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SMALL RING COMPOUNDS—XLI

CYCLOBUTENE CYCLOADDITIONS; SYNTHESIS AND REACTIVITY IN THE BICYCLO[2.2.0]HEXAN-2-ONE SERIES

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Abstract—Cyclobutene, prepared by base-induced elimination from tosyloxycyclobutane **19** undergoes cycloaddition with ethyl propiolate in the presence of $AlCl_3$ to provide ethyl bicyclo[2.2.0]hex-2-ene-2-carboxylate **20**. This cycloadduct at room temperature and in the presence of $AlCl_3$ undergoes forbidden ring opening into ethyl cyclohexa-1,3-diene-2-carboxylate **21**. The cycloaddition of cyclobutene with dichloroketene provides 3,3-dichlorobicyclo[2.2.0]hexan-2-one **24** and after reductive halogen removal the *endo* 3-chloro bicyclo[2.2.0]hexan-2-one **28** (the first study of this strained system). However, further dechlorination of **28** results in rearrangement and fragmentation reactions.

Due to its ring strain the bicyclo[2.2.0] hexane system is a challenging one; it was first obtained in 1960[1] and much of its chemistry has been explored (for a review see Ref. 2). However, in spite of different attempts the bicyclo[2.2.0]hexan-2-one **1** has not been described as far as we know. Most of the reactions which might be thought to lead to this strained cyclobutanone derivative failed because of the occurence of rearrangement or fragmentation reactions.

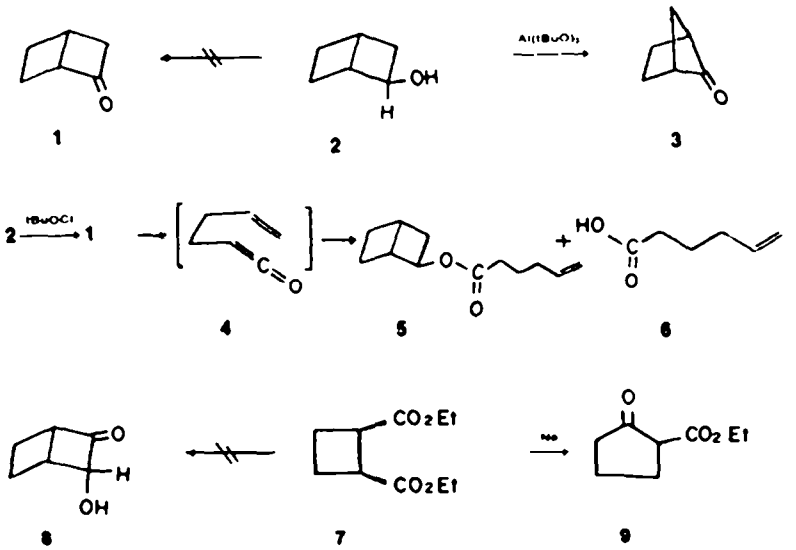
Thus for instance, McDonald and Reineke have reported that Oppenauer oxidation of *exo* bicyclo[2.2.0]hexan-2-ol **2** resulted in an oxidative rearrangement leading mainly to the bicyclo[2.1.1]hexan-5-one **3** and not to **1**.[3]

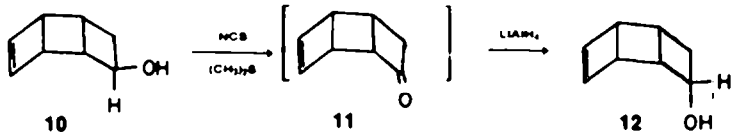
On the other hand, t-butyl hypochlorite oxidation of **2** at room temperature gave *exo*-bicyclo[2.2.0]hex-2-yl-5-hexenoate **5** and 5-hexenoïc acid **6**, presumably resulting from ring opening of **1** and trapping of the intermediate ketene **4** by alcohol **2** and water, respectively. When performed at 0°, the oxidation products exhibited infrared absorption at 1782cm^{-1} suggesting the presence of a cyclobutanone moiety, but attempts to collect the expected bicyclo[2.2.0]hexan-2-one **1** resulted in the complete disappearance of the characteristic IR band.[3]

Finally, attempted acyloin ring closure on *cis*-1,2-dicarbethoxycyclobutane **7** did not give the expected α-hydroxy ketone **8** but led, by an apparent fragmentation reaction to the 2-carbethoxycyclopentanone **9**.[4]

Recently, the lability of the bicylo[2.2.0]hexan-2-one system **1** has been illustrated by Paquette who reported the conversion of the *exo*-cyclobutanol **10** into the *endo*-isomer **12** from the direct hydride reduction of the oxidation product of **10** by N-chlorosuccinimide and dimethylsulfide, without isolation and description of the hypothetical intermediate ketone **11**.[5]

In order to test new pathway to **1** taking into account recent attractive reports of the literature concerning the reactions of non-activated alkenes, we have investigated the Lewis acid catalyzed cycloaddition of acetylenic esters[6–11] and the cycloaddition of reactive ketenes[14–16] with cyclobutene. The achievement of certain of these goals is reported in the present paper which includes a





new and convenient preparation of cyclobutene and its cycloaddition reactions with ethyl propiolate and dichloroketene which enable us to prepare and describe for the first time the 3-chloro and 3,3-dichloro derivatives of the bicyclo[2.2.0] hexan-2-one **1**.

