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NEW ROUTES TO 1,1-DICHLORO-4-METHYL-1,3-PENTADIENE

ISTVÁN BITTER, LÁSZLÓ TŐKE*, ZOLTÁN BENDE, ÉVA KÁRPÁTI-ÁDÁM
RUDOLF SOÓS[a]

Department of Organic Chemical Technology, Technical University,
H-1521 Budapest, Hungary
[a]Chinoin Pharmaceutical and Chemical Works, Ltd. H-1780 Budapest,
POB 49, Hungary

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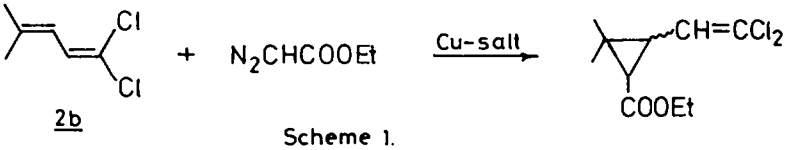
Abstract - 1,1,1-trichloro-2-hydroxy-4-methyl-pentene-3 (1b) was chlorinated to afford tri- and tetra-chlorinated compounds 2,3,4. Compounds 2 and 3 were transformed by reductive dechlorination into 1,1,-dichloro-4-methyl-1,3-pentadiene (2b). Another route starting from the same alcohol or its isomer was also developed.

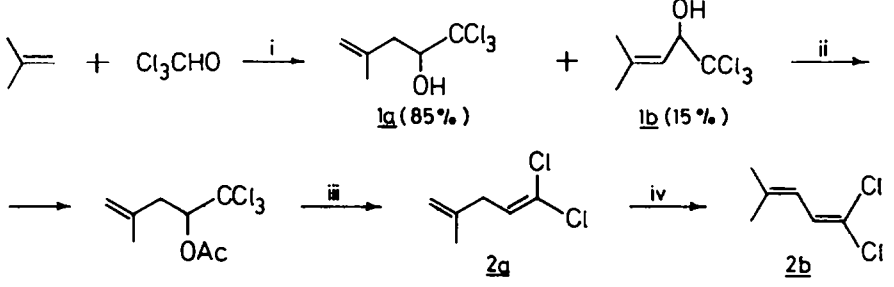
Pyrethroids exhibit a high degree of activity as insecticides while showing a low mammalian toxicity. The most potent representatives belong to the derivatives of 2,2-dimethyl-3-(2,2-dihalovinyl)-cyclopropanecarboxylates which have greater photostability than the natural pyrethroids[1]. Since the discovery of permethrin, 1-phenoxybenzyl-3-(2,2-dichlorovinyl)-2,2-dimethylcyclopropanecarboxylate[2], great efforts have been made for developing a commercially feasible synthesis of the acid moiety of permethrin[3]. Originally Farkas et al.described the preparation of ethyl-3-(2,2-dichlorovinyl)-2,2-dimethylcyclopropanecarboxylate by the reaction of ethyl diazoacetate and 1,1-dichloro-4-methyl-1,3-pentadiene (2b)[4] (Scheme 1).



2b

Scheme 1.

Since cyclopropanation can be readily accomplished with continuous process in large scale the success ot this procedure depends on the availability of diene 2b. In the past decade a great number of methods have been described for the synthesis of this compound. The first attempt was made by Farkas who started from isobutylene and chloral reaching only 35 % overall yield in a four step synthesis[4] (Scheme 2).



Scheme 2.

i: $AlCl_3$ (1a:1b 6:1); ii: Ac_2O + pyridin; iii: Zn, AcOH; iv: pTSA

Chloral and isobutylene are inexpensive starting materials therefore we tried to utilize them in new entries in order to avoide some disadvantages of Farkas's procedure.

