Synthesis of 7-Chloro- and 7-Hydroxybicyclo[5.2.2]undeca-1(9),10-dienes

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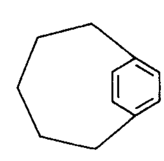
7-Chlorobicyclo[5.2.2]undeca-1(9),10-diene (**2a**) and the 7-hydroxy derivative **2b** were prepared by oxidative decarboxylation of tricyclo[5.2.2.$0^{1,7}$]undec-10-ene-8-carboxylic acids **6a** and **6b** followed by acid-catalyzed isomerization.

We have been interested in strained bicyclic molecules possessing bridgehead double bonds such as bridgehead dienes,[3] and [*n*]paracyclophanes.[4] Recently, Bickelhaupt and we succeeded in the characterization of [5]paracyclophane **1** at low temperature by ^{1}H NMR and UV spectra.[5] However, attempts to isolate **1** and its derivatives met with difficulties because of their lability.[6] As an extension of these works, we are interested in bicyclo[5.2.2]undeca-1(9),10-dienes **2** (X = leaving group) because **2** can be envisaged as 6,7-dihydro[5]paracyclophane system which formally lacks *the third* (bridgehead) double bond of **1**. Also, **2** may well serve as viable precursors to [5]paracyclophane **1**. This paper describes the synthesis of two derivatives, chloride **2a** and alcohol **2b**.



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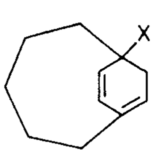
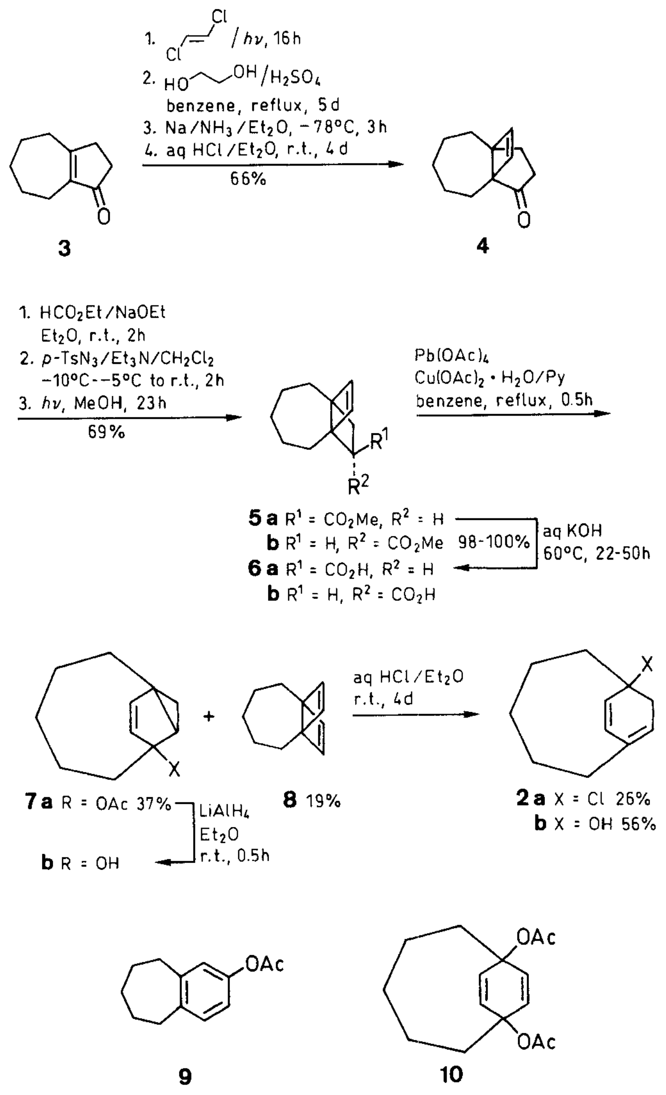