Preparation of cyclobutene

The literature contains many different reports of preparation of cyclobutene but, none of these methods appears to be of practical importance for the ready preparation of pure amounts of this small ring compound. Thus, cyclobutene has been obtained (a) by thermolysis of cyclobutyldimethylamine oxide[39-41] and of cyclobutylammonium hydroxide[40-42] (8 steps from malonate esters, 2.0% overall yield); (b) by pyrolysis of the cycloadducts of dimethylacetylenedicarboxylate with cyclooctatriene[43-45] (30–32% overall yield) or with cyclooctatetraene[46-48] (34–39% overall yield); (c) by photolysis of butadiene[49,50] (30% yield); (d) by lead tetra acetate oxidation[51] of cyclobutylcarboxylic acid[52] (11.8% overall yield); (e) by trialkylphosphite fragmentation of 1,2-cyclobutylthiocarbonate[53] (68% yield based on *cis*-1,2-dihydroxycyclobutane; (f) by ring expansion of cyclopropylcarbene[54] or from cyclobutylidene.[55,56]

In most cases, cyclobutene is contaminated with butadiene, bicyclobutane or methylenecyclopropane. So for instance, an other alternate pathway involving the base induced ring expansion of cyclopropylmethyltosylate **13** with potassium t-butoxide in dimethylsulfoxide leads to a 1:1 mixture of cyclobutene **14** and methylenecyclopropane **15**.[47]

In a search of a convenient source of cyclobutene, we have found that, contrary to **13**, the cyclobutyltosylate **19** can provide, in good yields, cyclobutene **14** free of its isomeric impurities.[58]. The procedure takes advantage of Robert's conversion of cyclopropylcarbinol into cyclobutanol.[59] Thus, cyclopropylcarbinol **16** which is commercially available or obtained readily from the hydride reduction of cyclopropanecarboxylic acid[60] or ester undergoes, upon treatment by aqueous hydrochloric acid at reflux for 3 hr, ring enlargement into cyclobutanol **17** in 92% yield (while after refluxing for 100 mn, a 72% yield only is reported by Robert[59]) contaminated with 3% of 3-butenol **18**.

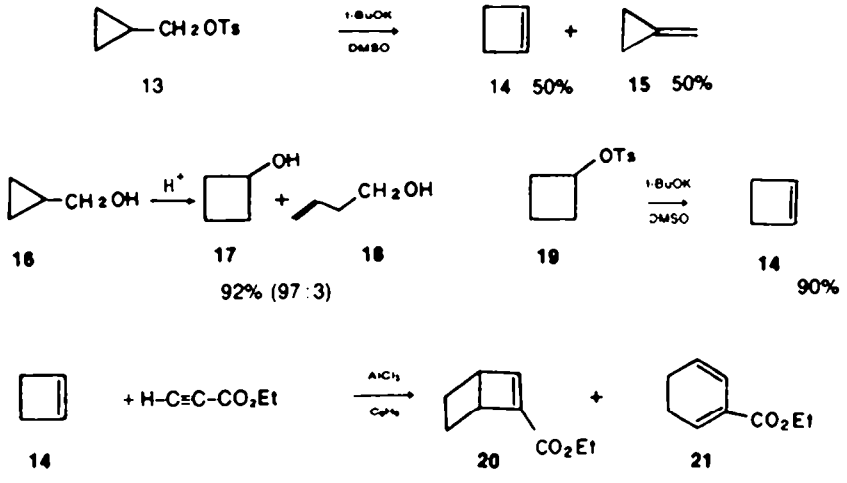
Then the tosyloxycyclobutane **19** is obtained by conventional means through the reaction of the mixture of **17** and **18** with tosylchloride in pyridine. After usual work-up, the pale yellow residue treated under high vacuum at room temperature for 3 hr gives the practically pure tosylate **19** in about 90% yield; the lack of 3-buten-1-ol derivatives is shown by the lack of olefinic protons in the NMR spectra of **19**. Upon treatment with potassium t-butoxide in dimethylsulfoxide at 70° the tosylate **19** undergoes base induced elimination to give cyclobutene **14**. The yield based on pure 1,2-dibromocyclobutane obtained by adding bromine to the collected cyclobutene (b.p. 2°) in a dry ice-cooled trap is 86–90%, the overall yield from cyclopropylcarbinol **16** is 70–75%.

The tosyloxycyclobutane **19** is quite stable, it can be prepared in large amounts, kept in the fridge to provide a convenient source of this gaseous small ring compound.[58]

Cycloaddition of cyclobutene with ethyl propiolate

It has been reported recently by Snider that acetylenic esters undergo in high yields Lewis acid catalyzed stereospecific[2 + 2]cycloaddition reactions with unactivated 1,2-disubstituted alkenes; while monosubstituted alkenes give mixtures of ene adducts and cycloadducts.[6-13] We have tested such a cycloaddition with cyclobutene itself.

As expected, cyclobutene **14** undergoes aluminium chloride catalyzed[2 + 2]cycloaddition with ethylpropiolate in benzene to provide ethyl bicyclo[2.2.0]hex-2-ene-2-carboxylate **20**, a potential precursor of **1**, along with ethyl cyclohexa-1,3-diene-2-carboxylate **21**. But the reaction is quite slow; thus, after 3 days at room temperature and atmospheric pressure **20** and **21**are obtained in 20 and 2% yield, respectively. While after 7 days, **21** is obtained alone in 30% yield from the ring opening of **20**.