RESULTS AND DISCUSSION

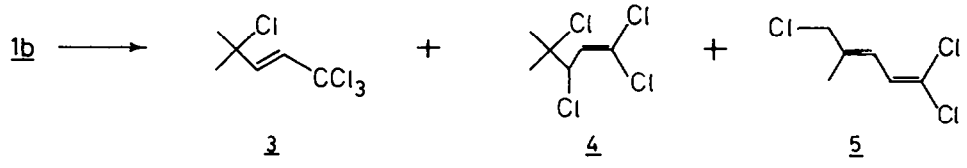
I. In an attempt to replace the OH group by chlorine in compound 1b the crystalline sample was treated with inorganic acid chloride resulting in formation of a mixture of at least five compounds. The molar ratios of the compounds were found to change during the chlorination process and the changes continued even after starting material 1b was comsumed. The three main components of the mixture were separated on preparative scale by combination of fractional distillation, in vacuo, and recrystallization. Structures 3,4 and 5 were assigned to these three components on the basis of analytical, IR, ^1H, ^{13}C-NMR and high resolution mass spectral[5] data. Table 1. summarizes the data of the chlorinations.

Table 1. Chlorination of 1b

Entry	Acid Chloride	Solvent	Total yield of 3+4+5 (%)	Ratio[d] (3+4):5	Procedure[e]
1[a]	$SOCl_2$	$(CH_2)_2Cl_2$	93	8o : 2o	A
2[a]	$SOCl_2$	$(CH_2)_2Cl_2$ or benzene	85	7o : 3o	B
3[a]	PCl_3	$(CH_2)_2Cl_2$	75	65 : 35	A
4[a]	PCl_5	$(CH_2)_2Cl_2$	7o	6o : 4o	B
5[a]	$POCl_3$	$(CH_2)_2Cl_2$ or toluene	7o	5 : 95	A
6	$POCl_3$	DMF	9o	3o : 7o	B
7[b]	$POCl_3$	$(CH_2)_2Cl_2$	75	25 : 75	A
8[c]	$ClSO_3H$	$(CH_2)_2Cl_2$	5o	3o : 7o	A

a=5 mol % DMF catalyst was used; b=5 mol % DMF catalyst and equimolar TEBAC was used (This experiment was needed for the elucidation of the mechanism. See ref.7); c=without DMF; d=The ratio is given for the time at which 1b was completely consumed; e=See Experimental section.

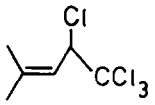
The product ratio was found to be very sensitive to the reaction conditions, mainly to the nature of the acide chloride, but also to the quantity of DMF catalyst. The reaction pathway is illustrated by Scheme 3.



3 4 5

Scheme 3

On heating 3 suffers irreversible rearrangement affording 4. In DMF catalysed reactions two further products 6 and 7 could be detected. GC-MS experiments[5] provided evidences for the structure of 6 which quantity is less then 1 %. Compound 7 could not be isolated in pure form as it easily transforms into 5 (details on the transformation see ref.7) but its structure was unequivocally determined by NMR spectrocopic methods.



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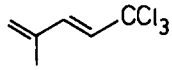

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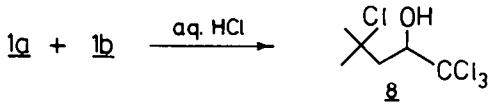
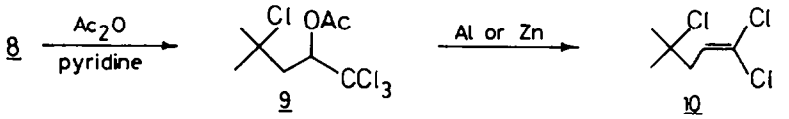
We attampted the reductive dechlorination of compounds 3,4 and 5 in order to get 1,1-dichloro-4-methyl-1,3-pentadiene (2b). Catalytic hydrogenation in the presence and absence of base, metal powder (Zn, Al, Fe) and chemical reductions /$(MeO)_2P(O)H$, $Na_2S_2O_4$/ have been tried. All methods failed in case of 5 but, luckily, the major compound 3 and its isomer 4 readily underwent reductive elimination. The simplest way of getting pure 1,3-diene 2b without 1,4-isomer 2a contamination is the reduction of the mixture of 3,4 and 5 with iron powder in protic media.

