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A SIMPLE SYNTHESIS OF TROPONES AND RELATED COMPOUNDS†

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Abstract - *Cyclohexa-2,4- and 2,5-dienones bearing at position 2 or 4 a dihalomethyl group (halogen = chlorine or bromine) are smoothly reduced by tri-butyltin hydride to furnish appropriately substituted tropones. Modification of the substituents permits access to a tropolone and to less substituted tropones. The mechanism of this ring expansion process has been discussed.*

The elucidation of the intricate structure of phomenoic acid[1] required the synthesis of certain model compounds such as 2,4,6,6-tetramethylcyclohexa-2,4-dienone 1. It seemed to us that such dienones should be available by reduction of dihalogeno- derivatives like 2 and 3. The latter are, of course, easily prepared. Unexpectedely radical reduction of 2 and 3 with tributyltin hydride provided a new and simple synthesis of tropones. A preliminary Communication has already been published.[2]

After the brilliant conception of the existance and the nature of tropones and tropolones,[3], many different syntheses were reported.[4,5,6]

The synthesis of cyclohexadienones of the type 2, 3 and of type 4, 5 is made using dihalocarbene reactivity and is well documented.[7] The compounds 2 and 4 are also well known.[7] Using dibromocarbene compounds 3 and 5 were easily prepared. Compound 8 is also known,[7] but the other dienones 12, 18, 19, 23 and 24 are new. Their preparation is described in the Experimental.

Reduction of 2, 3, 4 and 5 with tributyltin hydride did not afford even a trace of the expected dienone 1. Instead a nearly quantitative yield of 2,4,7-trimethyltropone 6 was obtained. This compound was characterised fully by spectroscopic data and also by comparison with an authentic specimen kindly furnished by Professor R. Noyori (Nagoya).

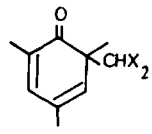
Similarly, 2,6-di-t-butyl-p-cresol was converted in good yield into the dienone [7]8, which afforded on reduction in the same way a high yield of 2,7-di-t-butyl-4-methyltropone 9.

We have also examined the possibility of converting a catechol into a tropolone using the same experimental procedure. Thus 3,5-di-t-butylcatechol 10 was readily converted to its monoisopropyl ether 11. This compound gave the dichlorocarbene derivative 12 which, on reduction with tributyltin hydride afforded in moderate yield the tropolone isopropyl ether 13. This process was not optimised.

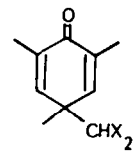
In connection with model structures for phomenoic acid 2,6-dimethylphenol 14 was reacted with formaldehyde to give the known alcohol[8] 15. This was oxidised by pyridinium chlorochromate to the aldehyde 16. Further transformation to the acetal 17 was facile. Reaction of the acetal 17 with dichlorocarbene and dibromocarbene gave the ortho-substituted dienones 18 and 19 respectively. Reduction in the usual way afforded the now expected tropone 20.

† Dedicated with respect to Prof. Hans Wynberg on the occasion of his sixtyfifth birthday.

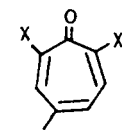
For the synthesis of certain naturally occuring troponoids, it is desirable to have a method that does not commence with a phenol substituted with three alkyl groups at positions 2,4- and 6-. Bromination of p-cresol 21 gave 2,6-dibromo-p-cresol 22. Reaction of the latter with dichloro- and dibromo-carbene gave the dihalomethyl derivatives 23 and 24 respectively. Reduction in the usual way gave the tropone 25 in satisfactory yield. The two bromines in 25 lend themselves to further manipulation[4] of this molecule.



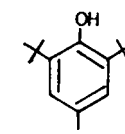
1 X = H
2 X = Cl
3 X = Br



4 X = Cl
5 X = Br



6 X = Me
9 X = t-Bu
25 X = Br



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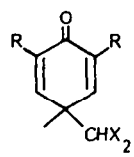
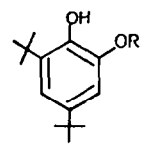
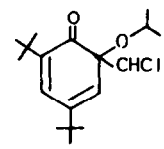


8 X = Cl, R = t-Bu
23 X = Cl, R = Br
24 X = R = Br



10 R = H
11 R = 



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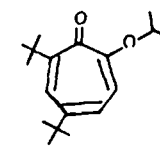