The same treatment of cyclobutene **14** with ethyl-propiolate and $AlCl_3$ performed in sealed tube at room temperature gives, after 5 days cyclohexadiene **21** (35%) along with a mixture of the Diels and Alder adducts **22** and **23** of diene **21** with ethyl propiolate (10%). After 17 days the adducts **22** and **23** are formed in 85% yield; they are separated by liquid chromatography and identified from their NMR spectra.

Due to steric considerations and the nature of the cycloaddition[6] the junction of the fused bicyclic ester **20** is *cis*; so, the ring opening of **20** into **21** is disrotatory and forbidden by the symmetry rules. Although it is known that ring strain lowers the temperature of the thermal ring opening of bicyclo[2.2.0]alkenes to 195°,[61] it is somewhat surprising that, in the presence of $AlCl_3$, such a rearrangement occurs at room temperature.

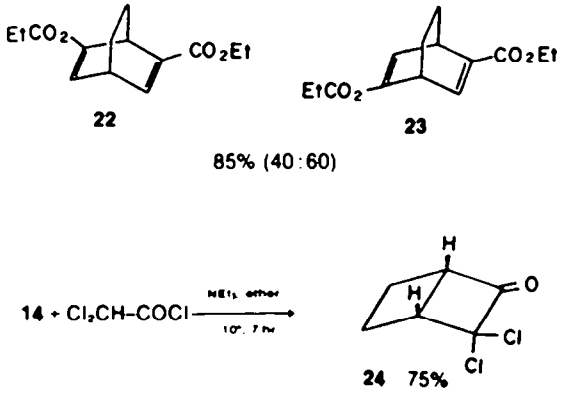
Whatever it may be, this Lewis acid catalyzed cycloaddition of cyclobutene with acetylenic esters does not appear to be of practical importance to enter the bicyclo[2.2.0]hexane system.

Cycloaddition of cyclobutene with dichloroketene. Synthesis of 3,3-*dichlorobicyclo*[2.2.0]*hexan-2-one*

More reactive than ketene itself, dichloroketene undergoes cycloaddition to various olefinic compounds to yield 2,2-dichlorocyclobutanones;[32] then, the reductive halogen removal provides readily cyclobutanones,[27-30] for which many useful transformations have been recently reported.[14-26,62]

The preparation of dichloroketene from dichloroacetyl chloride and triethylamine in the presence of cyclobutene resulted in the[2 + 2]cycloaddition products **24**.

The optimum conditions for this cycloaddition appear to be the slow addition of triethylamine to a dilute solution[31] of dichloroacetyl chloride and cyclobutene in ether at −10°. In these conditions 3,3-dichlorobicyclo[2.2.0]hexan-2-one **24** was obtained in 75% yield after purification by liquid chromatography allowing us to describe for the first time this system. Its IR spectrum in CCl_4 is characterized by a sharp carbonyl band at 1815 cm^{-1} and its NMR spectrum by two multiplets at 3.96 (H) and 3.38 ppm (H) for the two bridgehead protons and by a multiplet at 2.9–2.0 ppm for the four other protons of the fused cyclobutane ring.



Reduction of 3,3-*dichlorobicyclo*[2.2.0]*hexan-2-one. Synthesis of* 3-*chlorobicyclo*[2.2.0]*hexan-2-one*

Usually, chlorine atoms are easily removed from 2,2-dichlorocyclobutanones by zinc dust in acetic acid or tri-n-butyltin hydride to produce monochloro or non-halocyclobutanones, selectively.[21,25-33,63] Moreover, it has been shown that 7,7-dichlorobicyclo[3.2.0]hept-2-en-6-one **25** is reduced to yield first the *endo*-monochloro isomer **26** and then the cyclobutanone **27**.[29,30]

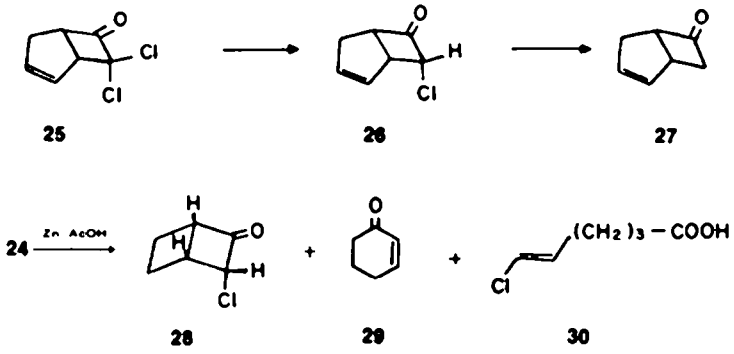
With the object of preparing the parent system **1** the chlorine atoms removal of the 3,3-dichlorobicyclo[2.2.0]hexan-2-one **24** has been attempted by means of zinc in acetic acid, silver-promoted zinc in methanol and tri-n-butyltin hydride reductions as also by palladium catalyzed hydrogenation.