2 a X = Cl
b X = OH

The synthesis is based on carbocation rearrangement of tricyclo[5.2.2.$0^{1,7}$]undec-10-ene-8-carboxylic acids ([5.2.2]-propellenecarboxylic acids) (**6a**) and (**6b**) by oxidative decarboxylation.[7,8] The acids **6a** and **6b** were prepared by ring contraction of [5.3.2]propellenone **4** which was prepared from the bicyclic enone **3**.[9] Oxidative decarboxylation of **6a** with lead(IV) acetate in the presence of copper(II) acetate gave cyclopropylcarbinyl-type acetate **7a** as the major product (37%) along with the propelladiene **8**[10] (19%). Similar reaction with **6b** gave essentially identical results. It should be noted that, in contrast with **6a** and **6b**, the higher homologue, [6.2.2]propellenecarboxylic acids, gave allylcarbinyl-type acetate and [6]paracyclophane.[7] A similar tendency has been observed in the oxidative decarboxylation of [*n*.2.2]propellanecarboxylic acids (*n* = 4–6) where cyclopropylcarbinyl-type products were formed in preference to allylcarbinyl-type with decreasing the ring size (*n*) of the propellane framework.[8] When the oxidation was carried out without copper(II) acetate, **7a** was given in 26% yield while propelladiene **8** was not obtained. It has been shown that copper(II)-catalyzed lead(IV) decarboxylation gives alkenes via oxidation of alkyl radical intermediates by copper(II) (oxidative elimination).[11] Instead, small amounts of byproducts, 2-acetoxy-6,7,8,9-tetrahydro-5*H*-benzocycloheptene (**9**) and 1,7-diacetoxybicyclo[5.2.2]undeca-8,10-diene (**10**), which are probably formed by further oxidation of **7a**,[12] were isolated in 8% and 4% yields, respectively.



Scheme

Finally, the cyclopropylcarbinyl-type product **7a** was converted to the dienes **2a** and **2b** by acid-catalyzed isomerization. Thus, reduction of **7a** with lithium aluminum hydride gave alcohol **7b** in 98 % yield. Treatment of **7b** with hydrochloric acid afforded **2a** and **2b** in 26 % and 56 % yield, respectively.

Tricyclo[5.3.2.$0^{1,7}$]dodec-11-en-8-one ([5.3.2]Propellenone) (4):
A solution of the enone **3**[9] (21.5 g, 0.143 mmol) in (*E*)-1,2-dichloroethylene (200 mL) was irradiated under N_2 with a 500 W high pressure mercury lamp in a Pyrex vessel for 16 h.The excess olefin was removed in vacuo and the residue was dissolved in benzene

(500 mL). Ethylene glycol (100 mL) and H_2SO_4 (5 mL) was added and the mixture was heated at reflux for 5 d with removal of H_2O with a Dean-Stark trap. The mixture was diluted with H_2O (500 mL) and the aqueous layer was extracted with benzene (300 mL). The combined organic phase was washed with $NaHCO_3$ solution (200 mL) and H_2O (200 mL) and then dried ($MgSO_4$). After removal of the solvent, the residue was dissolved in anhydr. Et_2O (400 mL) and NH_3 (1.4 L) was condensed at − 78 °C. Na (10.0 g, 0.43 mol) was added portionwise and the mixture was stirred for 3 h. Excess sodium was destroyed by NH_4Cl and the NH_3 was allowed to evaporate. The residue was dissolved in H_2O (800 mL) and Et_2O (500 mL) and the aqueous layer was extracted with Et_2O (200 mL). The combined organic layer was washed with H_2O (200 mL) and dried ($MgSO_4$). The residue after evaporation of the solvent was dissolved in Et_2O (1 L) and 1.2 N HCl (200 mL) was added. The two phase mixture was stirred at r.t. for 4 d. The aqueous phase was extracted with Et_2O (100 mL) and the combined organic layer was washed with $NaHCO_3$ solution (100 mL) and H_2O (300 mL) and then dried ($MgSO_4$). The solvent was evaporated and the residue was chromatographed on silica gel with Et_2O/petroleum ether (bp 40–60 °C) (3:97) eluent to give **4** as a colorless oil; yield 16.5 g (66 %).

MS: *m*/*z* (%) = 176 (M^+, 94), 133 (84), 105 (98), 91 (100).

IR (neat): ν = 3020, 1720, 1065, 735 cm^{-1}.

^1H NMR (CCl_4): δ = 1.10–2.40 (m, 13 H), 2.60–3.10 (m, 1 H), 6.03 (d, 1 H, *J* = 2 Hz), 6.23 (d, 1 H, *J* = 2 Hz).

Semicarbazone; mp 215–216 °C.