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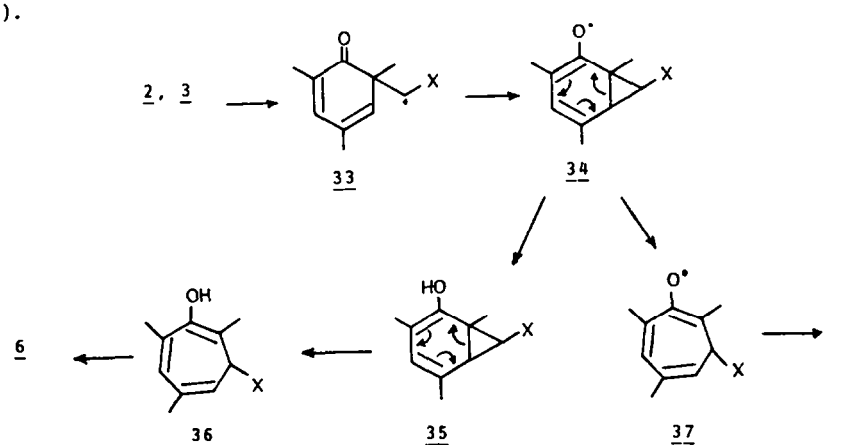
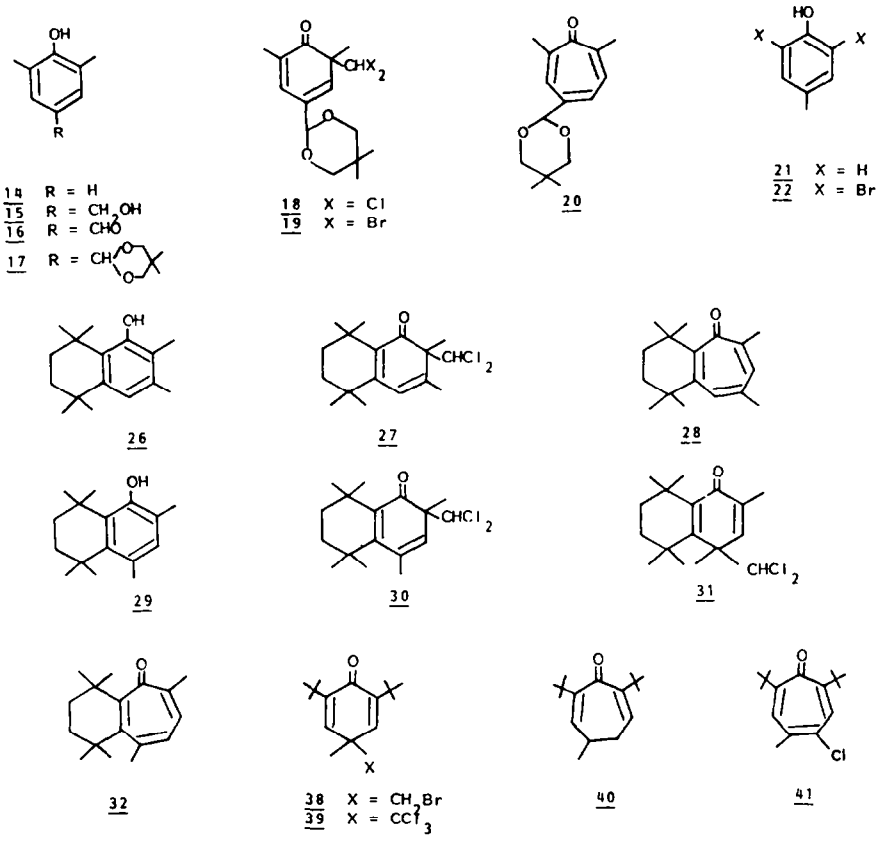
It was of interest to examine the scope of the reaction when more hindered molecules were used. Thus the phenol 26 gave the dichloromethyl derivative 27 which on reduction afforded the tropone 28 in excellent yield. Similarly the α-naphthol derivative 29 afforded 30 and 31. Reduction of 30 afforded 32 in good yield (82%). Reduction of 31 afforded 28 (28%) and 32 (42%).



Scheme 1

The mechanism of this tropone synthesis can be explained as in Scheme 1. For example 2 or 3 by reaction with a tributyltin radical would afford the radical 33 (X = Cl, or Br) which must cyclise to 34. From 34 two routes are possible. In the first the alkoxy radical is reduced to 35 which then rearranges to 36 and gives by ordinary ionic β-elimination tropone 6. Alternately 34 may rearrange to 37 which by reduction and elimination would afford 6.



Further evidence for the mechanism was given by the reduction of compounds 38 and 39. Phase transfer catalysed reaction of the anion of phenol 7 with a large excess of CH_2Br_2 afforded 38 in one step, but in modest yield (24%). Similarly, and surprisingly, the reaction of the same anion in methanol-sodium methoxide with bromotrichloromethane gave the desired trichloromethyl derivative 39 (46%). The mechanism of this reaction deserves further study.

Reduction of bromide 38 gave the dihydrotropone 40 (26%), thus showing that addition and rearrangement of the radical had indeed taken place. This confirms halogen is not reduced from 34 or 35 prior to rearrangement. Finally, reduction of 39 afforded the chlorotropone 41 as well as some of the parent tropone 9.

Experimental

General

All solvants were dried and distilled by standard procedures. Tri-n-butyltin hydride, purchased from Aldrich, was used without further purification. Melting points were taken on a Reichert hot stage apparatus and were uncorrected. Infrared spectra were recorded with either a Perkin Elmer 297 or 257 Spectrophotometer. Ultra-violet spectra were measured with either Jobin-Yvon type Duospac 203 or Perkin-Elmer Lambda S UV/vis spectrophotometer in methanol. Mass spectra were recorded on either an AEI-MS 9 or AEI MS 50 apparatus. NMR spectra were recorded at 60 MHz unless otherwise stated with either a Varian T60 or EM 360 spectrometer for solutions in deuterochloroform. Chemical shifts are in ppm downfield from tetramethylsilane as internal standard. 200 MHz spectra were recorded on a Bruker WM 200 spectrometer.

General Methods for Carbene Formation.

Method A : Sodium trihaloacetate as a source of dihalocarbene.[9] To a mixture of the phenol (10 mmoles), sodium trichloroacetate (or sodium tribromoacetate[10]) (25 mmoles) was added dry 1,2-dimethoxyethane (20 ml) under nitrogen. The solution was refluxed for 8 hrs. The reaction mixture was filtered on a small pad of silica gel. This silica gel pad was washed with ethylacetate. The solvant was evaporated under reduced pressure and the residue subjected to column chromatographic separation on silica gel using hexane and dichloromethane as eluants.