Thus, treatment of a solution of dichlorocyclobutanone **24** in glacial acetic acid with excess zinc dust affords, after 15 min at 0° as shown by gas chromatography, a mixture of monochloroketone **28** (25%) of 2-cyclohexenone **29** (3%) and of 6-chloro-5-hexenoïc acid **30** (5%); while at room temperature, the mixture of products **28**, **29** and **30** is obtained in 10, 3 and 20% yields, respectively.

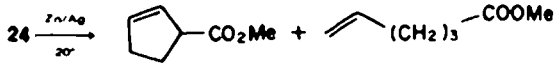
Dechlorination with zinc dust performed in a mixture of acetic acid and water at room temperature following a known procedure[18] gives only the acid **30** in 55% yield.

Hence, the reduction of **24** enables us to describe the 3-chlorobicyclo[2.2.0]hexan-2-one **28**. Its IR spectrum in CCl_4 exhibits a multiplied carbonyl band at 1792, 1802, 1815 and 1836 cm^{-1} and its NMR spectrum a multiplet at δ 4.32 ppm for the proton geminal to chlorine, a multiplet at 2.88 ppm for the two bridgehead protons and a multiplet at 2.40–1.85 ppm for the four other protons of the fused cyclobutane ring, in agreement with an expected endo-configuration for the chlorine atom of **28**.[29,30,64,65] The chlorocylobutanone **28** appears to be thermally stable in the gas phase since it can be purified by GLC at 140°.

With silver-promoted zinc dust in methanol (zinc-silver couple according to ref.[66], the dichloroketone **24**

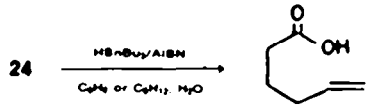


undergoes rearrangement into methyl cyclopentene-3-carboxylate **31**[67] and methyl 5-hexenoate **32**[68] in 50 and 5% yields, respectively.



31 50% **32** 5%

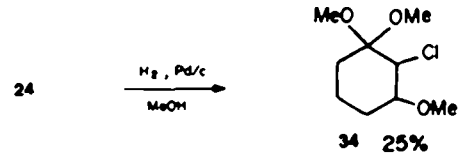
The reductive removal of chlorines from α,α-dichloroketones with tri-n-butyltin hydride[27,30-33,63] is known to proceed in the presence of azo bis(isobutyronitrile), via free radicals[69]; this hydride reacts with **24** in benzene or cyclohexane at reflux for 30 min or at room temperature for 12 h to give, after aqueous work-up, the 5-hexenoic acid **33** exclusively.



33

Treatment of **24** with hydrogen and palladium dispersed over carbon in methanol according to Ref. 24, gives besides the chloroketal **34** in 25% yield, a mixture of non-identified products.

It could be expected that removal of chlorines from the ketal **35** and subsequent deketalisation of **36** could offer a way to **1**, but unfortunately upon treatment with ethanol in the presence of pyridinium p-toluene-sulfonate,[70] **24** undergoes ring opening into the dichloroester **37**.

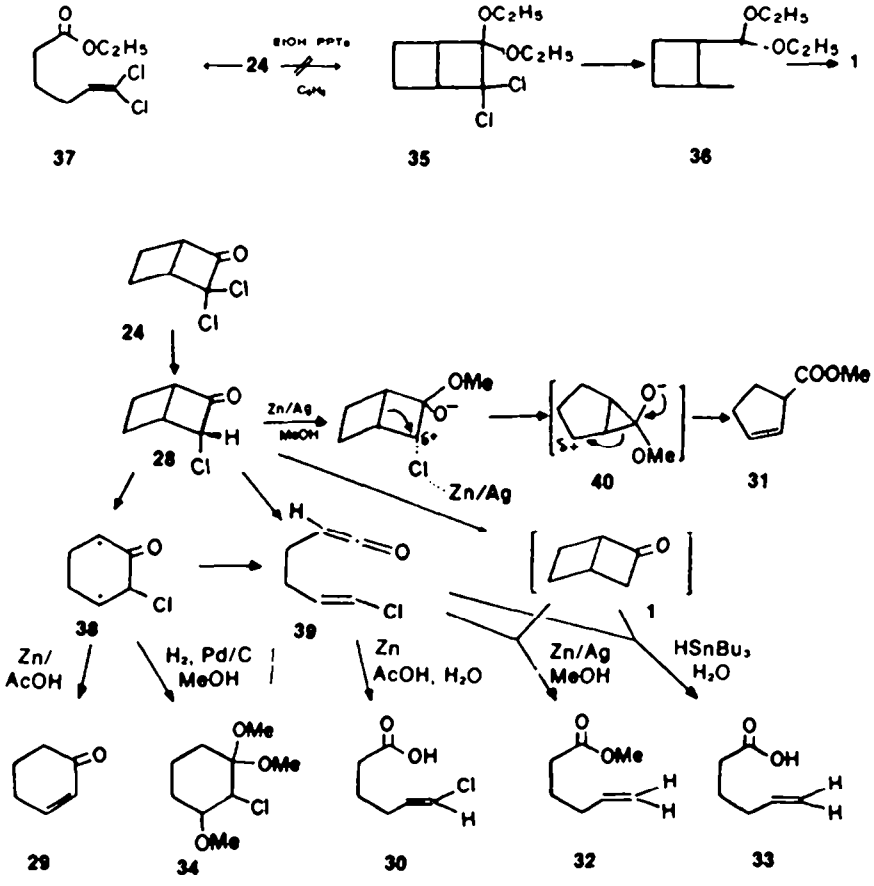


34 25%

Such a ring opening of a cyclobutanone ketal has been recently reported.[71] All the compounds obtained in the reductive reactions of **24** have been identified by comparison with authentic samples, by univocal synthesis and from their spectroscopic data.