$C_{13}H_{19}N_3O$	calc.	C 66.92	H 8.21	N 18.01
(233.3)	found	67.02	8.21	18.10

Methyl Tricyclo[5.2.2.0^{1,7}]undec-10-ene-8-carboxylates (5a) and (5b):

To a stirred suspension of 50 % NaH (3.27 g, 68.2 mmol) and EtOH (0.3 mL) in Et_2O (140 mL), a mixture of **4** (12.0 g, 68.0 mmol) and ethyl formate (7.57 g, 102 mmol) was added dropwise. The mixture was stirred at r.t. for 2 h while another Et_2O (150 mL) was added to affect efficient stirring. H_2O (600 mL) was added and the aqueous layer was washed with Et_2O (200 mL) and acidified with 6 N HCl. The oil separated was taken up in Et_2O (700 mL) and the ether layer was washed with H_2O (200 mL) and dried ($MgSO_4$). Evaporation of the solvent gave the corresponding hydroxymethylene derivative (14.0 g) as a yellow solid [IR (KBr): ν = 3600–2300, 1680, 1600 cm^{-1}]. To a solution of the above ketone and Et_3N (13.9 g, 138 mmol) in CH_2Cl_2 (53 mL) was added *p*-TsN_3[13] (13.8 g, 70.0 mmol) at − 10 to − 5 °C. The mixture was stirred for 2 h while being slowly warmed up to r.t. A solution of KOH (4.6 g, 82.6 mmol) in H_2O (50 mL) was added and the mixture was stirred for 30 min. The organic layer was separated and washed with KOH solution (300 mL) and H_2O (700 mL) and then dried ($MgSO_4$). Removal of the solvent in vacuo gave a yellow oil [17 g; IR (neat): ν = 2060, 1650 cm^{-1}] which was dissolved in MeOH (250 mL). The solution was irradiated with a 500 W high pressure mercury lamp in a Pyrex vessel for 23 h. The solvent was evaporated and the residue distilled under reduced pressure (88–92 °C/2 Torr) to give a mixture of **5a** and **5b** in a ratio of 3:2: yield 9.67 g (69 %). The epimers were separated by silica gel chromatography with Et_2O/petroleum ether (bp 40–60 °C) (2:98) as eluent.

5a (*exo* isomer):

MS: *m*/*z* (%) = 206 (M^+, 7), 147 (51), 105 (74), 91 (100).

IR (neat): ν = 3020, 1730, 1320, 1205, 1190, 1170, 780, 740 cm^{-1}.

^1H NMR (CCl_4): δ = 1.00–2.30 (m, 12 H), 2.76 (dd, 1 H, *J* = 9, 7 Hz), 3.52 (s, 3 H), 5.96 (d, 1 H, *J* = 2 Hz), 6.20 (d, 1 H, *J* = 2 Hz).

$C_{13}H_{18}O_2$	calc.	C 75.69	H 8.80
(206.3)	found	75.29	8.93

5b (*endo* isomer):

MS: *m*/*z* (%) = 206 (M^+, 6), 147 (46), 105 (32), 91 (100).

IR (neat): ν = 3020, 1730, 1350, 1335, 1190, 1165, 760 cm^{-1}.

^1H NMR (CCl_4): δ = 0.90–2.10 (m, 11 H), 2.23 (dd, 1 H, *J* = 12, 6 Hz), 2.75 (dd, 1 H, *J* = 8, 6 Hz), 3.61 (s, 3 H), 6.22 (s, 2 H).

$C_{13}H_{18}O_2$	calc.	C 75.69	H 8.80
(206.3)	found	75.36	8.95

Tricyclo[5.2.2.0^{1,7}]undec-10-ene-8-carboxylic Acids (6a) and (6b):

A mixture of **5a** or **5b** and 2 % aq KOH was stirred at 60 °C for 22 h (for **5a**) or 50 h (for **5b**). The solution was washed with Et_2O (200 mL), acidified with 6 N HCl, and extracted with Et_2O (200 mL). The extract was washed with H_2O (100 mL), dried ($MgSO_4$), and the solvent evaporated to give acid **6a** or **6b** with 98 or 100 % yield which was recrystallized from petroleum ether (bp 40–60 °C).

6a (*exo* isomer); mp 73–74 °C.

MS: *m*/*z* (%) = 192 (M^+, 14), 148 (33), 105 (53), 92 (50), 91 (100).

IR (KBr): ν = 3600–2300, 1690, 1320, 1240, 910, 790, 780, 750 cm^{-1}.