Method B : Phase transfer method.[11] The phenol (10 mmoles), cetyltrimethylammonium bromide (0.1 mmoles) and the haloform (33 mmoles) were stirred at 50°C, while sodium hydroxide solution (77 mmoles of NaOH) in water (7 ml) was added drop by drop during 10 minutes. After four hours ice-cold water was added and the mixture was extracted with ether. The combined ether layers were washed with water, saturated sodium chloride solution and dried over sodium sulphate. After removal of solvant under reduced pressure, the residue was subjected to purification on a silica gel column using a gradient of dichloromethane in hexane.

Method C : Ultra-sonication method.[10] To the phenol (10 mmoles), cetyltrimethylammonium bromide (0.1 mmole) the haloform (33 mmoles), sodium hydroxide solution (77 mmoles of NaOH) in water (7 ml) was added. This mixture was subjected to ultrasonication for about 30 minutes. The work-up and separation were carried out as described in Method B.

2,4,6-Trimethyl-6-dichloromethyl-2,4-cyclohexadienone[7] *2.*

This known compound was obtained from 2,4,6-trimethylphenol using the above three methods. Methods A (22%), B (59%), and C (60%).

2,4,6-Trimethyl-6-dibromomethyl-2,4-cyclohexadienone 3.

From 2,4,6-trimethylphenol and bromoform this compound was obtained (Method B) as a colourless thick liquid (28%); $\nu_{max.}$ (neat) 1638, 1360 cm^{-1}; $\lambda_{max.}$ 319 nm (ε 3,766); δ 1.28 (3H, s, CH_3), 1.90 (3H, S, CH_3), 2.03 (3H, S, CH_3), 5.91 (H, s, $CHBr_2$), 6.22 (H, s, H), 6.72 (H, s, H); m/z 310, 308 ($M^{+\cdot}$), 306, 229, 227 ($M^{+\cdot} - Br_2$), 148 ($M^{+\cdot} - Br_2$). (Found: C, 39.21; H, 3.89; Br. 51.77; O, 5.36. Calc. for $C_{10}H_{12}Br_2O$: C, 38.99; H, 3.93; Br, 51.88; O, 5.19%).

2,4,6-Trimethyl-4-dichloromethyl-2,5-cyclohexadienone[7] *4.*

This known compound was prepared from 2,4,6-trimethylphenol 1. Methods A (28%), B (17 %) and C (23%).

2,4,6-Trimethyl-4-dibromomethyl-2,5-cyclohexadienone 5.

This compound was prepared from 2,4,6-trimethylphenol 1 and bromoform as in method B (24%). It was crystallised from hexane and dichloromethane, m.p. 65-66°; $\nu_{max.}$ (Nujol) 1640 cm^{-1}; 1360 cm^{-1}; $\lambda_{max.}$ 246 nm (ε 10,786); δ 1.40 (3H, s, CH_3), 1.95 (6H, s, $2CH_3$), 5.56 (H, s, $CHBr_2$), 6.60 (2H, s, 2H); m/z 310, 308 ($M^{+\cdot}$), 306, 229, 227 ($M^{+\cdot}$ - Br), 148 ($M^{+\cdot}$ - Br_2). (Found: C, 39.40; H, 3.94; Br, 51.06; O, 5.86. Calc. for $C_{10}H_{12}Br_2O$: C, 38.99; H, 3.93; Br. 51.88; O, 5.19%).

2,6-Di-t-butyl-4-methyl-4-dichloromethyl-2,5-cyclohexadionone[7] *8.*

This known compound was prepared from 2,6-di-t-butyl-4-methylphenol 7 and chloroform as in method B (79%). It was crystallized from hexane, m.p. 79-80°, $\nu_{max.}$ (Nujol) 1640, 1365 cm^{-1}; $\lambda_{max.}$ 283 nm (ε 11,584).

2,6-Di-t-butyl-6-isopropyloxyphenol 11.

To a solution of 3,5-di-t-butylcatechol 10 (10 mmoles) in dry acetonitrile (35 ml) was added anhydrous potassium carbonate (3 g), 18-crown-6-ether (0.1 mmole) and isopropylbromide (12.5 mmoles). The mixture was heated to 80°C and stirred overnight. The usual work-up and separation on a silica gel column (gradient of dichloromethane in hexane) gave 2,4-di-t-butyl-6-isopropyloxyphenol 11 (92%) as a colourless liquid, $\nu_{max.}$ (neat) 3500, 1595, 1200-1000 cm^{-1} (several bands); $\lambda_{max.}$ 284 nm (ε 2,352); δ 1.35 s and 1.48 s. 2,4-di-t-butyl and two methyls of isopropyl group, 4.30 to 4.55 (H, m, $CHMe_2$), 6.05 (H, s, OH), 6.88 (H, s, H), 7.00 (H, s, H); m/z 265 ($M^{+\cdot}$), 249 ($M^{+\cdot}$ -CH_3), 233, 222, 207. (Found: C, 77.15; H, 10.69; O, 11.98. Calc. for $C_{17}H_{28}O_2$: C, 77.22; H, 10.67; O, 12.10%).

2,4-Di-t-butyl-6-isopropyloxy-6-dichloromethyl-2,4-cyclohexadienone 12.

