

## A New Approach to the Synthesis of Catena-compounds

H. LARKEM and A. LARKEM \*

*Department of Chemistry, University of Annaba, Annaba-23000, Algeria*

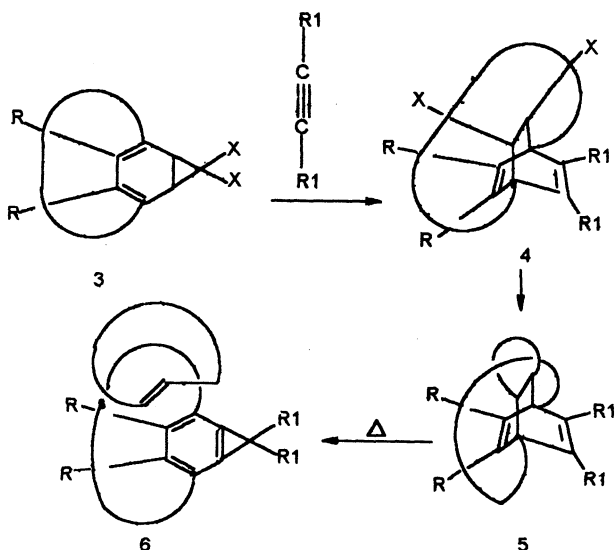
*Email: larkem\_a@yahoo.fr*

This paper describes the preparation of the macrocyclic cyclopentadienone (2), which was accomplished by the following method from diacetylenic ketone. Benzil was condensed with a long chain ketone to give (1) and the macrocycle (2) formed in a subsequent step.

**Key Words:** Synthesis, Cyclopentadienone, Diacetylenic ketone.

### INTRODUCTION

In a new approach to the directed synthesis of catena-compounds<sup>1,2</sup>, it was proposed to prepare a cyclohexa-1,3-diene (3), incorporating a macrocycle, two sterically bulky groups R and two functional groups X with *trans* stereo-chemistry. Diels-Alder addition of disubstituted acetylene would then be expected to occur on the least hindered face of (3), giving structure (4). Attachment of a long chain to the X groups, followed by ring-closure, would produce a precatenane (5), which on thermolysis would undergo a retro-Diels-Alder reaction to give the catenane (6).