^1H NMR ($CDCl_3$): δ = 1.10–2.40 (m, 12 H, d at 2.04, *J* = 8 Hz), 2.99 (t, 1 H, *J* = 8 Hz), 6.11 (d, 1 H, *J* = 2 Hz), 6.28 (d, 1 H, *J* = 2 Hz), 8.30–9.80 (br s, 1 H).

$C_{12}H_{16}O_2$	calc.	C 74.97	H 8.39
(192.3)	found	74.99	8.45

6b (*endo* isomer); mp 90–91 °C.

MS: *m*/*z* (%) = 192 (M^+, 5), 148 (21), 147 (23), 105 (56), 92 (45), 91 (100).

IR (KBr): ν = 3600–2300, 1690, 1325, 1295, 1230, 1215, 940, 770, 760 cm^{-1}.

^1H NMR ($CDCl_3$): δ = 0.80–2.10 (m, 11 H), 2.05 (dd, 1 H, *J* = 13, 8 Hz), 2.90 (dd, 1 H, *J* = 8, 5 Hz), 6.23 (s, 2 H), 7.80–9.60 (br s, 1 H).

$C_{12}H_{16}O_2$	calc.	C 74.97	H 8.39
(192.3)	found	74.84	8.44

Oxidative Decarboxylation of 6a and 6b with Lead Tetraacetate:

A solution of **6a** and **6b** (3:2 mixture, 5.00 g, 26.3 mmol), $Cu(OAc)_2 \cdot H_2O$ (2.64 g, 13.2 mmol), and pyridine (1.04 g, 13.2 mmol) in benzene (200 mL) was heated at reflux. To this solution was added $Pb(OAc)_4$ (21.0 g, 47.3 mmol) portionwise. The mixture was heated for 0.5 h, filtered, and the filtrate was washed with 1 N HCl (100 mL), $NaHCO_3$ solution (100 mL) and H_2O (100 mL) and dried ($MgSO_4$). The solvent was evaporated and this residue was chromatographed on silica gel. Elution with petroleum ether (bp 40–60 °C) gave propelladiene **8**[10] (733 mg, 19 %) and with Et_2O/petroleum ether (3:97) acetate **7a** (2.00 g, 37 %). A control experiment with either **6a** or **6b** resulted in almost identical results.

7-Acetoxytricyclo[5.2.2.0^{1,9}]undec-10-ene (**7a**):

MS: *m*/*z* (%) = 206 (M^+, 2), 164 (35), 146 (51), 131 (74), 118 (46), 108 (42), 107 (100).

IR (neat): ν = 3030, 1730, 1360, 1240, 1040, 1025, 780, 735, 710 cm^{-1}.

^1H NMR ($CDCl_3$): δ = 0.60–0.80 (m, 2 H), 0.80–2.40 (m, 14 H, s at 1.98), 5.36 (d, 1 H, *J* = 6 Hz).

^{13}C NMR ($CDCl_3$): δ = 21.1 (t), 22.1 (q), 24.6 (d), 26.5 (t), 28.1 (t), 31.4 (t), 32.2 (t), 34.2 (t), 39.6 (t), 95.5 (s), 129.2 (d), 139.4 (d), 170.6 (s).

$C_{13}H_{18}O_2$	calc.	C 75.69	H 8.80
(206.3)	found	75.86	8.92

Reaction of a mixture of **6a** and **6b** as described above without using $Cu(OAc)_2$ gave unreacted **6a** and **6b** (1.58 g, enriched by **6b**), **7b** (986 mg, 26 %), 2-acetoxy-6,7,8,9-tetrahydro-5*H*-benzocycloheptene (**9**) (307 mg, 8 %), and 1,7-diacetoxybicyclo[5.2.2]undeca-8,11-diene (**10**) (177 mg, 4 %). (Yields are based on the acids consumed).

9; mp 62–63 °C.

MS: *m*/*z* (%) = 204 (M^+, 13), 162 (100).

IR (KBr): ν = 1760, 1605, 1590, 1220, 1200, 1165, 910, 815 cm^{-1}.

^1H NMR ($CDCl_3$): δ = 1.50–2.00 (m, 6 H), 2.24 (s, 3 H), 2.75 (br d, 4 H, *J* = 10 Hz), 6.78 (d, 1 H, *J* = 8 Hz), 6.81 (s, 1 H), 7.08 (d, 1 H, *J* = 8 Hz).