2,4-Di-t-butyl-6-isopropyloxyphenol 11, treated with chloroform as in method B, gave the title compound (37%) as a thick liquid, $\nu_{max.}$ (neat) 1650, 1365 cm^{-1}; $\lambda_{max.}$ 332 nm (ε 3,712); δ 1.00 (3H, d, CH_3), 1.12 (3H, d, CH_3), 1.28 (18H, s, 2,4-di-t-butyl), 3.4 to 3.8 (H, m, $CHMe_2$), 5.81 (H, s, $CHCl_2$), 6.31 (H, d, H), 7.02 (H, d, H); m/z 348 ($M^{+\cdot}$), 346, 306, 304, 291, 289.

(Found: C, 62.08; H, 8.26; Cl, 20.63; O, 8.94. Calc. for $C_{18}H_{28}Cl_2O_2$: C, 62,24; H, 8.21; Cl, 20.42; O, 9.20%).

4-Hydroxy-3,5-dimethylbenzylalcohol[8] *15.*

To an ice-cold aqueous solution (15 ml) of sodium hydroxide (6 g) was added 2,6-dimethylphenol 14 (100 mmoles). To this ice-cold solution 35% formaldehyde solution (200 ml) was added. The temperature was raised slowly to 30°C and kept for 2.5 hrs. After cooling in an ice-salt bath and careful neutralisation to pH 7.25, the solution was extracted with dichloromethane. The organic phase was then washed with water, dried over sodium sulphate and concentrated under reduced pressure. The concentrate was impregnated onto silica gel which was loaded on to a silica gel column and eluted with a hexane-dichloromethane solvant system to obtain compound 15 as a white crystalline solid (76%), m.p. 105°C (ethanol-dichloromethane), $\nu_{max.}$ (Nujol) 3420, 1598, 1365 cm^{-1}.

4-Hydroxy-3,5-dimethylbenzaldehyde 16.

To a mixture of sodium acetate (7 mmoles) and pyridinium chlorochromate (35 mmoles) was added dry dichloromethane (50 ml) and the mixture was stirred for 15 minutes. Then under nitrogen was added 4-hydroxy-3,5-dimethylbenzylalcohol 15 (22 mmoles). The reaction was stirred for two hours and then dry ether (50 ml) was added. The supernatant layer was decanted and the gummy mass was washed with ether 3x20 ml. The combined ether layer was washed with water, dried over sodium sulphate and concentrated under reduced pressure. The concentrate was further purified on a silica gel column using hexane and dichloromethane as eluants. 4-Hydroxy-3,5-dimethylbenzaldehyde 16 was a crystalline solid (64%), m.p. 119-120°C (dichloromethane-ethanol), $\nu_{max.}$ (Nujol) 3420, 1660, 1595, 1365 cm^{-1}; $\lambda_{max.}$ 220, 276 nm (ϵ 7,522, ϵ, 7,656 respectively); δ 2.31 (6H, s, $2CH_3$), 5.25 (H, s, OH), 7.04 (2H, s, 2H aromatic), 9.76 (H, s, CHO); m/z 150 ($M^{+\cdot}$), 149, 121, 107, 91, 77. (Found: C, 71.69; H, 6.71; O, 21.58. Calc. for $C_9H_{10}O_2$: C, 71.98; H, 6.70; O, 21.31%).

2,2-Dimethylpropan-1,3-diol Acetal of Aldehyde 16.

Aldehyde 16 (4 mmoles), 2,2-dimethylpropan-1,3-diol (6 mmoles) and p-toluenesulphonic acid (0.1 mmole) were dissolved in dry benzene 25 ml. Using a Dean-stark apparatus the solution was refluxed for 20 hrs. The usual work-up and separation on a silica gel column afforded compound 17 in quantitative yield as a crystalline solid, m.p. 109-110°C (hexane), $\nu_{max.}$ (Nujol) 3350, 1600, 1385 cm^{-1}; $\lambda_{max.}$ 219 nm (ϵ 8,916); δ 0.82 (3H, s, CH_3), 1.35 (3H, s, CH_3), 2.33 (6H, s, $2CH_3$), 3.80 (4H, d, $2CH_2$), 4.97 (H, s, OH), 5.45 (H, s, H-C(=O)-O), 7.33 (2H, s, 2H), aromatic); m/z 236 ($M^{+\cdot}$), 235, 221, 150 ($M^{+\cdot}$ - $C_5H_{10}O$), 91. (Found: C, 70.91; H, 8.56; O, 20.44. Calc. for $C_{14}H_{19}O_3$: C, 71.15; H, 8.35; O, 20.31%).

Synthesis of 2,4-Cyclohexadionone 18.

The reactionof the phenol 17 with sodium trichloroacetate (Method A) gave the derivative 2,4-cyclohexadienone 18 (30%). This was a crystalline solid, m.p. 117-118° (hexane); $\nu_{max.}$ (Nujol) 1650, 1385 cm^{-1}; $\lambda_{max.}$ 310 nm (ϵ 2,666); δ 0.80 (3H, s, CH_3), 1,30 (6H, s, $2CH_3$), 1.95 (3H, s, CH_3), 3.65 (4H, s, $2CH_2$), 5.05 (H, s, $CHCl_2$), 6.06 (H, s, H), 6.60 (H, s, H), 7.10 (H, s, H-C(=O)-O); m/z 322, 320, 318 ($M^{+\cdot}$), 285, 283, 235 ($M^{+\cdot}$ - $CHCl_2$), 197, 169, 91. (Found: C, 56.37; H, 6.28; Cl, 22.12; O, 14.79. Calc. for $C_{15}H_{20}Cl_2O_3$: C, 56.43; H, 6.31; Cl, 22.21; O, 15.03%).

