Cyclodienones. Part 8.[1] Hydrolysis of 5-Oxo-2,4-di-t-Butylcyclopenta-1,3-dienecarbonitrile

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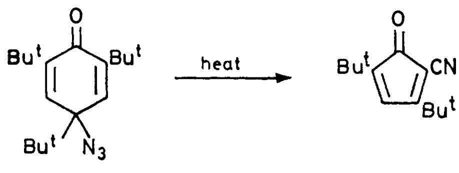
The acid-catalysed hydrolysis of 5-oxo-2,4-di-t-butylcyclopenta-1,3-dienecarbonitrile (2) gave the novel products 3,3a,6,6a-tetrahydro-3,3,3a-trimethyl-5-t-butyl-1*H*-cyclopenta[*c*]furan-1,6-dione (5), 4,5-dimethyl-7-t-butylbicyclo[3.3.0]octa-3,6-diene-2,8-dione (6), and 2-carbamoyl-5-isopropylidene-3-methylcyclopent-2-enone (7), but not the expected carboxylic acid (3). Treatment of compound (5) with 10% NaOH followed by acidification with 10% HCl gave, in 88% yield, the unexpected 2-methyl-5-oxo-4-t-butylcyclopent-1-enecarboxylic acid (8) which, on thermolysis, gave 3-methyl-5-t-butylcyclopent-2-enone (9) and 4-methyl-2-t-butylcyclopent-3-enone (10) in 51 and 36% yields, respectively.

The base catalysed hydrolysis of compound (2) has also been attempted.

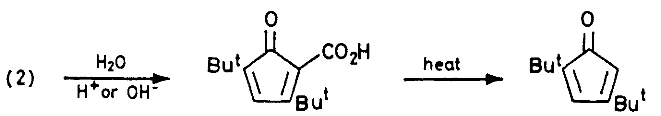
DURING an investigation of the decomposition of 4-azido-2,4,6-tri-t-butylcyclohexa-2,5-dienone (1), the formation of the cyclopentadienone (2) was observed in the thermolysis of compound (1) (Scheme 1). It was expected



(1) (2)

SCHEME 1

that hydrolysis of compound (2) would afford the corresponding carboxylic acid (3) which would then give the known compound (4) by decarboxylation (Scheme 2). However, the acid-catalysed hydrolysis of compound (2)



(3) (4)

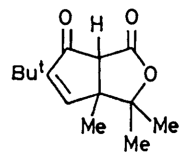
SCHEME 2

gave novel products, but not compound (3); furthermore, treatment of compound (2) with alkali afforded the corresponding salts, but not compound (3). The results are presented in this paper.

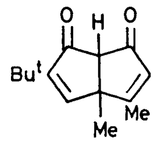
RESULTS AND DISCUSSION

In Acidic Media.—The acid-catalysed hydrolysis of compound (2) was carried out under various conditions and the results are summarized in Table 1.

Treatment of compound (2) with concentrated H_2SO_4 in refluxing acetic acid for 3 h gave the novel product (5) in 72% yield rather than compound (3), the expected product. The structure of compound (5) was assigned on the basis of elemental analysis and spectral results. A molecular model of (5) suggests that it adopts a *cis*-configuration.



(5)



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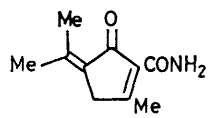


(7)

Under all other conditions employed, lower yields of compound (5) were obtained; in the presence of concentrated H_2SO_4 (run 4), however, two further products resulted, compounds (6) and (7), together with some tar. The structures of (6) and (7) were assigned on the basis of their elemental analyses and spectral results.