II. The Prins reaction of chloral and isobutylene results in the mixture of 1a and 1b in very good yield. 1a can be isomerised into 1b in the presence of 1 % p-toluene sulfonic acid at 80-120°C affording a mixture of 85 % 1b and 15 % 1a[6]. Although pure 1b can be gained by recrystallization from hexane it was accompanied by 25-30 % loss of the material. Anyhow, we decided to develop a new synthetic strategy in order to avoid isomerization during the whole synthesis. First HCl addition was carried out with the 1a, 1b isomer mixture resulting in single compound 8 in quantitative yield (Scheme 4).



Scheme 4.

Chlorination of 8 with usual inorganic acid chlorides ($SOCl_2$, $POCl_3$ etc.) failed therefore the hydroxyl group had to be acetylated (by standard method) so that the dichlorovinyl group could be smoothly formed (Scheme 5).



Scheme 5.

We have tried the reductive elimination of 9 with the methods mentioned previously but only Al and Zn powder proved to be effective and selective concerning the CCl_3 group. In case of Al powder trace of Hg^{2+} salt was necessary to promote the reaction which was accompanied by deacetylation process giving back 5-8 % of 8.

We expected that the preformed C=C double bond of 8 would affect on the direction of the HCl elimination contributing the exclusive formation of the

conjugated 1,3-diene 2b. Exactly, the elimination with ethanolic sodium ethylate procceeded as it was expected affording exclusively 1,1-dichloro-4-methyl-1,3-pentadiene (2b).

EXPERIMENTAL

The ^{1}H and ^{13}C NMR spectra were recorded in $CDCl_3$, in the PFT mode (16 K date points for the FID) at 99.6 and 25.0 MHz, respectively, with internal deuterium lock, at ambient temperature using a JEOL FX-100 multinuclear spectrometer. The chemical shifts were determined on the δ scale with tetramethyl silane as internal standard. IR spectra were recorded by a SPECORD IR 75 spectrophotometer. Gaschromatography was performed on a Hewlett-Packard 5750 instrument equipped with a flameionization detector and a 2m stainless steel, 3 % QF1 column.

Chlorination of 1,1,1-trichloro-2-hydroxy-4-methyl-pentene-3 (1b)

General procedures A) To the stirred mixture consisting of 20.35 g (0.1 mol) 1b, 80 cm^3 solvent and 0.4 cm^3 (5 mmol) DMF 0.11 mol inorganic acid chloride was added at 50-60°C over a period of 20 minutes. After the addition was completed the mixture was kept boiling of 1-1.5 h, then cooled to room temperature and washed successively with portions of 100 cm^3 water, sodium carbonate solution (of about 10 %) and saturated aqueous calcium chloride and finally dried over anhydrous calcium chloride. After evaporation of the solvent the remaining product was fractionated under reduced pressure.

B) To the mixture of 0.11 mol acid chloride in 15 cm^3 DMF or in 80 cm^3 solvent containing 0.4 cm^3 (5 mmol) DMF, 20.35 g (0.1 mol) of 1b or solution of 0.1 mol of 1b in 30 cm^3 solvent was added over 20 minutes at 30-35°C or 50-60°C, respectively. The mixture was warmed up and was kept stirring in oil bath of 100°C for 1-1.5 h. The mixture was worked up as in A) but when DMF had been used as solvent the mixture was first poured in 200 cm^3 water and extracted with 80 cm^3 benzene. Mixtures of products containing 3 or 5 as major components were collected in the boiling range of 90-96° or 95-104°C/18 torr, respectively. Materials of analytical purity were obtained for 3 by crystallization at -30°C and subsequent recrystallization from n-hexane (mp.: 39-40°C, bp.: 92-93°C/18 torr), and for 5 by repeated fractionation of the product mixture containing the highest amount of 5 (Table 1, entry 5, bp.: 101-2°C/18 torr).