Synthesis of 2,4-Cyclohexadienone 19.

Sodium tribromoacetate reacted with the phenol 17 (Method A) to give compound 19 (46%). This was a crystalline solid, m.p. 112-113° (hexane); $\nu_{max.}$ (Nujol) 1650, 1385 cm^{-1}; $\lambda_{max.}$ 310 nm (ϵ 4,200), δ 0.80 (3H, s, CH_3), 1.32 (6H, s, $2CH_3$), 1.96 (3H, s, CH_3), 3.64 (4H, s, $2CH_2$), 5.05 (H, s, $CHBr_2$), 6.10 (H, s, H), 6.61 (H, s, H), 7.12 (H, s, H-C(=O)-O); m/z 410, 408 ($M^{+\cdot}$), 406, 329 ($M^{+\cdot}$ - Br), 327, 243, 241, 235 ($M^{+\cdot}$ -$CHBr_2$). (Found: C, 44.02; H, 4.77; Br, 39.17; O, 11.20. Calc. for $C_{15}H_{20}Br_2O_3$: C, 44.14; H, 4.93; Br, 39.16; O, 11.76%).

4-Methyl-2,6-dibromophenol 22.

To t-Butylamine (40 mmoles) in toluene (30 ml) cooled to -30°C was added dropwise bromine (20 mmoles). After cooling to -70°C p-cresol 21 (10 mmoles) in dichloromethane (10 ml) was added dropwise. The reaction mixture was then allowed to warm to room temperature over a period of 6 hrs. Water (50 ml) was added to the reaction mixture and with the help of 10% NaOH (150 ml) the solution was transferred to a separating funnel. Once again the organic layer was extracted with 10% NaOH solution (2x150 ml). The combined alkaline extract, colled in ice-salt bath was neutralised with dilute HCl. The neutralised solution was extracted with dichloromethane (4x150 ml). The dichloromethane extract was dried over sodium sulphate and concentrated. The product was loaded on to a silica gel column and separation was effectuated by using a gradient of dichloromethane in hexane. 4-Methyl-2,6-dibromophenol 22 was obtained as a white crystalline compound (89%), m.p. 48-49° (hexane-dichloromethane); $\nu_{max.}$ (Nujol) 3400, 1560, 740 cm^{-1}; $\lambda_{max.}$ 296 nm (ϵ 2,508); δ 2.28 (3H, s, CH_3), 5.78 (H, s, OH), 7.36 (2H, s, 2H); m/z 268, 266 ($M^{+\cdot}$), 264, 187 ($M^{+\cdot}$), 185.

4-Methyl-2,6-dibromo-4-dichloromethyl-2,5-cyclohexadienone 23.

4-Methyl-2,6-dibromophenol 22 used as under Method B yielded 4-methyl2,6-dibromo-4-dichloromethyl-2,5-cyclohexadionone 23 as a crystalline compound (46%), m.p. 172-174° (dichloromethane), $\nu_{max.}^{-1}$ (Nujol) 1660, 700 cm^{-1}; $\lambda_{max.}$ 262 nm (ε 8,775), δ 1.64 (3H, s, CH_3), 5.89 (H, s, $CHCl_2$), 7.60 (2H, s, 2H), m/z 351, 349 ($M^{+\cdot}$), 347, 345, 316, 314, 312, 310, 268, 266, 264, 187, 185. (Found: C, 29.08; H, 1.69; Br, 44.81; Cl, 20.30; O, 4.77. Calc. for $C_8H_6Br_2Cl_2O$: C, 27.54; H, 1.73; Br, 45.81; Cl, 20.33; O, 4.59%).

4-Methyl-2,6-dibromo-4-dibromomethyl-2,5-cyclohexadienone 23.

Prepared by Method B from 4-methyl-2,6-dibromophenol 22 and bromoform, this was a crystalline compound (32%), m.p. 165-166° (dichloromethane), $\nu_{max.}^{-1}$ (Nujol) 1660, 700 cm^{-1}; $\lambda_{max.}$ 262 nm (ε 7,712); δ 1.66 (3H, s, CH_3), 5.80 (H, s, $CHBr_2$), 7.60 (2H, s, 2H); m/z 442, 440, 438 ($M^{+\cdot}$), 436, 434, 361, 359 ($M^{+\cdot}$ - Br), 357, 355, 267, 265 ($M^{+\cdot}$ - $CHBr_2$). (Found: C, 22.02; H, 1.26; Br, 73.06; O, 3.88. Calc. for $C_8H_6Br_4O$: C, 21.95; H, 1.38; Br, 73.01; O, 3.65%).

1-Oxo-2-dichloromethyl-2,3,5,5,8,8-hexamethyl-1,2,5,6,7,8-hexahydronaphthalene 27.