Surprisingly, a solution of compound (5) in 10% NaOH when acidified with 10% HCl solution resulted in the formation of the carboxylic acid (8) in 88% yield rather than in recovery of compound (5). Heating of

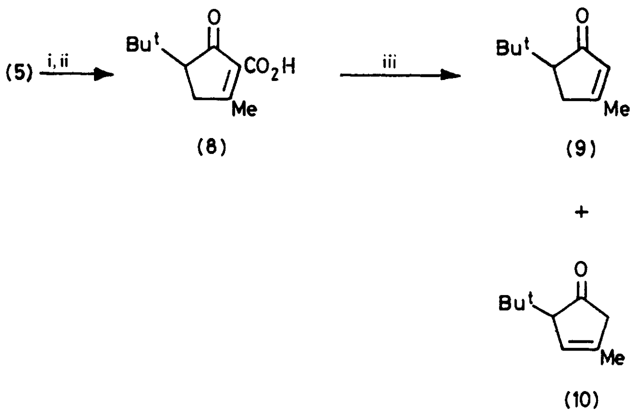
TABLE 1

Hydrolysis of compound (2)

Expt.	Acid	T/°C	t	Product (%)
1	Conc. H_2SO_4–AcOH (4 : 25 v/v)	Reflux	3 h	(5), 72
2	50% H_2SO_4	Reflux	5.5 h	(5), 59
3	75% H_2SO_4	90 [a]	20 min	(5), 28
4	Conc. H_2SO_4	90 [a]	5 min	(5), 1; (6), [b]; (7), 16

[a] Temperature of water-bath. [b] Trace.

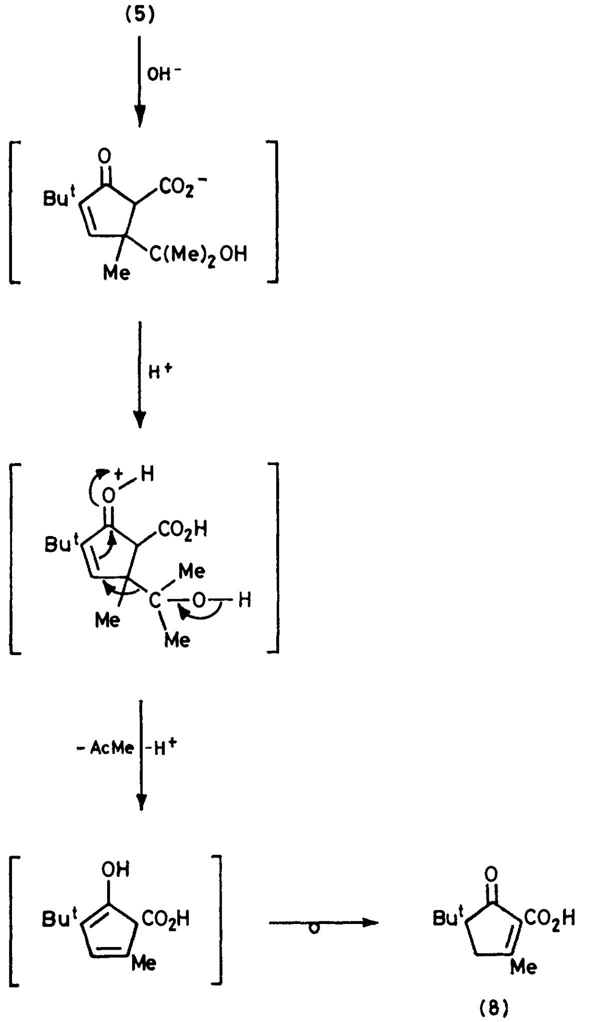
compound (8) in pyridine afforded the cyclopent-2-enone (9) and the cyclopent-3-enone (10) in 51 and 36% yields, respectively (Scheme 3). Elemental analyses and spectral results support the structural assignments for compounds (8), (9), and (10) which appear to belong to