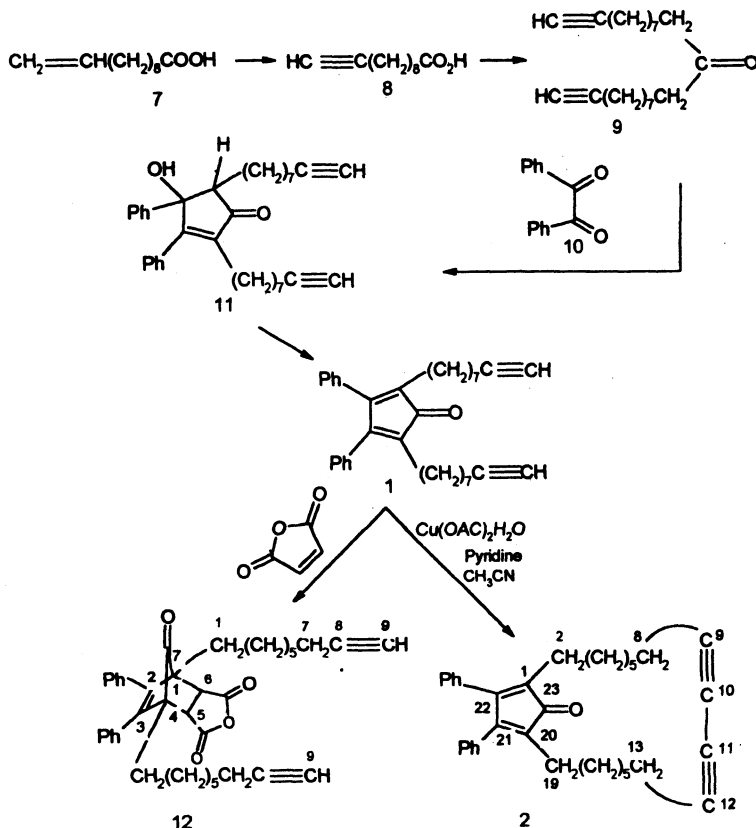


It was thought that the preparation of a suitable cyclohexa-1,3-diene system (3) would be accomplished as mentioned later on. Alternatively, benzil (10) could be condensed with a long chain ketone<sup>3, 4</sup> of the type (9) giving rise to the compound 1.

The chosen starting material for this long chain ketone was undec-10-ynoic acid (8) which could be converted into heneicososa-1,20-diyne-11-one (9) by known procedure<sup>5</sup>.

## RESULTS AND DISCUSSION

For the preparation of the macrocyclic cyclopentadienone (2), undec-10-ynoic acid (8) was the chosen starting material. Undec-10-ynoic acid (8) is known to be best prepared (on a large scale) from the readily available undec-10-enoic acid by the addition of bromine followed by elimination using potassium hydroxide in ethanol<sup>6</sup>, but the yields were poor (usually 30% or less)<sup>7</sup>. Somewhat higher yields (38–49%) were obtained with sodamide in liquid ammonia<sup>7</sup> or in white spirit (55%)<sup>8</sup>. Excellent yields of terminal acetylenes, however, have been achieved by the use of potassium *t*-butoxide in hydrocarbons containing 18-crown-6.<sup>9</sup> The conversion of the acetylene acid (8) into the diacetylenic ketone (9) has been achieved according to reported method<sup>5</sup>.

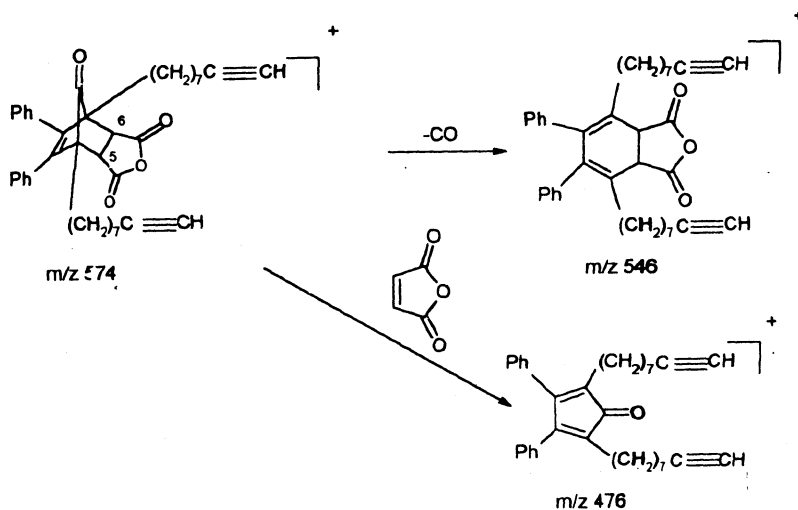


Scheme-1

Furthermore, a general method for the preparation of cyclopentadienones (cyclones) involves a double Aldol-type condensation between a suitable 1,2-diketone and a monoketone containing the  $\text{CH}_2\text{COCH}_2$  grouping<sup>3</sup>. In the present investigation, the ketone (**9**) was reacted slowly with benzil (**10**) in the presence of potassium hydroxide to give hypothetical compound carbinol (**11**). This was isolated by chromatography and dehydrated with thionyl chloride in pyridine to afford the cyclone (**1**). The spectral evidence was consistent with the expected structure (**1**).

The maleic anhydride adduct **12** was characterized by its mass spectrum which showed a base peak at  $m/z$  574 (100%) (molecular ion) and a peak at  $m/z$  546 (33%) corresponding to the loss of carbon monoxide from the molecular ion ( $M$   $m/z$  574) and another fragment ion at  $m/z$  476 (64%) of base peak ( $M$ -maleic anhydride).