1,1,1,4-Tetrachloro-4-methyl-pentene-2 (3)

IR (neat) /cm^{-1}/: 3000, 1460, 1380, 1285, 1085, 960, 850, 775, 730.
^{1}H NMR: 1.73 (s,6,CH_3), 6.27 (d,1,J=14.6Hz=CH-CCl(CH_3)$_2$), 6.43 (d,1,J=14.6 Hz, =CH-CCl_3).
^{13}C NMR: 32.2 (CH_3), 65.3 ((CH_3)$_2$C-Cl), 94.0 (CCl_3), 132.4, 137.8 (CH=CH).
MS: m/e=220(4, M^+), 185 (66), 149(32), 113(37), 103(15,M-CCl_3), 77(100, (CH_3)$_2$CCl).

1,1,5-Trichloro-4-methyl-1,3-pentadiene (5)

IR (neat) /cm^{-1}/: 2850, 1560, 1440, 1250, 900, 820.
^{1}H NMR: 1.85 (d,3,J=2Hz, CH_3), 4.03(s,2,CH_2Cl) 6.19 (dq,1,J=10 Hz, 2Hz, CH_3-C=CH), 6.55 (d,1,J=10Hz, -CH=CCl_2).
^{13}C NMR: 15.4 (CH_3), 51.5 (CH_2Cl), 123.1, 124.6 (=CH-CH=), 132.4 (CCl_2), 137.5 (CH_3-C=).
MS: m/e 184 (42,M^+), 149 (86), 113(67), 77(100).
To produce a sample of pure 4, compound 3 was transformed by thermal rearrangement to 4 (140-150°C, 6 h) and the resulting product was fractionated (bp.:97-8°C/18torr).

1,1,3,4-Tetrachloro-4-methyl-pentene-1 (4)

IR (neat) /cm^{-1}/: 2980, 1610, 1450, 1390, 1370, 1110, 850, 775, 740
^{1}H NMR: 1.70 (s,6,CH_3), 4.70 (d,1,J=9.5Hz, CHCl), 6.12 (d,1,J=9.5Hz, =CH).
^{13}C NMR: 28.8, 30.4 (CH_3), 65.5 (CHCl), 69.8 ((CH_3)$_2$CCl), 126.1 (=CCl_2), 126.5 (=CH).
MS: m/e=220 (2, M^+), 185(19), 149(8), 77(100).

Mixture containing 67-75 % 7 and 33-25 % 3 was obtained according to method B) (Table 1, entry 2). The reaction was not carried to completion, 20 minutes after the addition of the reactants the mixture was worked up; the fraction of boiling range 88-92°C/18 torr was collected and the majority of 3 was removed by crystallization at -30°C.

1,1,1-Trichloro-4-methyl-2,4-pentadiene (7)

(From the mixture of 70 mol % 7 and 30 mol % 3)
^{1}H NMR: 1.87 (s,3,CH_3), 5.21 (s,2,H_2C=), 6.10 (d,1,J=15 Hz, ⟩CH=), 6.71 (d,1,J=15 Hz, =HC-CCl_3).

^{13}C NMR: 18.5 (CH_3), 94.8 (CCl_3), 122.6 ($H_2C=$), 132.6, 133.9 (-CH=CH-), 138.9 (=C-CH_3).
MS: The same as that of 5.

1,1-Dichloro-4-methyl-1,3-pentadiene (2b) from the mixture of 3,4,5.