CONCLUSION

Cyclobutene undergoes cycloaddition with dichloroketene to provide 3,3-dichlorobicyclo[2.2.0]hexan-2-one **24** and after reductive halogen removal the *endo*-3-chloro bicyclo[2.2.0] hexan-2-one **28**. However, although thermally stable at 140°, this monochloro-cycloadduct **28** does not constitute a convenient intermediate for synthesis of the parent ketone **1**. The formation of the products obtained in the different reductive chlorine removals attempted from **24** can be interpreted in the Scheme I.



Scheme 1. The formation of the products of reductive chlorine removal from the 3,3-dichloro bicyclo[2.2.0]hexan-2-one **24**.

As shown in this Scheme I, the products of these reductive reactions imply the breaking or migration of the central σ bond of the 3-chlorobicyclo[2.2.0]hexan-2-one **28**. Hence, it is formed a biradical **38** leading either to the cyclohexan-2 one **29** by chlorine removal (Zn in AcOH) or to the methylchlorocyclohexanone ketal **34** (H_2, Pd/C in MeOH). On the other hand, a retro[2 + 2]cycloaddition from **28** or **38** gives the chloroketene **39** which is readily trapped by water to give the chloroacid **30** (Zn, AcOH + H_2O); while the non-chlorinated acid and methyl ester **33** and **32** derive from ketene **39** by trapping by water ($HSnBu_3$, H_2O) and methanol (Zn/Ag, MeOH) respectively and subsequent chlorine removal. However, the direct formation of **32** and **33** from the ring opening of the bicyclo[2.2.0]hexanone **1** itself, cannot be excluded. Finally, ionisation of chlorine by silver-promoted zinc in methanol induced a ring contraction process to the bicyclo[3.1.0]hexane derivative **40** followed by ring opening of this intermediate cyclopropylcarbinyl cation into the methyl cyclopentene-3-carboxylate **31** (Zn/Ag, MeOH).

It must be underlined, that in our hands cyclobutene does not undergo cycloaddition reactions with monochloroketene[29,30] or with the new ketene equivalents such as ketene iminium[72] or methyl α-methyl-thioacrylate in presence of $AlCl_3$.[73]

EXPERIMENTAL

Cyclobutanol **17**

To a stirred soln of 600 ml H_2O and 57.3 ml (0.68 mol) conc HCl was added 57.6 g (0.8 mol) of cyclopropylcarbinol **16**. The mixture was refluxed for 3–3.5 h. After cooling in ice the mixture was neutralized (24 g, 0.6 mol NaOH were added and the neutralization was completed with $NaHCO_3$). The aqueous layer was saturated with NaCl and extracted several times with ether (or extracted continuously); the organic layers were combined, dried over $MgSO_4$, to give after removed of the solvent and distillation of the residue 51.8–52.9 g (90–92%) of **17** b.p. 123–124°, contaminated with 3% of 3-butene-1 ol.[25] NMR (CCl_4): δ 4.46 (s, OH), 4.18 quintuplet (1H, J = 7.5 Hz), 2.5 – 0.8 (m, 6H).

Tosyloxycyclobutane **19**

The tosyloxycylobutane **19** was obtained by the reaction of the cyclobutanol **17** with 1.1 equivalent of tosylchloride in pyridine at 0° for 48 h. After usual work up, the yellow pale residue treated under high vacuum (3.10^{-2} mm Hg) at room temperature for 3 h, gave the pure tosyloxycyclobutane **19** in 90% yield, without impurities. NMR (CCl_4): δ 7.76 (d, J = 8.3 Hz, 2H), 7.34 (d, J = 8.3 Hz, 2H), 4.76 (quintuplet, J = 7.5 Hz, 1H), 2.48 (s, 3H), 2.8 – 1.1 (m, 6H).

Cyclobutene **14**

A soln of 6.78 g (30 mmol) of tosyloxycyclobutane **19** in 10 ml of dry, DMSO was added dropwise over 10 min to a stirred mixture of 8.4 g (75 mmol) of t-BuOK in 120 ml of dry DMSO at 70° under argon. After stirring and heating for 100 min the evolved gas was carried in argon into a solid CO_2 trap (−80°) and 1.39 – 1.46 g (86–90%) cyclobutene **14** (b.p. 2°) was obtained. The yield was based on the pure 1,2-dibromocyclobutane obtained by addition of bromine to **14**. NMR (CCl_4): δ 4.47 (m, 2H), 3.1 – 2 (m, 4H). Mass spectrum: *m/e*: 216 (22, M^+ + 2); 214 (M^+, 41); and 133 (M^+–HBr, 82); 135 (M^+–HBr, 62); 53 (M^+ + 2–2HBr, 100).

The overall yield of cyclobutene **14** based on cyclopropylcarbinol **16** was 70–75%, purity 98–99%.