Attention was then turned to the cyclization of **1** to produce **2**. The classical Eglinton-Galbraith procedure<sup>10</sup> was adopted. It involves the use of copper(II) acetate in pyridine to effect intramolecular oxidative coupling of the diacetylene in the presence of ether as a co-solvent.



In the present investigation, acetonitrile was used as the co-solvent and special high-dilution condition was found to be unnecessary. Thus, slow addition of a solution of diacetylene (**1**) in acetonitrile to a refluxing solution of the catalyst gave rise to the macrocyclic cyclone (**2**) as an orange oil in 79% yield. The spectral evidence indicated that cyclization has been achieved.

## EXPERIMENTAL

Unless otherwise stated, the following conditions apply. Thin layer chromatography (TLC), using silica plates, was the tool following up the reaction mixture

during and after each process, the plates being examined under UV light at 254 or 336 nm. Column chromatography was carried out on either silica gel (60–120 mesh) or Merck kieselgel (60 H). Infrared spectra were recorded on a Perkin-Elmer 1420 spectrophotometer. Mass spectra were recorded on an AET MS9 Instrument updated with VG ZAB components. Nuclear magnetic resonance spectra were recorded on a JEOL G × 270 instrument using TMS as the internal standard.

### Undec-10-ynoic Acid (8)

A solution of undec-10-enoic acid (7) (50.0 g, 0.27 mol) in sodium-dried ether (230 mL) was cooled in an ice-salt bath ( $-10^{\circ}\text{C}$ ) while bromine (42.6 g, 0.27 mol) was added dropwise with stirring, at such a rate that the temperature did not rise above  $0^{\circ}\text{C}$ . The ether was then removed under reduced pressure and the formed dibromide was taken up in sodium-dried toluene (135 mL). This solution was added slowly to vigorously stirred slurry of potassium *t*-butoxide (100 g) in dry toluene (400 mL) containing 18-crown-6 (0.15 g), with cooling in a water-bath. When the initial reaction had subsided down, the mixture was stirred at  $60\text{--}65^{\circ}\text{C}$  (bath temperature) for 2 h, cooled and ice was added. The mixture was then acidified with concentrated HCl (135 mL). The toluene layer was separated and the aqueous layer was extracted with toluene (35 mL); the combined toluene solutions were washed with water (65 mL), dried ( $\text{MgSO}_4$ ) and evaporated under reduced pressure. The residue was finally distilled, giving the acetylenic acid (8) (33.2 g, 67%), (b.p.  $110\text{--}120^{\circ}\text{C}/0.04$  mm Hg), which crystallized in the receiver. IR ( $\text{cm}^{-1}$ )  $\nu_{\text{max}}$  (Nujol): 3325  $\nu(\text{OH})$ , 3298  $\nu(\equiv\text{CH})$ , 2115  $\nu(\text{C}\equiv\text{C})$ , 1707  $\nu(\text{CO})$ .  $^1\text{H}$  NMR (270 MHz;  $\text{CDCl}_3$ ): 2.35 (2H, t,  $\underline{J} = 7.5$  Hz,  $2 \times \text{H-2}$ ), 2.18 (2H, td,  $\underline{J} = 7$  and 2.5 Hz;  $2 \times \text{H-9}$ ), 1.94 (1H, t,  $\underline{J} = 2.5$  Hz, H-11), 1.75–1.2 ppm (12 H, m). The preparation was repeated several times on various scales; the yields were 63–69%.

