

3-ACETYL AND 3-CARBOXY DERIVATIVES OF 7,10,14-TRI-*t*-BUTYL-1,8-BISDEHYDRO[14]-ANNULENE AND THE pK_a' -VALUE OF THE LATTER COMPOUND

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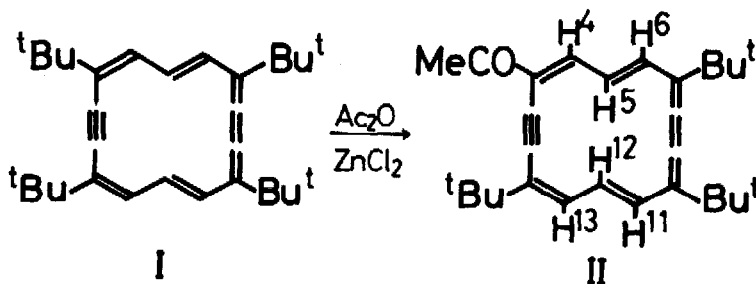
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Formation of 3-substituted derivatives by various substitution reactions of 1,8-bisdehydro[14]annulene (1) suggests that the most reactive sites in the bisdehydro[14]annulene ring are the positions adjacent to *sp*-hybridized carbon atoms. Considering the fact that *t*-butyl cation has been known to be a nice leaving group (2), we have tried the replacement of *t*-butyl groups in 3,7,10,14-tetra-*t*-butyl-1,8-bisdehydro[14]annulene (I) (3) under conditions of electrophilic substitution reactions.

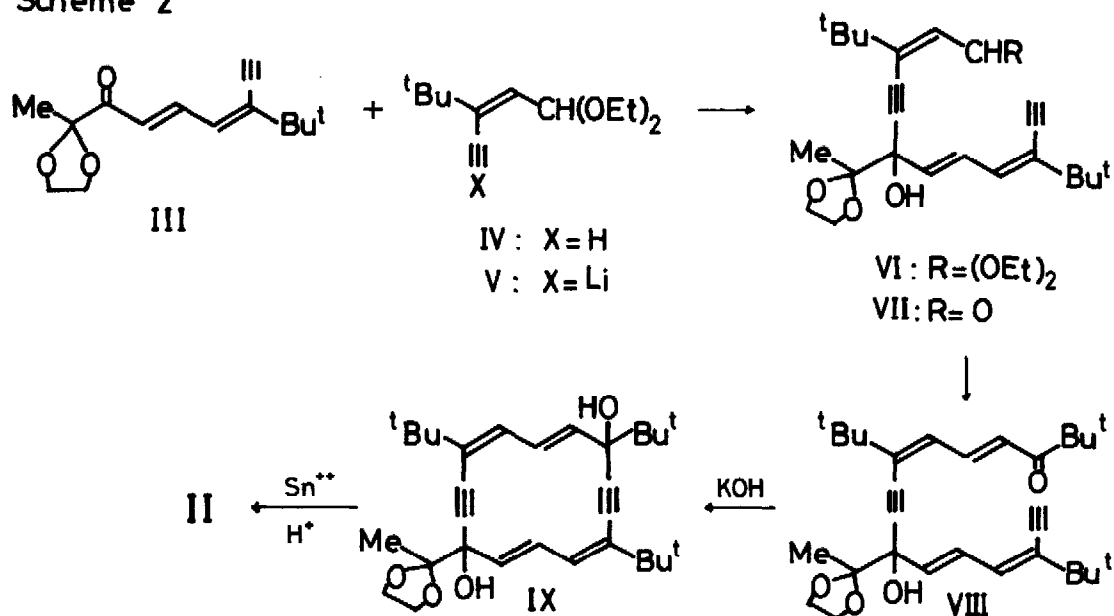
After several experimentations, it was found that 3-acetyl-7,10,14-tri-*t*-butyl-1,8-bisdehydro[14]annulene (II) can be obtained under limited reaction conditions (Scheme 1). Anhydrous zinc chloride (560 mg) was added to a stirred solution of tetra-*t*-butylbisdehydro[14]annulene (I, 152 mg) in 1,1,2,2-tetrachloroethane (60 ml) and acetic anhydride (60 ml) maintained at 140°C. After 30 sec., the reaction mixture was poured onto ice-water to quench the reaction, and extracted with ether. The product dissolved in hexane-benzene was chromatographed on silica gel (Merck, 50 g), and eluted with the same mixed solvent to give recovered I (115 mg, 76%). Further elution with benzene yielded acetylannulene (II, reddish brown crystals; 12 mg, 8.2%, 33.6% based on consumed I; mp 191.0-192.0°C; Mass: m/e 388 (M^+); UV: λ_{max} (THF) 238 (ϵ 6830), 273sh (8090), 284.5 (10800), 341.5 (110000), 481 (20700), 542 (1400), 561 (1310), 612 (7190) nm; IR (KBr-disk): 2080, 2020 ($C\equiv C$), 1661 ($C=O$), 980 (*trans* $C=C$) cm^{-1} ; nmr ($CDCl_3$): 14.16dd ($J=13.5, 14.5, H^5$), 13.88t ($J=13.5, H^{12}$), 8.13s, 8.11s, 8.09s,