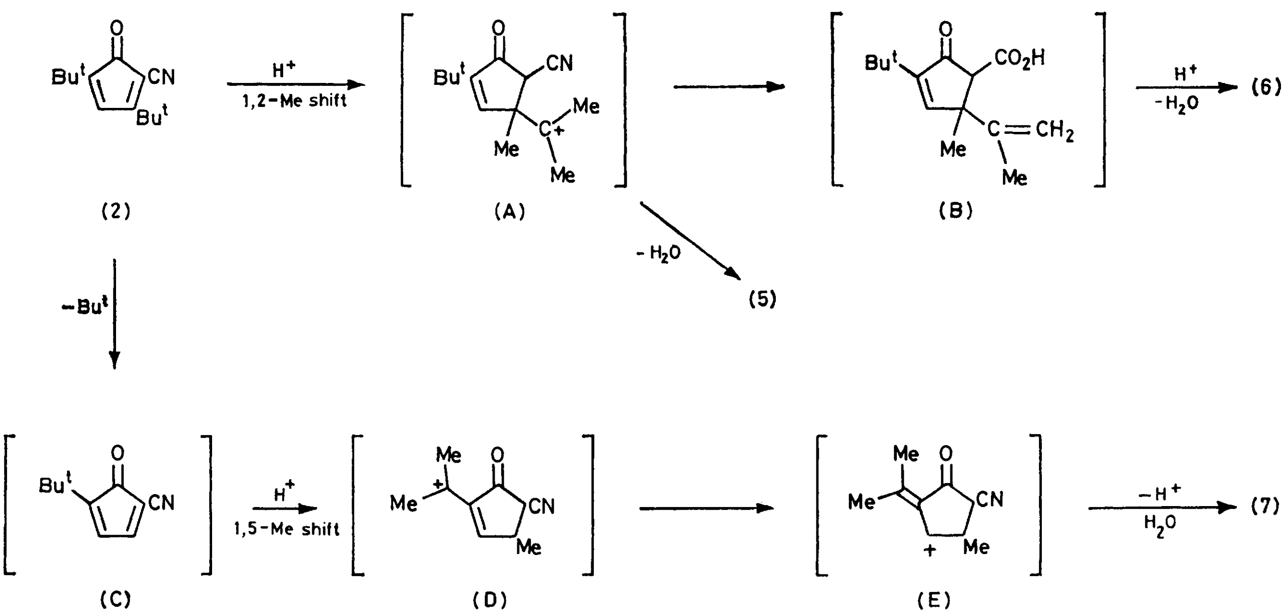
SCHEME 3 *Reagents*: i, 10% NaOH; ii, 10% HCl; iii, heat, pyridine

the Jasmonoid family;[2] indeed, compounds (9) and (10) smell of peppermint. The formation of compounds (8), (9), and (10) from compound (5) supports our structural assignment for the latter. The reaction pathway for the formation of the acid (8) from compound (5) is tentatively proposed as that shown in Scheme 4. A reaction path for the formation of compounds (5), (6), and (7) from compound (2) is tentatively proposed in Scheme 5.

Since the intermediate (A) should be more stable than the intermediate (C), except in the presence of concentrated sulphuric acid, compound (5) would be the sole product. That compound (6) was formed only when the hydrolysis of compound (2) was carried out in con-

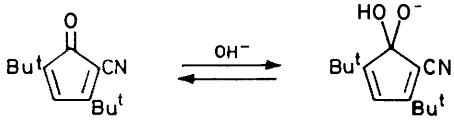


SCHEME 4



SCHEME 5

centrated sulphuric acid suggests that formation of the intermediate (B) from the intermediate (A) must be more difficult than that of compound (5). Compound (7) should also be formed only in strong acidic media because intermediate (C) might be less stable than intermediate (A).



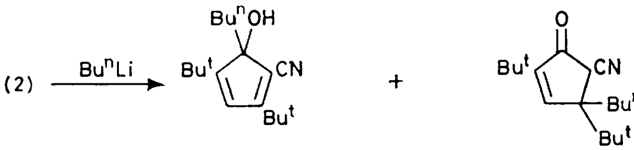
(2) (11)

Reddish-orange Colourless

SCHEME 6

In Alkaline Media.—Addition of 10% aqueous NaOH solution to an ethanolic solution of compound (2) resulted in immediate discharge of the reddish-orange colour. The reaction was reversible on the addition of 10% aqueous HCl with almost quantitative recovery of starting material (Scheme 6). Similar results were obtained with $Ba(OH)_2$, Na_2CO_3, 1,5-diazabicyclo[5.4.0]-undec-5-ene, and NaOEt, but not $NaHCO_3$.