$C_{13}H_{16}O_2$	calc.	C 76.44	H 7.90
(204.3)	found	76.25	7.89

10; mp 107–108 °C.

MS: *m*/*z* (%) = 264 (M^+, 2), 204 (17), 162 (100), 107 (29).

IR (KBr): ν = 1730, 1250, 1220, 1020, 875, 790 cm^{-1}.

^{1}H NMR ($CDCl_3$): δ = 1.30–1.80 (m, 6 H), 1.90–2.20 (m, 10 H, s at 1.98), 6.12 (s, 4 H).

$C_{15}H_{20}O_4$ calc. C 68.16 H 7.63
(264.3) found 67.91 7.58

7-Chloro- and 7-Hydroxybicyclo[5.2.2]undeca-1(9),10-dienes (2a) and (2b):

To a suspension of $LiAlH_4$ (40 mg, 1.05 mmol) in Et_2O (2 mL) was added a solution of **7a** (247 mg, 1.19 mmol) in the same solvent (5 mL). The mixture was stirred at r. t. for 0.5 h before the addition of H_2O (1 mL) followed by 1 N HCl (1 mL). The aqueous layer was extracted with Et_2O (20 mL) and the extract was washed with H_2O (10 mL) and dried ($MgSO_4$). Evaporation of the solvent gave alcohol **7b** as a waxy solid.

MS: *m*/*z* (%) = 164 (M^+, 28), 121 (31), 108 (41), 107 (100).

IR (KBr): ν = 3300, 3040, 1140, 1080, 1060, 1045, 780, 730 cm^{-1}.

^{1}H NMR ($CDCl_3$): δ = 0.60 (d, 2 H, *J* = 5 Hz), 0.8–2.4 (m, 12 H), 5.10 (d, 1 H, *J* = 6 Hz), 5.84 (d, 1 H, *J* = 6 Hz).

^{13}C NMR ($CDCl_3$): δ = 20.6 (t), 26.0 (d), 26.6 (t), 28.3 (t), 31.6 (t), 32.2 (t), 34.0 (s), 43.8 (t), 87.0 (s), 132.9 (d), 138.8 (d).

$C_{11}H_{16}O$ calc. C 80.44 H 9.83
(152.2) found 80.22 9.76

To an ether extract (40 mL) of reduction product derived from **7a** (886 mg, 4.74 mmol) was added 1 N HCl (20 mL) and the two phase mixture was stirred at r.t. The organic phase was separated and washed with $NaHCO_3$ (10 mL) and H_2O (10 mL). After being dried ($MgSO_4$), the solvent was evaporated. Flash chromatography with Et_2O/petroleum ether (bp 40–60 °C) (20 : 80) eluent afforded chloride **2a** (227 mg, 26 %) as a colorless oil and alcohol **2b** (441 mg, 56 %) as a waxy solid.

2a:

MS: *m*/*z* (%) = 184 (M^+, 8), 182 (26), 147 (38), 125 (42), 91 (100).

IR (neat): ν = 3020, 975, 770, 740 cm^{-1}.

^{1}H NMR ($CDCl_3$: δ = 0.70–2.60 (m, 11 H), 2.88 (br d, 1 H, *J* = 16 Hz), 5.66 (dd, 1 H, *J* = 7, 3 Hz), 5.96 (AB quart, 2 H, *J* = 10 Hz).

$C_{11}H_{15}Cl$ calc. C 72.32 H 8.28
(182.7) found 72.41 8.43

2b:

MS: *m*/*z* (%) = 164 (M^+, 27), 121 (30), 108 (44), 107 (100).

IR (KBr): ν = 3300, 3040, 1100, 1045, 860, 750 cm^{-1}.

^{1}H NMR ($CDCl_3$): δ = 0.80–2.70 (m, 13 H), 5.65 (dd, 1 H, *J* = 7, 3 Hz), 5.85 (AB quart, 2 H, *J* = 10 Hz).

^{13}C NMR ($CDCl_3$): δ = 27.1 (t), 30.3 (t), 30.9 (t), 34.8 (t), 39.0 (t), 45.6 (t), 76.1 (s), 120.0 (d), 129.3 (d), 136.7 (d), 138.5 (s).

$C_{11}H_{16}O$ calc. C 80.44 H 9.83
(152.2) found 80.04 9.97

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