Scheme 1



(*t*-Bu), 6.70s (-COCH₃), 0.68d, 0.66d (*J*=13.5, H¹¹, H¹³), 0.48d (*J*=13.5, H⁴), 0.05d (*J*=14.5, H⁶); 2,4-dinitrophenylhydrazone, brown crystals, mp >300°C (4,5). The structure of II was further confirmed by another synthesis (Scheme 2). Ethylene ketal of acetoin (colorless liquid, bp 88-89°C/24 mmHg) prepared in the usual way was oxidized with chromium trioxide in aqueous acetone containing sulphuric acid to give biacetyl monoethylene ketal (colorless liquid, bp 90-92°C/55 mmHg). The aldol condensation of 3-*t*-butyl-2-penten-4-ynal (6) with biacetyl monoethylene ketal yielded III (lemon yellow crystals, mp 63.2-63.7°C). Diethyl acetal of 3-*t*-butyl-2-penten-4-ynal (IV) (7) was converted into the lithio derivative (V) with butyllithium. The reaction of III with V in ether afforded VI which was hydrolyzed with 1% aqueous tartaric acid to give VII (pale yellow viscous liquid, 61% based on IV). The ketal aldehyde (VII) in ethanol was mixed with pinacolone in the presence of sodium hydroxide, and the product was chromatographed on silica gel (Merck). Elution with benzene-ether (8:2) yielded VIII (pale yellow crystalline powder, 69%). A solution of VIII in tetrahydrofuran was added to a suspension of potassium hydroxide in liquid ammonia, and the reaction mixture was worked up in the usual manner. Crude IX (light brown crystalline solid) was treated at -55°C with stannous chloride dihydrate in ether saturated with hydrogen chloride. Acetylannulene (II, 10% based on VIII), thus prepared, was found to be identical in every respect to II prepared by the route shown in Scheme 1.

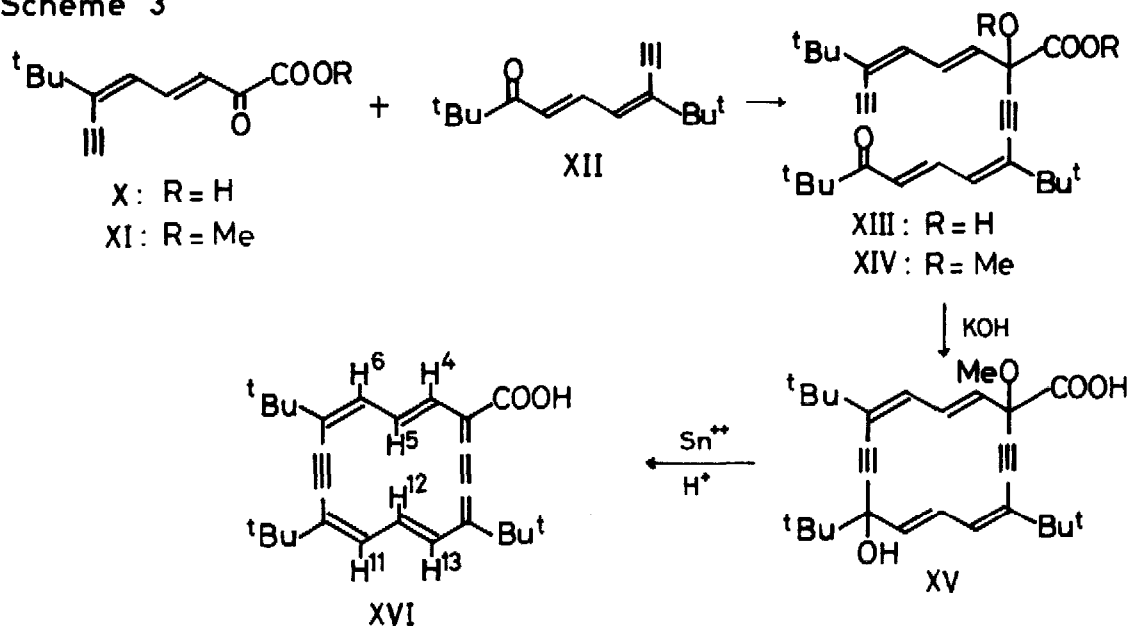
Scheme 2



Conversion of the acetylannulene (II) into carboxyannulene seemed to be of considerable interest, because electronic character of 1,8-bisdehydro[14]-annulene nucleus should be reflected upon the dissociation constant of the carboxy-