Ethyl bicyclo[2.2.0]*hex-2-ene-2-carboxylate* **20**

To a mixture of 254 mg (1.9 mmol) of $AlCl_3$ (0.5 M) and 230 mg (4.25 mmol) of cyclobutene **14** prepared as above in 5 ml of dry benzene was added dropwise a soln of 373 mg (3.8 mmol) of ethyl propiolate in 2 ml dry benzene. The flask was fitted with a condenser at −45°. The reaction mixture was stirred for 3 days at 12° and worked up in the usual manner to yield 300 mg (51%) of crude product. Purification by column chromatography (20 g of silica gel, eluting with 97:3 petroleum ether–Et_2O) gave 116 mg (20%) of **20** followed by 10 mg (< 2%) of **21**. The spectral data of **20** are: NMR (CCl_4): δ 6.89 (d, J = 2 Hz, 1H), 4.14 (q, J = 7.3, 2H), 3.7 – 2.9 (m, 2H), 2.6 – 2 (m, 2H), 2.14 (m, 2H), 1.28 (t, J = 7.3 Hz, 3H). IR (CCl_4) $\nu_{C=O}$ 1710 cm^{-1}; $\nu_{C=C}$ 1635 cm^{-1}. MS *m/e* (rel. intensity) 152 (M^+; 38); 79 (M^+ – COOEt, 100); 77 (77).

Ethyl cyclohexa-1,3-diene-3-carboxylate **21**

The reaction described above gave after 7 days at 12° the corresponding ring opening product **21** in 30% yield after chromatography. NMR (CCl_4): δ 6.82 (t, H), 6.35 (d, of t, J = 10.7 Hz, 1H), 5.79 (d of t, J = 10.7 Hz, 1H), 4.16 (q, 2H), 2.24 (t, of d, 4H), 1.29 (t, 3H). IR (CCl_4): $\nu_{C=O}$ 1710; $\nu_{C=C}$ 1638 and 1626 cm^{-1}. MS *me* (rel. intensity 152 (M^+, 24); 79 (100); 77 (69); 51 (26).

Diethyl bicyclo[2.2.2]*hexa-2,5-diene-2,6-dicarboxylate* **22**

The reaction described above performed in a sealed tube at room temperature for 5 days, gave after purification by column chromatography **21** in 35% yield and 10% of Diels–Alder products **22** and **23** in 40:60 ratio. The reaction performed in the same conditions, for 17 days, yields 5% of **21** and 85% of **22** and **23** in 40:60 ratio, based on ethyl propiolate.

The spectral data of visquous **22** are: NMR (CCl_4): δ 7.17 (d, d, 2H, J = 2 Hz, J = 6.8 Hz), 4.72 (m, CH), 4.16 (q, 2 CH, J = 7 Hz), 3.87 (m, CH), 1.55 – 1.1 (m, s, 4H), 1.3 (t, 6H). IR (CCl_4): $\nu_{C=O}$ 1710; $\nu_{C=C}$ 1628 and 1600 cm^{-1}. MS *m/e* (rel. intensity): 250 M^+, 2); 177 (M^+–CO_2Et, 100); 149 (70).

Diethyl bicyclo[2.2.2]*hexa-2,5-diene-2,5-dicarboxylate* **23**

The spectral data of pure **23** recristallized in pentane are: NMR (CCl_4); δ 7.25 (d, d, J = 1.75 Hz, J = 6.8 Hz, 2H); 4.29 (d, d, J = 6.8 Hz, 2CH); 4.13 (q, $2CH_2$); 1.55 – 1.1 (m, 4H); 1.27 (t, $2CH_3$). IR: $\nu_{C=O}$ 1705 (s); $\nu_{C=C}$ 1628 and 1600 cm^{-1}. Ms *m/e* (rel. intensity) 250 (M^+, 0.6); 177 (M^+–CO_2Et, 100); 149 (M^+-28-CO_2Et, 91). Calc for $C_{14}H_{18}O_4$: C, 67.18; H, 7.25; O, 25.56. Found: C, 67.35; H, 7.35; O, 25.31%.

3,3,-*Dichlorobicyclo*[2.2.0]*hexan-2-one* **24**

Into a soln of 2.48 g (0.017 mol) of freshly-distilled dichloroacetylchloride (prepared from dichloroacetic acid and thionylchloride) in 300 ml of anhydrous ether cooled at −30° was distilled, under an argon atmosphere, 1.40–1.45 g (26–27 mmol) of cyclobutene prepared from 6.78 g (30 mmol) of tosyloxycyclobutane **19** as described above. To the mixture, kept at −10° by immersion in a cooling bath, was added dropwise over a 6–7 h period a soln of 1.84 g (0.018 mol) of triethylamine (distilled over CaH_2) in 100 ml of dry ether. A faster rate of addition results in more polymerization of dichloroketene and lower yields of cycloadducts. After the addition was completed, the reaction mixture was stirred at 13° for an additional 14 h. Then, 5 ml of cold water was added, the organic phase was decanted and the aqueous layer extracted twice with 40 ml of ether. The combined organic layers were washed with 2 ml of N HCl and then with 1 ml of a saturated solution of $NaHCO_3$, dried over $MgSO_4$, filtered, concentrated to give 2.24 g of crude product 79% yield based on dichloroacetylchloride. Purification by column chromatography (50 g of silical gel, eluting with 99:1 pentane–Et_2O) gave 2.10 g (75%) of **24**. NMR (CCl_4); δ 3.95 (d, d, t, 1H), 3.37 (d, d, t, 1H); 3.1 – 1.9(m, 4H). IR (CCl_4) $\nu_{C=O}$ 1815 cm^{-1}. MS: *m/e* (rel. intensity) 164 (M^+, 0.1); 65 (12.6); 55 (100). Calc for $C_6H_6OCl_2$: C, 43.67; H, 3.66; O, 9.69; Cl, 42.96. Found: C, 43, 41; H, 3.75; O, 9.79; Cl, 42.94%. Calc 163.979567. Found: 163.9808; $C_5H_6Cl_2$ (M–CO)$^+$: calc 135.984653. Found: 135.9841