### Heneicosa-1,20-diyne-11-one (9)

This was prepared essentially as described by Bergeson *et al.*<sup>5</sup> A mixture of undec-10-ynoic acid (8) (22.0 g, 0.12 mol), thionyl chloride (16.3, 10.0 mL) and dry toluene (40 mL) was heated slowly to reflux temperature and then refluxed for 2 h. The toluene and excess of thionyl chloride were removed under reduced pressure and more toluene was distilled from the residue. The resulting acid chloride was immediately taken up in dry ether (100 mL) and the solution was cooled in ice-water while dry triethylamine (12.2 g, 11.4 mL) was added slowly (during 4 min) with stirring and continued for 1 h and the mixture was left overnight at room-temperature, then treated with 2% aqueous sulphuric acid (30 mL). The organic material was collected in dichloromethane, the solution was dried ( $\text{MgSO}_4$ ), evaporated and the residue was refluxed for 2 h with 2% aqueous potassium hydroxide (200 mL). The product was extracted with ether and the ethereal solution was washed with water, dried ( $\text{MgSO}_4$ ) and evaporated. The crude ketone (9) (16.3 g) was subjected to dry column 'flash' chromatography (using suction) on silica (Merck 60H). Elution with ethyl acetate-light petroleum (b.p.  $30\text{--}40^{\circ}\text{C}$ ) (1 : 3) gave the ketone (9) (9.40, 51%) as pale yellow oil, which

crystallized on standing. A sample purified by repeated recrystallization from methanol at 0°C had m.p. 43.5–45°C (Lit.<sup>4</sup> 46–47°C). IR ( $\text{cm}^{-1}$ )  $\nu_{\text{max}}$  (Nujol) : 3295  $\nu(\equiv\text{CH})$ , 2115  $\nu(\text{C}\equiv\text{C})$ , 1705  $\nu(\text{CO})$ .  $^1\text{H}$  NMR (270 MHz;  $\text{CDCl}_3$ ): 2.38 (4H, t,  $\underline{J}$  = 7.5 Hz; H-10 and H-12), 2.19 (4H, td,  $\underline{J}$  = 7 and 2.5 Hz; H-3 and H-19), 1.94 (2H, t,  $\underline{J}$  = 2.5 Hz; H-1 and H-21), 1.75–1.1 ppm (24H, m).

### 2,5-Di (non-8-ynyl)-3,4-diphenylcyclopenta-2,4-dienone (1)

To a solution of the diacetylenic ketone (9) (9.40 g, 0.03 mol) in ether (25 mL) a cold solution of potassium hydroxide (10.0 g) in methanol (75 mL) was added, followed by benzil (10) (6.50 g, 0.03 mol) and the mixture was stirred at room-temperature for 89 h, when a white precipitate was formed. The mixture was poured into water (300 mL) and extracted with dichloromethane (200 mL) and the extract was washed with water and dried ( $\text{MgSO}_4$ ). The solvent was evaporated under reduced pressure and the residue was crystallized from methanol to recover benzil (2.2 g). Dry-column 'flash' chromatography of the methanol-soluble fraction on silica (Merck 60H) (using suction) then gave the carbinol (11) (3.30 g) eluted with 200 mL of ethyl acetate-light petroleum (b.p. 60–80°C) (3 : 2) respectively. Acidification of the aqueous layer after the above extraction with dichloromethane gave recovered ketone (9) (2.3 g). The carbinol (11) (3.30 g) was taken up in dry pyridine (5 mL) and thionyl chloride (0.90 g, 0.55 mL) was added slowly, with swirling and cooling in ice water; the solution became red and crystals separated. The mixture was left for 24 h at room temperature and then acidified with 10% aqueous hydrochloric acid. Extraction with light petroleum (b.p. 40–60°C), followed by washing the extract with water, drying ( $\text{MgSO}_4$ ) and removal of the solvent under reduced pressure, gave the crude cyclone (1) (8 g, 54%) as a red oil. IR ( $\text{cm}^{-1}$ )  $\nu_{\text{max}}$  (Nujol): 3310  $\nu(\equiv\text{CH})$ , 2115  $\nu(\text{C}\equiv\text{C})$ , 1700  $\nu(\text{CO})$ . MS  $m/z$ : 476  $\nu(\text{M};$  base peak).  $^1\text{H}$  NMR (270 MHz,  $\text{CDCl}_3$ ): 7.4–6.8 (10H, m; Ar-H), 2.25 (4H, t,  $\underline{J}$  = 7.5 Hz; 4  $\times$  H-1), 2.14 (4H, td,  $\underline{J}$  = 7 and 2.5 Hz; 4  $\times$  H-7), 1.92 (2H, t,  $\underline{J}$  = 2.5 Hz; 2  $\times$  H-9), 1.6–1.0 ppm (20H, m).