To a stirred solution of the chlorinated product (85 g, 90 % of 3 + 4 and 10 % of 5, by GLC) in 400 cm^3 benzene and 200 cm^3 methanol, iron powder (26.8 g, 0.48 gatom) was added and refluxed for 2 h. The methanol was distilled out of the resultant mixture, after cooling the precipitated iron (II) chloride was filtered off and washed with benzene. The filtrate was washed with 2 x 150 cm^3 of diluted HCl, water, saturated $NaHCO_3$ solution and brine subsequently. After drying over Na_2SO_4 the solvent was evaporated and the residue distilled in vacuo to give 2b (37 g, 60 % b.p.: 65-68°C/18 torr.)
No 1,4-diene (2a) was detected by GLC.

1,1,1,4-Tetrachloro-2-hydroxy-4-methyl-pentene (8)

To 100 cm^3 of conc.HCl 1,1,1-trichloro-2-hydroxy-4-methyl-pentene-4 (1a) or 1,1,1-trichloro-2-hydroxy-4-methyl-pentene-3 (1b) or their mixture (50.9 g, 0.25 mol) was added dropwise under vigorous stirring at 25-35°C. Almost immediately white solid was precipitated. Stirring was continued for 3 h, the material was filtered off, washed with water and dried on air to give 8 (58.8 g, 98 % m.p.: 79-81°C).

^1H NMR ($CDCl_3$): 1.71 (s,6, $(CH_3)_2C$); 2.02 (dd, 1, CH_2, J_{gem}=15Hz, J=8Hz), 2.56 (dd,1,CH_2, J=1, 5Hz); 4.43 (dd, 1, CHOH); 3, 11 (s,1,OH)
^{13}C NMR ($CDCl_3$): 32.2 and 34.1 (CH_3), 46.9 (CH_2); 68.7 (CCl), 80.4 (C-OH); 103.6 (CCl_3). Anal.Calcd. for $C_6H_{10}OCl_4$ (239.96) C 30.02; H 4.17; Cl 59.16; Found: C 30.20; H 4.25; Cl 59.21.

1,1,1,4-Tetrachloro-2-acetoxy-4-methyl-pentane (9)

To a solution of 9 (48.0 g, 0.2 mol) in 50 cm^3 pyridine acetic anhydride (25.5 g, 0.25 mol) was added dropwise at 25°C and stirred for 4 h at 60°C. After standard work up the material was extracted with 2 x 100 cm^3 of benzene, dried over Na_2SO_4. Solvent was evaporated and the remaining oil distilled in vacuo to give 10 (48.0 g, 85 %, b.p.: 126-128°C/18 torr).
IR (film): 1760 cm^{-1} (C=O)
^1H NMR ($CDCl_3$): 1.70 (s,6, $(CH_3)_2$), 2.10 (dd, 1, CH_2) 2.61 (dd,1,CH_2); 2.15 (s, 3,CH_3CO), 5.05 (dd,1,CHO).

1,1,4-Trichloro-4-methyl-pentene-1 (10)

To a solution of 9 (28.2 g, 0.1 mol) and NH_4Cl (5.0 g) in 80 cm^3 methanol zinc powder (7.2 g, 0.11 gatom) was added at reflux temperature under stirring. After 2h additional boiling the resultant mixture was filtered, the filtrate was combined with diluted HCl, extrated with 2 x 100 cm^3 of ethylene chloride. The organic layer was washed with water, aquous $NaHCO_3$, dried over Na_2SO_4, and concentrated then distilled in vacuo to give 10 (15.0 g 80 %, b.p.: 74-76°C/18 torr).
^1H NMR ($CDCl_3$): 1.60 (s,6,$(CH_3)_2$); 2.62 (d,2,CH_2, J=7Hz), 6.08 (t,1,CH=).

1,1-Dichloro-4-methyl-1,3-pentadiene (2b) from 10.

10 (18.75 g 0.1 mol) was refluxed in 80 cm^3 of ethanolic sodium ethylate (2.5 g Na, 0.11 gatom) for 2-3 h, the endpoint of elimination was checked by GLC. After standard work up the residue was distilled to give 2b (12.0 g 80 % b.p.: 58-61°C/12 torr). No 1,4-diene (2b) was detected by GLC.

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