The reaction of 1-naphthol 26 with chloroform under method B gave the dienone 27 (45%) as a colourless liquid, $\nu_{max.}^{-1}$ (neat) 1650 cm^{-1}, $\lambda_{max.}$ 322 nm (ε 4,600), δ 1.23 (6H, s, $2CH_3$), 1.27 (6H, s, $2CH_3$), 1.33 (3H, s, CH_3), 1.56 (4H, d, $2CH_2$), 2.17 (3H, d, CH_3, J = 1.5 Hz), 6.17 (H, d, H, J = 1.5 Hz), 6.26 (H, s, $CHCl_2$); m/z 316 [($M^{+\cdot}$ + 1)$^{+\cdot}$], 314, 301, 299, 281, 279, 231. (Found: C, 64.94; H, 7.77; Cl, 22.69; O, 5.03. Calc. for $C_{17}H_{24}Cl_2O$: C, 64.76; H, 7.67; Cl, 22.49; O, 5.07%).

Products from 2,4,5,5,8,8-Hexamethyl-5,6,7,8-tetrahydro-1-naphthol 29.

Treatment of 1-naphthol 29 under method B gave two major products : isomer 30 (42%), a colourless liquid, $\nu_{max.}^{-1}$ (neat) 1645 cm^{-1}; $\lambda_{max.}$ 320, 240 nm (ε 9,707), δ 1.28 to 1.44 (14H, m, $5CH_3$), 1.72 (4H, s, $2CH_2$), 1.98 (3H, s, CH_3), 6.62 (H, s, $CHCl_2$), 6.73 (H, s, H); m/z 316 [($M^{+\cdot}$ +1)$^{+\cdot}$], 314, 301, 299, 281, 279, 231. (Found: C, 65.12; H, 8.14; Cl, 22.67. Calc. for $C_{17}H_{24}Cl_2O$: C, 64.76; H, 7.67; Cl, 22.49; O, 5.08%). The second isomer 31 (21%) was a colourless liquid, $\nu_{max.}^{-1}$ (neat) 1645 cm^{-1}, $\lambda_{max.}$ 242 nm (ε 10.200); δ 1.22 (3H, s, CH_3), 1.42 (3H, s, CH_3), 1.48 (6H, s, $2CH_3$), 1.58 (3H, s, CH_3), 1.85 (4H, s, $2CH_2$), 2.06 (3H, s, CH_3), 5.90 (2H, s, 2H); m/z 316 [($M^{+\cdot}$ +1)$^{+\cdot}$], 314, 301, 299, 281, 279, 231. (Found: C, 64.75; H, 7.49; Cl, 23.35; O, 4.78. Calc. for $C_{17}H_{24}Cl_2O$: C, 64.76; H, 7.67; Cl, 22.49; O, 5.08%).

General Procedure for Tropone Synthesis.

A mixture of dihalomethylcyclohexadionone (1 mmole) and azabis-isobutyronitrile (0.1 mmole) was dissolved in dry benzene (20 ml). To this mixture tri-n-butyltin hydride (2.5 mmoles) was added dropwise at room temperature under nitrogen atmosphere. Temperature of the reaction mixture was raised slowly to 80°C and maintained for 4 hrs. Then solvant was removed under reduced pressure. Preliminary purification of the concentrate was done on silica gel preparative plates and final purification was done on HPLC.

2,4,7-Trimethyltropone[12] *6.*

Tri-n-butyltin hydride reacted with all the following four cyclohexadienones : 2, 3, 4 and 5, under the experimental conditions as described in the general procedure to yield quantitatively 2,4,7-trimethyltropone as a colourless liquid, $\nu_{max.}^{-1}$ (neat), 1622, 1598, 1560 cm^{-1}; $\lambda_{max.}$ 237, 328 nm (ε 7,850). Shoulder at 342 nm; δ 2.11 (9H, s, $3CH_3$), 6.62 and 7.18 AB system. J_{AB} = 8Hz, 7.25 (H, s, H), m/z 148 ($M^{+\cdot}$), 120, 105, 91, 77, identical with an authentic specimen kindly provided by Professor R. Noyori.

2,7-Di-t-butyl-4-methyltropone[7] *9.*

4-Methyl-2,6-di-t-butyl-4-dichloromethyl-2,5-cyclohexadienone 8 and tri-n-butyltin hydride reacted as per the general procedure affording 2,7-di-t-butyl-4-methyltropone (91%) as a white crystalline solid, m.p. 38°-39°, $\nu_{max.}^{-1}$ (Nujol) 1638, 1620, 1595 cm^{-1}; $\lambda_{max.}$ 289 nm (ε 7,295); δ 1.35 (9H, s, t-butyl), 1.39 (9H, s, t-butyl), 2.23 (3H, s, CH_3), 6.57 and 6.59 (AB system, J_{AB} = 8Hz); m/z 276 ($M^{+\cdot}$), 219 ($M^{+\cdot}$-t-butyl).

2,4-Di-t-butyl-7-isopropyloxytropone 13.

The reaction between tri-n-butyltin hydride and 2,4-di-t-butyl-6-isopropyloxy-6-dichloromethyl-2,4-cyclohexadienone 12 under the experimental conditions of the general procedure gave 2,4-di-t-butyl-7-isopropyloxytropone 13 (43%). This was a colourless liquid, $\nu_{max.}^{-1}$ (neat) 1645 cm^{-1}; $\lambda_{max.}$ 318 nm (ε 5,476), δ 1.32 s and 1.46 s. (2,4-di-t-butyl and two methyls of isopropyl group), 4.46 to 4.87 (H, m, H-CMe_2), 6.86 and 7.47. (AB system J_{AB} = 6Hz), 7.66 (H, s, H); m/z 276 ($M^{+\cdot}$), 219 ($M^{+\cdot}$-t-butyl). (Found: C, 78.21; H, 10.28; O, 11.39. Calc. for $C_{18}H_{28}O_2$: C, 78.21; H, 10.21; O, 11.57%).

