—C3); 5.92/*bd* (*J* = 6), 1 pr. (H—C5); 2.20/*d* (*J* = ~1), 3 pr. ($CH_3$—C6); $\delta$ (Hz).

c) *Reduction of 6-trichloromethyl-4-phenyl-2-pyrone* (**16**). Reduction of 0.289 g (1 mmole) **16** with 0.4 g (~6 mmoles) of zinc in 10 ml acetic acid as described before, but heated under reflux for 2 h, gave 0.135 g (72%) of a solid residue, which crystallized from hexane to give pure *6-methyl-4-phenyl-2-pyrone* (**19**), m.p. 88–90°. – UV. ($C_2H_5OH$): Max. 226 (19810), 266 (13490), 313 (1110) nm ($\varepsilon$). – IR. ($CHCl_3$): C=O 1715; C=C 1640 $cm^{-1}$. – NMR. ($CDCl_3$): 7.55/*m*, 5 pr. (ArH—C4)[2]); 6.37/*bs*, 2 pr. (H—C3; H—C5); 2.32/*d* (*J* = ~1), 3 pr. ($CH_3$—C6); $\delta$ (Hz).

d) *Reduction of 6-trichloromethyl-4-(4'-methyl-pent-3'-enyl)-2-pyrone* (**17**): Reduction of 0.59 g (2 mmoles) **17** with 0.8 g (~12 mmoles) zinc in 10 ml acetic acid as described for a) gave 0.17 g (44%) *6-methyl-4-(4'-methyl-pent-3'-enyl)-2-pyrone* (**20**), b.p. 105–110°/0.1 Torr (bulb tube). This product, however, contained some starting material, as seen by NMR.

A pure sample of **20** was obtained in the following experiment: Reduction of 1.18 g (4 mmoles) **17** with 1.6 g (~24 mmoles) of zinc in 20 ml of acetic acid was performed as above, but heated under reflux for 2.5 h. Bulb tube distillation (with extensive decomposition) at 150–200°/0.1 Torr gave 0.38 g of a brown oil. This crude distillate consisted mainly of two compounds with very similar Rf values. They could be separated by TLC.-A.

The faster moving compound was *3,8,8-trimethyl-5,6,7,8-tetrahydro-isocoumarin* (**21**), yield 0.20 g (26%), b.p. 105–110°/0.02 Torr (bulb tube). – UV. ($C_2H_5OH$): Max. 292 (7300) nm ($\varepsilon$). – IR. (neat): C=O 1710; C=C 1653 $cm^{-1}$. – NMR. ($CDCl_3$): 5.62/*bs*, 1 pr. (H—C4)[2]); 2.37/*m*, 2 pr. (2×H—C5); 2.12/*d* (*J* ~ 1), 3 pr. ($CH_3$—C3); 1.60/*m*, 4 pr. (2×H—C6; 2×H—C7); 1.38/*s*, 6 pr. (2×$CH_3$—C8); $\delta$ (Hz).

The slower moving compound was *6-methyl-4-(4'-methyl-pent-3'-en-yl)-2-pyrone* (**20**), yield 0.1 g (13%), b.p. 115–120°/0.07 Torr (bulb tube). – UV. ($C_2H_5OH$): Max. 293 (6100) nm ($\varepsilon$). – IR. (neat): C=O 1730; C=C 1650 $cm^{-1}$. – NMR. ($CDCl_3$): 5.77/*bs*, 2 pr. (H—C3; H—C5)[2]); 5.06/*m*, 1 pr. (H—C3'). 2.30/*m*, 4 pr. (2×H—C1'; 2×H—C2'); 2.19/*d* (*J* = ~1), 3 pr. ($CH_3$—C6); 1.70/*s*, 3 pr. ($CH_3$—C4'); 1.60/*s*, 3 pr. ($CH_3$—C4'); $\delta$ (Hz).

e) *Reduction of 6-trichloromethyl-4-methyl-2-pyrone* (**5**) *with one mole-equivalent of zinc*. Reduction of 1.14 g (5 mmoles) **5** in 10 ml of acetic acid with 0.37 g (5 mmoles) of zinc, with stirring at room temperature for only 1 hour, gave, after usual working up, 0.7 g of an oil which, according to GC.-A, was a mixture of 4 compounds, three of which were identified by their retention time, in comparison with authentic samples, as 4,6-dimethyl-2-pyrone (**1**), 6-dichloromethyl-4-methyl-2-pyrone (**6**) and the starting material (**5**). The 4th component had a retention time between those of **1** and **6**, and was thus assumed to be 6-chloromethyl-4-methyl-2-pyrone.

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## 3. Über die Struktur eines neuartigen Indolalkaloids, des Talbotins

141. Mitteilung über Alkaloide [1]

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Herrn Dr. *O. Isler,* Basel, zum 60. Geburtstag gewidmet

(2. XI. 70)

*Summary.* From the leaves of the African Apocynacea *Pleiocarpa talbotii Wernham* a novel indole alkaloid, talbotine, $C_{21}H_{24}N_2O_4$, has been isolated. Talbotine (**1**) contains a secondary $N_{(b)}$-atom and a cyclic hemiacetal group. Catalytic hydrogenation leads to 19,20-dihydrotalbotine (**6**), hydrogenation in the presence of formaldehyde gives $N_{(b)}$-methyl-19,20-dihydrotalbotine (**8**). In the presence of sodium methoxide and methanol, **1** is converted into the lactone **12** and the methyl ester **13**. In these reactions carbon 17 is lost as formic acid. These data, together with the analyses of the NMR. spectra of talbotine and its derivatives as well as the interpretation of the various types of the mass spectral fragmentation, lead to formula **1** for the alkaloid.

Dehydrogenation of talbotine methyl ether (**3**) with palladium and maleic acid gives the $\beta$-carboline derivative **26**. The $N_{(b)}$-methiodide of the latter is converted into $N_{(b)}$-methyl-talbotine methyl ether on reduction with sodium borohydride. From these data as well as from the analyses of NMR. and IR. spectra the complete relative stereochemistry of talbotine could be derived. Application of the *Horeau* method to the nitrogen atom b of the methyl ether **3** on the one hand and to the hydroxyl group on C17 in $N_{(b)}$-methyl-19,20-dihydrotalbotine (**8**) on the other hand gives consistent results and establishes *S* configuration of centre 15.

Die Blätter der bisher chemisch noch nicht untersuchten, in Westafrika heimischen Apocynacee *Pleiocarpa talbotii Wernham* enthalten mehrere Indolalkaloide. Die vorliegende Arbeit betrifft das Talbotin, das Hauptalkaloid der Droge, für welches die Strukturformel **1** abgeleitet wird. Talbotin steht in keiner nahen Verwandtschaft mit den zahlreichen, verschiedenen Typen angehörenden Indolalkaloiden aus anderen *Pleiocarpa*-Species (vgl. [2]).

Talbotin liess sich aus den getrockneten Blättern in einer Ausbeute von 0,9% isolieren. Das Alkaloid, $C_{21}H_{24}N_2O_4$ ($M$ = 368), Smp. 212°, $[\alpha]_D = -200°$ ($CHCl_3$), besitzt ein Indolchromophor; in 0,05 N alkoholischer Salzsäure erfährt die Absorption eine hypsochrome Verschiebung um einige nm, was charakteristisch ist für Py-tetra-