Reduction of **24** *by zinc in acetic acid*

A solution of 600 mg (3.6 mmol) of dichloroketone **24** in 0.4 ml of glacial acetic acid was added dropwise under an argon atmosphere to a stirred mixture of 1.58 g (24 m atom g.) of powdered zinc in 1.7 ml of glacial AcOH cooled at 0° – 5°. After 15 min as shown by GLC, all the compound was consumed. The cold

reaction mixture was diluted with 10 ml of ether, and the zinc residue was filtered off. The ethereal layer was washed with a saturated solution of Na_2CO_3 to remove the acetic acid and dried over $MgSO_4$, and then concentrated by distillation to give 375 mg (*ca.* 80%) of crude product. Purification either by gas chromatography at 140° (column SE 30) or by liquid chromatography (20 g of silica gel, eluting with 95:5 (pentane–Et_2O) gave 117 mg (25%) of 3-chlorobicyclo[2.2.0]hex-2-one **28**, 10 mg (*ca.* 3%) of 2-cyclohexenone **29** and 24 mg (*ca.* 5%) of 6-chloro-5-hexenoïc acid **30** with the following spectral data: endo 3-chlorobicyclo[2.2.0]hexan-2-one **28**: NMR (CCl_4): δ 4.32 (t, H), 2.88 (m, 2H) and 2.40 – 1.85 (m, 4H). IR (CCl_4): $\nu_{C=O}$ 1792, 1802, 1815 and 1836 cm^{-1}. MS *m/e* (rel. intensity) 104 ($M^+ - 28$, 0.8); 67 ($M^+ - COCl$, 100); 55 (95). A calc 130.0185. Found: 130.0195; C_6H-Cl (M–CO) Calc 102.0236. Found 102.0235; C_6H-O [M–Cl]$^+$ Calc 95.0496. Found 95.0496. The endo configuration of **28** was determined by comparison with the reduction of 7,7-dichlorobicyclo[3.2.0] hept-2-en-6-one **2**.[29,30] 2-Cyclohexenone **29**: spectral data (IR, NMR, MS) of **29** were identical with the data of an authentical sample of 2-cyclohexenone. trans 6-Chloro-5-hexenoïc acid 30: NMR (CCl_4): δ 11.47 (s, –COOH), 6.04 (d, J = 7.3 Hz, H), 5.8 (d, t, J = 7.3 and 6.6 Hz, H), 2.7 – 1.3 (m, 6H). IR (CCl_4): $\nu_{C=O}$ 1715 and $\nu_{C=C}$ 1635 cm^{-1}. MS *m/e* (rel. intensity) 148 (M^+, 0.5), 113 (M^+–Cl, 25); 112 (M^+–HCl, 22); 60 (100); 39 (56).

Unequivocal synthesis of **30**

Into a solution of 228 mg (2 mmol) of 5-hexenoïc acid (prepared easily by saponification of the corresponding nitrile,[*] or following the procedure of Rubottom[68] in 15 ml of CH_2Cl_2 was bubbled Cl_2 at room temperature.[25] After 30 min the reaction was complete, as shown by TLC. Then the reaction mixture was poured into 15 ml of a 5% sodium thiosulfate solution and extracted three times with 100 ml of CH_2Cl_2. The organic layers were combined, washed with 2 ml of NaCl saturated solution, dried over $MgSO_4$, filtered and evaporated to give 350 mg of 5,6-dichlorohexanoïc acid 93% yield. Chromatography of the residual solid on 15 g of silica gel and elution with 85:15 pentane–ether led to 315 mg of the pure 5,6-dichlorohexanoïc acid in 85% yield. IR (neat): $\nu_{C=O}$ 1712 cm^{-1}. NMR (CCl_4): δ 11.25 (s, b, COOH), 4.3 – 3.3 (m, 3H), 2.7 – 2.2 (m, 2H), 2.2 – 1.45 (m, 4H).

A mixture of 185 mg (1 mmole) of 5,6-dichlorohexanoïc acid, 400 mg (7 mmole) of KOH and 5 ml of abs EtOH was stirred at reflux for 2 h,[76] cooled to 0°, and acidified by 2 M HCl. The mixture was extracted 3 times with 30 ml of ether. The organic layers were combined, dried over $MgSO_4$, filtered and evaporated. Chromatography of the residual oil on 20 g of silica gel and elution with 85:15 pentane–ether led to 90 mg ≈ 60% yield of trans-6-chloro-5-hexenoïc acid. IR (CCl_4): $\nu_{C=O}$ 1715 and $\nu_{C=C}$ 1635 cm^{-1}. NMR (CCl_4): δ 11.18 (s, H), 6.05 (d, J = 7.3 Hz, H), 5.8 (d, t, J = 7.3 Hz, H), 2.7 – 1.3 (m, 6H). MS *m/e* (rel. intensity) 148 (M^+, 0.5); 113 (M^+–Cl, 25), 60 (CH_3COOH, 100).