### 1,4-Di(non-8-ynyl)-7-oxo-2,3-diphenylbicyclo [2.2.1] hept-2-ene-cis-endo-5,6-dicarboxylic acid anhydride (12)

A mixture of the cyclone (1) (1.37 g,  $3 \times 10^{-3}$  mol) and maleic anhydride (0.82 g,  $8 \times 10^{-3}$  mol) in dry toluene (10 mL) was heated under reflux for 24 h. The solvent was removed under reduced pressure and the residue was chromatographed on silica (Merck 60H). Elution with ethyl acetate-light petroleum (b.p. 40–60°C) (1 : 8) gave the adduct (12) as a pale yellow oil (1.16 g, 70%). IR ( $\text{cm}^{-1}$ )  $\nu_{\text{max}}$  (Nujol): 3310  $\nu(\equiv\text{CH})$ , 2115  $\nu(\text{C}\equiv\text{C})$ , 1864 and 1773  $\nu(\text{anhydride CO})$ , 1779  $\nu(\text{bridge CO})$ . MS  $m/z$ : 546 (M-CO), 476 (M-maleic anhydride).  $^1\text{H}$  NMR (270 MHz,  $\text{CDCl}_3$ ): 7.5–7.0 (10H, m; Ar-H), 3.76 (2H, s, H-5 and H-6), 2.25–1.85, 10H, m, with features at 2.15 (td,  $\underline{J}$  = 7 and 2.5 Hz, 4  $\times$  H-7 in side-chain) and 1.93 (t,  $\underline{J}$  = 2.5 Hz; 2  $\times$  H-9), 1.7–1.0 ppm (20H, m).

### 21,22-Diphenylbicyclo [18.2.1] tricoso-1(22), 20-dien-9,11-diyn-23-one (2)

Copper(II) acetate monohydrate (0.50 g) was dissolved in pyridine (10 mL),

and acetonitrile (15 mL) was added. To this the stirred and refluxing solution was added during 4.5 h a solution of the cyclone (1) (0.25 g) in acetonitrile (5 mL); heating was then discontinued and the mixture was stirred overnight. Most of the acetonitrile was removed under reduced pressure; water (30 mL) was added and the product was collected in light petroleum (b.p. 40–60°C). The extract was washed with 2% aqueous sulphuric acid, dried (MgSO<sub>4</sub>) and evaporated to give the crude cyclone (2) 0.35 g, which was chromatographed on silica gel using ethyl acetate-light petroleum (1 : 3) as eluent to give the title compound (2) 0.19 g, 79% as an orange oil. IR (cm<sup>-1</sup>)  $\nu_{\max}$  (Nujol): 1695  $\nu$ (CO). MS *m/z* 474 (M; base peak). <sup>1</sup>H NMR (270 MHz; CDCl<sub>3</sub>): 7.35–6.85 (10H, m; Ar-H), 2.4–2.1 (8H, m; 2 × H-2), 2 × H-19 (4H at 2.27,  $J = 7.5$  Hz), 2 × H-8 and 2 × H-13), 1.55–1.15 ppm (20H, m).

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*Contact:*

Adria Congrex

Via Virgilio 30, 47838 Riccione (RN), Italy

Tel.: (+39-0541) 691-150; Fax: (+39-0541) 692-232

E-mail: l.banini@adriacongrex.it

URL: www.adriacongrex.it