The reaction of compound (2) with Bu-Li at −78 °C in tetrahydrofuran (THF) afforded compounds (12) and (13) in 43 and 22% yields, respectively (Scheme 7).



(12) (13)

SCHEME 7

The salt (11) described above, is stable and was isolated, but not purified. The crude compound (11) (Na salt) did not show a C=O signal in its i.r. spectrum. From the above results and a comparison of the spectral data of compound (12) with that of the salt (11), the structure of the salt is proposed as (11).

Attempted hydrolysis of compound (2) with NaOH under refluxing conditions was not successful, giving an almost quantitative yield of starting material.

EXPERIMENTAL

Hydrolysis of Compound (2) *with Concentrated* H_2SO_4 *in Acetic Acid.*—After a solution of compound (2) (4 g, 18 mmol) and concentrated H_2SO_4 (8 ml) in acetic acid (50 ml) had been refluxed for 3 h, it was poured into a large volume of ice–water and left overnight. The resultant precipitate was filtered off to give 3,3a,6,6a-*tetrahydro*-3,3,3a-*trimethyl*-5-*t-butyl*-1H-*cyclopenta*[c]*furan*-1,6-*dione* (5) as plates (from hexane), m.p. 108—109 °C; ν (KBr) 1 770 and 1 710 cm^{-1} (C=O); δ_H ($CDCl_3$) 1.20 (9 H, s), 1.30, 1.44, and 1.46 (each 3 H, s), 3.24 (1 H, d, *J* 1 Hz), and 7.16 (1 H, d, *J* 1 Hz); δ_C ($CDCl_3$) 20.0 (q), 22.6 (q), 26.8 (q), 31.9 (s), 51.2 (s), 61.5 (d), 86.4 (s), 151.8 (s), 157.5 (d), 108.6 (s), and 197.4 p.p.m. (s); *m/e* 236 (M^+) (Found: C, 71.15; H, 8.5. $C_{14}H_{20}O_3$ requires C, 71.16; H, 8.53%).

Hydrolysis of Compound (2) *with* 50% H_2SO_4.—A suspension of compound (2) (0.296 g, 1.4 mmol) and 50% H_2SO_4 (20 ml) was refluxed for 5.5 h. The reaction mixture was treated and worked up as described above to give compound (5) (0.189 g, 59%).

Hydrolysis of Compound (2) *with* 75% H_2SO_4.—A suspension of compound (2) (1 g, 4.6 mmol) in 75% H_2SO_4 (20 ml) was heated on a water-bath (*ca.* 90 °C). After *ca.* 10 min, the reaction mixture became a solution. After the solution had been heated for an additional 10 min, it was poured into a large volume of ice–water and extracted with $CHCl_3$. The $CHCl_3$ extract was dried (Na_2SO_4) and then evaporated under reduced pressure to leave a residue to which a small amount of cooled methanol was added to give compound (5) (0.3 g, 28%).

Hydrolysis of Compound (2) *with Concentrated* H_2SO_4.—After a suspension of compound (2) (2.28 g, 10 mmol) in concentrated H_2SO_4 (45 ml) had been heated on a water-bath (*ca.* 80 °C) for 5 min, it was poured into a large volume of ice–water, neutralized with $NaHCO_3$, and then extracted with $CHCl_3$. The $CHCl_3$ extract was dried (Na_2SO_4) and evaporated under reduced pressure to leave the residue to which a small amount of cooled methanol was added to give 2-*carbamoyl*-5-*isopropylidene*-3-*methylcyclopent*-2-*enone* (7) (0.12 g) as prisms (from MeOH), m.p. 214—215 °C; ν 3 325 and 3 150 (NH), and 1 680 and 1 670 cm^{-1} (C=O); δ_H ($CDCl_3$) 1.92, 2.32, and 2.60 (each 3 H, s), 3.16 (2 H, s), and 5.50br and 8.52br (each 1 H, s, disappeared with D_2O); *m/e* 179 (M^+) (Found: C, 66.75; H, 7.4; N, 7.7. $C_{10}H_{13}NO_2$ requires C, 67.02; H, 7.31; N, 7.31%).