annulene. Hypohalite (8) and iodine-pyridine-sodium hydroxide oxidation (9) of II gave unsatisfactory results, although some indications of formation of XVI could be obtained by electronic spectroscopy. Accordingly, we have developed another reaction sequence leading to XVI (Scheme 3). Product of the aldol condensation of *t*-butylpentenynal (6) with pyruvic acid (X) was treated with diazomethane to yield methyl ester (XI, yellow liquid, 40% based on the pentenynal). A solution of ethynyl ketone (XII) (6) in tetrahydrofuran was added at $-70 \sim -80^\circ\text{C}$ under nitrogen atmosphere over 10 min.-period to a solution of lithium diethylamide in the same solvent prepared from diethylamine and butyllithium. After the mixture had been stirred for 5 min., a solution of XI in the same solvent was added over a period of 15 min. After stirring for further 30 min., the reaction mixture was worked up in the usual way, and the product was chromatographed on silica gel (Merck). Elution with benzene-ether (95:5-90:10) yielded ketoalcohol (XIII, pale yellow crystals, mp $66.0\text{--}67.5^\circ\text{C}$ (from hexane-ether), 58%). Treatment of XIII in tetrahydrofuran with dimethyl sulphate in the presence of powdered potassium hydroxide gave methoxy derivative (XIV, pale yellow crystals, mp $106.5\text{--}108.5^\circ\text{C}$ (from hexane-ether), 69%). Crude XV obtained by the cyclization of XIV by means of potassium hydroxide in liquid ammonia was converted into carboxyannulene (XVI) on treatment at -40°C under nitrogen atmosphere with stannous chloride dihydrate in ether saturated with hydrogen chloride. XVI was obtained as reddish brown crystals (mp $243\text{--}245^\circ\text{C}$ (dec.); 59%; Mass: m/e 390 (M^+); IR (KBr-disk): 2100 ($\text{C}\equiv\text{C}$), 1668 ($\text{C}=\text{O}$) cm^{-1} ; nmr (CDCl_3): -0.12d ($J=14.0$, 1H , H^4), 0.40d ($J=14.0$, 1H , H^6), 0.61d ($J=14.0$, 2H , H^{11} , H^{13}), 8.04s (9H ,

Scheme 3



t-Bu), 8.09s (18H, t-Bu), 14.07t ($J=14.0$, 1H, H^{12}), 14.29t ($J=14.0$, 1H, H^5); UV: λ_{\max} (THF) 272sh (ϵ 5510), 282.5sh (8270), 308.5sh (32200), 335 (13600), 476 (19100), 537 (1070), 557 (1070), 605 (7220) nm). The nmr spectrum indicates that the carboxyannulene (XVI) is strongly diatropic showing outer proton signals at low field and those of inner protons at fairly high field.

The dissociation constant of XVI was determined by spectrophotometric method using 0.2N sulphuric acid-99% ethanol (1:1), 0.7N acetic acid + 0.2N sodium acetate-99% ethanol (1:1) and 0.2N sodium hydroxide-99% ethanol (1:1) solutions. The spectral range of 320 to 610 nm was used for the pK_a' determination. Iso-*st*ebic points were observed at 336, 375, 474 and 590 nm. The pK_a' -value for XVI was found to be 5.92 ± 0.11 (at 18°C). The pK_a' -values for benzoic and *p*-*t*-butylbenzoic acids measured under the same conditions were found to be 5.55 ± 0.04 and 5.64 ± 0.07 , respectively. It has been well-known that the dissociation of acetylene and allene carboxylic acids are much more larger than their ethylenic and saturated analogues, *e.g.*, the pK_a' -values for 3-pentynoic acid [$CH_3C \equiv CCH_2COOH$], 5-hexen-3-ynoic acid [$H_2C=CHC \equiv CCH_2COOH$] (10) and allene carboxylic acid [$H_2C=C=CHCOOH$] (10) have been reported to be 3.60, 3.37 and 3.69, respectively. Consequently, the fact that the dissociation of carboxyannulene (XVI) is much smaller than those of acetylenic and allenic acids and is similar to those of benzoic and substituted benzoic acids can be regarded as a reflection of highly delocalized aromatic π -electron system in 1,8-bisdehydro[14]annulene ring.

References and Notes

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