2,7-Dibromo-4-methyltropone 25.

Following the general procedure the reduction of cyclohexadienones 23 and 24 led to the formation of tropone 25 in 40% and 70% yield respectively. The tropone 25 was a crystalline solid, m.p. 127-128°C (dichloromethane), ν_{max} (Nujol) 1655 cm^{-1}; λ_{max} 265, 340 nm (ε 8,732), δ 2.42 (3H, s, CH_3), 6.08 and 8.07 (AB system, J_{AB} = 10Hz), 8.17 (H, s, H); m/z 280, 278 (M^+), 276, 252, 250, 248, 199, 197, 171, 169, 90, 89. (Found: C, 35.13; H, 2.12; Br, 57.42; O, 5.67. Calc. for $C_8H_6Br_2O$: C, 34.57; H, 2.17; Br, 57.50; O, 5.75%)

2,7-Dimethyl-4-[2-(1,3-dioxolanyl)-5,5-dimethyl]tropone 20.

When cyclohexadienones 18 or 19 were treated with tri-n-butyltin hydride in accordance with the general procedure tropone 20 was obtained (25%). This tropone was a colourless thick liquid, ν_{max} (neat) 1645 cm^{-1}; λ_{max} 322 nm (ε 8,570), δ 0.80 (3H, s, CH_3), 1.28 (3H, s, CH_3), 2.32 (6H, s, $2CH_3$), 3.66 (4H, m, $2CH_2$), 5.15 (H, s, H-C<O,O>), 7.10 and 7.28 (AB system, J_{AB} = 10 Hz), 7.50 (H, s, H); m/z 248 ($M^{+\cdot}$), 219, 162 ($M^{+\cdot}$ - $C_5H_{10}O$), 134 ($M^{+\cdot}$ - $C_6H_{11}O_2$). (Found: C, 71.43; H, 8.66; O, 19.82. Calc. for $C_{15}H_{20}O_3$: C, 72.55; H, 8.11; O, 19.33%).

2,4,6,6,9,9-Hexamethyl-6,7,8,9-tetrahydrobenzocycloheptatrien-1-one 28.

When cyclohexadienone 27 was treated with tri-n-butyltin hydride under the experimental conditions as described for tropone synthesis tropone 28 was obtained (80%).

The same tropone was also obtained (28%) from cyclohexadienone 31 when it was treated under the same experimental conditions (see below). Tropone 28 was a crystalline compound, m.p. 91-92° (hexane), ν_{max} (Nujol) 1640 cm^{-1}; λ_{max} 329 nm (ε 3,700), δ 1.21 (6H, s, $2CH_3$), 1.32 (6H, s, $2CH_3$), 1.36 to 1.73 (4H, m, $2CH_2$), 2.13 (3H, s, CH_3), 2.18 (3H, s, CH_3), 6.51 (H, s, H), 6.62 (H, s, H); m/z 244 ($M^{+\cdot}$), 299, 216, 201, 173, 159. (Found: C, 83.39; H, 10.07; O, 6.30. Calc. for $C_{17}H_{24}O$: C, 83.55; H, 9.90; O, 6.55%).

2,5,6,6,9,9-Hexamethyl-6,7,8,9-tetrahydrobenzocycloheptatrien-1-one 32.

The cyclohexadienone 31 in the presence of tri-n-butyltin hydride under the conditions of tropone synthesis was transformed into tropones 28 (see above) and 32 (42%). The same tropone 32 (82%) was also obtained from cyclohexadienone 30 under the same experimental conditions. Tropone 32 was a crystalline solid, m.p. 86-87° (hexane), ν_{max} (Nujol) 1640 cm^{-1}; λ_{max} 326 nm (ε 2,539); δ 1.24 (12H, s, $4CH_3$), 1.4 to 1.7 (4H, m, $2CH_2$), 2.06 (3H, s, CH_3), 2.13 (3H, s, CH_3), 6.15 (2H, s, 2H); m/z 244 ($M^{+\cdot}$), 229, 216, 201, 173, 159. (Found: C, 83.57; H, 9.87; O, 6.29. Calc. for $C_{17}H_{24}O$: C, 83.55; H, 9.90; O, 6.55%).

2,6-Di-t-butyl-4-methyl-4-bromomethyl-2,5-cyclohexadienone 38.

2,6-Di-t-butyl-4-methylphenol 7 (20 mmoles) and cetyltrimethylammoniumbromide (1 mmole) were dissolved in dibromomethane (7 ml). Solution heated to 50°C and then was added drop by drop a sodium hydroxide solution (200 mmoles of NaOH) in water (27 ml). The reaction mixture was stirred overnight. Crushed ice was then added to the reaction mixture and it was then extracted with ether. The ether layer was dried over sodium sulphate and then concentrated. The concentrate was applied to a silica gel column and eluted with a gradient of dichloromethane in hexane to obtain 2,6-di-t-butyl-4-methyl-4-bromomethyl-2,5 cyclohexadienone 38 (24%) as a white crystalline compound, m.p. 66-67° (hexane); ν_{max} (Nujol) 1650, 1365 cm^{-1}; λ_{max} 242 nm (ε 8,138); δ 1.29 (18H, s, two t-butyls), 1.36 (3H, s, CH_3), 3.41 (2H, s, CH_2Br), 6.52 (2H, s, 2H); m/z 314, 312 ($M^{+\cdot}$), 233 ($M^{+\cdot}$ - Br), 220, 219, 205, 177, 161. (Found: C, 61.60; H, 7.97; Br, 25.50; O, 5.21. Calc. for $C_{16}H_{25}BrO$: C, 61.34; H, 8.04; Br, 25.51; O, 5.11%).