After compound (7) had been filtered off, the filtrate was chromatographed on silica gel using a mixture of ethyl acetate and chloroform (1 : 6) as eluant to give compound (5) (20 mg, 1%), compound (7) (26 mg), and a trace of 4,5-*dimethyl*-7-*t-butylbicyclo*[3.3.0]*octa*-3,6-*diene*-2,8-*dione* (6) as pale yellow prisms, m.p. 109—111 °C; ν (KBr) 1 710 (C=O) and 1 620 cm^{-1} (C=C); δ_H ($CDCl_3$) 1.14 (9 H, s), 1.46 (3 H, s), 2.12 (3 H, d, *J* 1.5 Hz), 3.06 (1 H, s), 5.60 (1 H, q, *J* 1.5 Hz), and 7.08 (1 H, s) (Found: *m/e* 218.1288. Calc. for $C_{14}H_{18}O_2$: *M*, 218.1296).

Preparation of 2-*Methyl*-5-*oxo*-4-*t-butylcyclopentenecarboxylic Acid* (8).—After a suspension of compound (5) (0.55 g, 2.3 mmol) in 5M NaOH (10 ml) had been heated on a water-bath (*ca.* 90 °C) for 10 min, it was poured into a large volume of ice–water, acidified with dilute HCl (1 : 1), and then extracted with $CHCl_3$. The $CHCl_3$ extract was washed with water, dried (Na_2SO_4), and then evaporated under reduced pressure to give the *acid* (8) (0.4 g, 88%) as prisms (from hexane), m.p. 74.5—75 °C; ν (KBr) 1 740 and 1 670 (C=O), and 1 620 cm^{-1} (C=C); δ_H ($CDCl_3$) 1.00 (9 H, s), 2.45 (1 H, dd, *J* 3.5 and 6.0 Hz), 2.56 (1 H, dd, *J* 3.5 and 20 Hz), 2.63 (3 H, s), and 2.84 (1 H, dd, *J* 6 and 20 Hz); δ_C ($CDCl_3$) 13.6 (q), 27.2 (q), 33.7 (s), 37.8 (t), 55.0 (d), 128.2 (s), 162.0 (s), 192.35 (s), and 212.5 p.p.m. (s) (Found: C, 67.2; H, 8.2. $C_{11}H_{16}O_3$ requires C, 67.32; H, 8.22%).

Thermolysis of the Acid (8).—After a solution of the acid (8) (9.5 g, 50 mmol) in pyridine (100 ml) had been heated on an oil-bath (*ca.* 130—135 °C) for 50 min, it was poured into a large volume of ice–water, acidified with dilute HCl (1 : 1), and then extracted with diethyl ether. The diethyl ether extract was dried (Na_2SO_4) and then evaporated under reduced pressure at room temperature to give a pale yellow oil (6.5 g) which smelt of peppermint. The oil obtained was purified by chromatography (silica gel; $CHCl_3$) to give two compounds (9) and (10) in a 5 : 7 distribution (by g.c.), which were identified as 3-methyl-5-t-butylcyclopenta-2-enone (9), a pale yellow liquid; ν (NaCl) 1 700 (C=O) and 1 640 cm^{-1} (C=C); δ_H ($CDCl_3$) 0.98 (9 H, s), 2.08 (3 H, s), 2.16 (1 H, dd, *J* 3.5 and 6.0 Hz), 2.34 (1 H, dd, *J* 3.5 and 20 Hz), 2.60 (1 H, dd, *J* 6 and 20 Hz), and 5.80 (1 H, q, *J* 1.5 Hz); δ_C ($CDCl_3$) 19.6 (q), 27.3 (q), 33.1 (s), 36.9 (t), 55.8 (d), 131.3 (d), 176.0 (s), and 210.6 p.p.m. (s); *m/e* 152 (M^+); and 4-methyl-2-t-butylcyclopent-3-enone (10), a liquid; ν (NaCl) 1 750 cm^{-1} (C=O); δ_H ($CDCl_3$) 0.94 (9 H, s), 1.86 (3 H, m), 2.56 (1 H, m), 2.68 br (2 H, s), and 5.68 (1 H, m); δ_C ($CDCl_3$) 17.5 (q), 27.2 (q), 34.5 (s), 47.45 (t), 63.2 (d), 125.2 (d), 138.1 (s), and 217.5 p.p.m. (s); *m/e* 152 (M^+).