Reduction of **24** *by silver–zinc couple in methanol*

To a stirred suspension of silver-zinc couple, prepared as described[66] from 500 mg of zinc dust and 15 ml of anhydrous silver acetate was added dropwise a solution of 165 mg of **24** (1 mmol) in 0.3 ml of methanol. As shown by GLC the reaction was complete after being vigorously stirred at room temp for 30 min. The zinc was filtered off and washed with 10 ml of methanol. The solvent was then evaporated under reduced pressure to give a residue. Purification by gas chromatography at 152°C (column SE 30) gave 63 mg (50%) of methyl cyclopentene-3-carboxylate **31**, 7 mg (5%) of methyl-5-hexenoate **32**. Methyl cyclopentene-3-carboxylate **31**: NMR (CCl_4): δ 5.70 (m, 2H), 3.60 (s, 3H), 3.42 (m, 1H) and 2.7 – 1.7 (m, 4H). IR (CCl_4): $\nu_{C=O}$ 1745 and $\nu_{C=C}$ 1618 cm^{-1}. MS *m/e* (rel. intensity) 126 (M^+, 16); 67 (M^+–COOMe, 100), according to the literature.[67] Methyl 5-hexenoate **32**: NMR (CCl_4): δ 6.20 – 5.3 (m, 1H), 5.06), (m, H), 4.84 (m, H), 3.6 (s, 3H) and 2.7 – 1.3 (m, 6H). IR (CCl_4): $\nu_{C=O}$ 1745 and $\nu_{C=C}$ 1645 cm^{-1}. MS *m/e* (rel. intensity) 128 (M^+, 6); 74 (CH_3COOMe); 69 (M^+–HCOOMe, 61) and 43 (92%), according to the literature.[68]

Reduction of **24** *by tri-n-butyltin hydride*

A solution of 100 mg (0.6 mmol) of **24**, 10 mg of azobis(isobutyronitrile) and 528.5 mg (1.8 mmol) of tri-n-butyltin hydride in 0.350 ml of anhydrous benzene or cyclohexane was refluxed under argon. As shown by the formation in the NMR spectra of multiplets at δ 6.2 – 5.4 and 5.25 – 4.6 ppm, the reaction was complete within 30 min. After work-up with a solution of potassium fluoride in water (10%), distillation gave 62 mg (90%) of 5-hexenoïc acid **33**, identified by comparison of its spectral data with literature.[65] The reaction performed at room temperature for 12 h gave **33** in 100% yield.

Reduction of **24** *by hydrogen in presence of palladium*

A mixture of 165 mg (1 mmol) of **24**, 20 mg Pd/C (10%) in 3 ml MeOH was hydrogenated under atmospheric pressure. The reaction was stopped after 2 h, when 45 ml of hydrogen (2 equivalents) had been absorbed. Then, the mixture was filtered, methanol evaporated under reduced pressure and the residue dissolved in 15 ml of ether. The organic phase was washed with saturated bicarbonate solution with water, and dried over $MgSO_4$. Removal of solvent under reduced pressure gave 150 mg of crude product. Purification by liquid chromatography (eluting with 95:5 pentane–ether) yielded, besides unidentified products, 50 mg (25%) of a compound identified as the 2-chloro-1,1,3-trimethoxycyclohexane **34** from its spectral data: NMR (CCl_4) δ 4.22 (d, H), 4.0 – 3.0 (m, H), 3.28 (s, OCH_3), 3.18 (s, OCH_3), 3.13 (s, OCH_3), 2.1 – 1.2 (m, 6H). MS *m/e* (rel. intensity) 193 ($M^+ - CH_3$, 1.6), 177 (M^+–OCH_3, 62); 141 (72); 101 (CH_2=CH–$^+$C(OMe), 100).

Ethyl 6,6-dichloro-5-hexenoate **37**

In a 5 ml round-bottomed flask fitted with a Dean and Stark Collector was refluxed a solution of 165 mg (1 mmol) of **24** in 3 ml of dry benzene and 1 ml of ethanol containing 30 mg of pyridinium p-toluene sulfonate.[70]

The reaction was complete within 14 h as shown by the absence of **24** by GLC. The solvent was removed under reduced pressure, and 10 ml of ether were added to the residue. The organic layer was washed with saturated aq $NaHCO_3$, dried over $MgSO_4$ and concentrated to yield, after liquid chromatography on silica gel 180 mg (85%) of ethyl 6,6-dichloro-5-hexenoate **37**. NMR (CCl_4): δ 5.79 (t, J = 7.3 Hz, H), 4.05 (q, J = 7.3 Hz, 2H), 2.2 (m, 4H), 1.75 (m, 2H), 1.25 (t, J = 7.3 Hz, 3H). IR (CCl_4): $\nu_{C=O}$ 1740 and $\nu_{C=C}$ 1625 cm^{-1}. MS *m/e* (rel. intensity) 210 (M^+, 8.5%), 165 (M^+ – OC_2H_5, 26.7); 167 (14.5); 88 (100); 60 (66).

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