2,6-Di-t-butyl-4-methyl-4-trichloromethyl-2,5-cyclohexadienone 39.

2,6-Di-t-butyl-4-methylphenol 7 (20 mmoles) was dissolved in methanol (20 ml) under nitrogen atmosphere. To this sodium methoxide (2.7 g) in dry methanol (40 ml) was added drop by drop. Then under vigorous stirring trichlorobromomethane (8 ml) was added drop by drop. The reaction mixture was heated to 60° and maintained there for two hrs. The reaction mixture was filtered and the filtrate evaporated to dryness. The residue was transferred to a separating funnel with the help of water and extracted with ether. The layer was washed with water and dried over sodium sulphate. The solvant was evaporated under reduced pressure and the concentrate was impregnated onto silica gel which was further loaded on silica gel column. Elution with a gradient of dichloromethane in hexane gave 2,6-di-t-butyl-4-methyl-4-trichloromethyl-2,5-cyclohexadienone 39 (46%) as a white crystalline solid, m.p. 69-70° (hexane:dichloromethane); ν_{max} (Nujol) 1655, 1370 cm^{-1}; λ_{max} 242 nm (ε 10,608); δ 1.30 (18H, s, two-t-butyls), 1.66 (3H, s, CH_3), 6.85 (2H, s, 2H); m/z 341, 339, 337 ($M^{+\cdot}$), 305, 303, 301 ($M^{+\cdot}$ - Cl), 266 ($M^{+\cdot}$ - Cl_2), 251, 219 ($M^{+\cdot}$ - CCl_3), 177, 163. (Found: C, 56.74; H, 6.76; Cl, 31.59; O, 4.48. Calc. for $C_{16}H_{23}Cl_3O$: C, 56.90; H, 6.86; Cl, 31.50; O, 4.73%). This compound was mentioned, but not characterised, before.[13]

Reaction of Tri-n-butyl tinhydride on 2,6-Di-t-butyl-4-methyl-4-bromomethyl-2,5-cyclohexadienone 38.

Cyclohexadienone 38 (0.5 mmole) and AIBN (0.1. mmole) were dissolved in toluene (10 ml) under nitrogen atmosphere. To this was added tri-n-butyltin hydride (0.6 mmole). The solution was heated to reflux and maintained for 72 hours. The solvant was removed under reduced pressure. The concentrate was purified on silica gel preparative plates using hexane and dichloromethane (1:1) as solvant system. Further purification was carried out on HPLC [partisil M9 10/50 C8 column] to obtain 2,7-di-t-butyl-4-methyl-2,6-cycloheptadienone 40 (26%) as a thick colourless liquid, ν_{max} (neat) 1660, 1365 cm^{-1}; λ_{max} 241 nm (ε 5,632); δ 1.06 (3H, d, CH_3), 1.15 (18H, s, 2,6-di-t-butyl), 2.10 (1H, ddd, -C-H), 2.24 (H, ddd, -C-H), 2.45 (H, m, CH_3-C-H), 5.74 (H, d, =C-H), 6.14 (H, dd, =C-H); m/z 234 ($M^{+\cdot}$), 219 ($M^{+\cdot}$ - CH_3), 177 [$M^{+\cdot}$ -t-butyl]. (Found: C, 82.52; H, 10.54; O, 7.12. Calc. for $C_{16}H_{24}O$: C, 82.70; H, 10.41; O, 6.89%).

Reaction of Tri-n-butyltin hydride with 2,6-Di-t-butyl-4-methyl-4-trichloromethyl-2,5-cyclohexadienone 39.

To cyclohexadienone 39 (1 mmole) and AIBN (0.1 mmole) in dry benzene (10 ml) under a nitrogen atmosphere was added tri-n-butyltin hydride (3.75 mmoles) drop by drop with the help of a syringe at room temperature. The reaction mixture was heated to 80°C and maintained for four hrs. The solvant was removed under reduced pressure. The concentrate was applied to silica gel preparative plates; ether:dichlromethane 1:9 was used as a solvant system. The following two compounds were isolated : i) 2,7-di-t-butyl-4-methyltropone 9 with the same characteristics as mentioned above, ii) 2,7-di-t-butyl-4-methyl-5-chlorotropone 41 as a white crystalline solid, m.p. 63-64° (hexane); ν_{max} (Nujol) 1665 cm^{-1}; λ_{max} 289 (ε 6,695); δ 1.32 (18H, s, two t-butyl), 2.27 (3H, s, CH_3), 6.64 (H, s, H), 6.80 (H, s, H); m/z 266 ($M^{+\cdot}$), 251 ($M^{+\cdot}$ - CH_3), 231 ($M^{+\cdot}$ - Cl), 195. (Found: C, 72.02; H, 8.69; Cl, 13.29; O, 5.99. Calc. for $C_{16}H_{23}ClO$: C, 71.75; H, 8.61; Cl, 13.29; O, 5.89%).

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