Elemental analyses of compounds (9) and (10) could not be carried out because of the high volatility of these compounds.

Titration of Compound (2) *with Alkali Solution*.—A solution of compound (2) (*ca.* 100 mg) in pure ethanol (10 ml) was titrated with 0.23M NaOH or 0.17M $Ba(OH)_2$ solution. In each case, the equivalence point was determined by a change of the colour from reddish orange to colourless.

Reaction of Compound (2) *with* Bu-Li.—To a solution of compound (2) (0.895 g, 4.1 mmol) in dry THF (20 ml) was added at −78 °C, a solution of Bu-Li in hexane (2.5 ml; Bu-Li–hexane, 1 mmol : 0.63 ml) under a stream of nitrogen. The reaction mixture was stirred for 1.5 h and then a further portion of Bu-Li–hexane (0.5 ml) solution was added. After 1 h, another portion of Bu-Li–hexane (0.2 ml) solution was added to the reaction mixture. After the reaction mixture had been left for an additional 3.5 h, it was poured into a large volume of ice–water, acidified with dilute HCl (1 : 1), and then extracted with $CHCl_3$. The $CHCl_3$ extract was dried (Na_2SO_4) and then evaporated under reduced pressure to leave a residue which was chromatographed on silica gel, using $CHCl_3$ as eluant, to afford 5-*butyl*-5-*hydroxy*-2,4-*di*-*t*-*butylcyclopenta*-1,3-*dienecarbonitrile* (12) (0.486 g, 43%) as a pale yellow liquid; ν (NaCl) 3 450 (OH) and 2 200 cm^{-1} (CN); δ_H ($CDCl_3$) 0.7—1.1 (5 H, m), 1.24 and 1.28 (each 9 H, s), 1.30—2.20 (5 H, m, 1 H disappeared with D_2O), and 6.40 (1 H, s); δ_C ($CDCl_3$) 13.9, 22.6, 25.0, 34.25, 28.9 (q), 30.3 (q), 35.0 (s), 35.8 (s), 90.6 (s), 113.2 (s), 116.5 (s), 125.6 (d), 165.8 (s), and 167.0 p.p.m. (s); *m/e* 275 (M^+) (Found: C, 78.7; H, 10.8; N, 5.2. $C_{18}H_{29}NO$ requires C, 78.49; H, 10.61; N, 5.09%); and 2-*butyl*-5-*oxo*-2,4-*di*-*t*-*butylcyclopenta*-3-*enecarbonitrile* (13) as prisms (from hexane), m.p. 88—89 °C; ν (KBr) 2 250 (C≡N) and 1 720 cm^{-1} (C=O); δ_H ($CDCl_3$) 0.70—1.00 (5 H, m), 1.00 and 1.19 (each 9 H, s), 1.30—1.96 (4 H, m), 3.44 (1 H, s), and 7.00 (1 H, s); δ_C ($CDCl_3$) 13.8, 23.0, 27.6, 30.6 (Bu), 25.9 (q), 28.3 (q), 32.1 (s), 44.7 (d), 54.0 (s), 116.5 (s), 151.3 (s), 158.5 (d), and 196.9 p.p.m. (s); *m/e* 219 (M^+ − 56) (Found: C, 78.8; H, 10.7; N, 4.9. $C_{18}H_{29}NO$ requires C, 78.49; H, 10.61; N, 5.09%).

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