Chem. Pharm. Bull.
28(6)1932—1934(1980)

Studies on the Syntheses of Spiro-dienone Compounds. VII.[1] Novel Synthesis of the Spiro[4.5]decane Carbon Framework

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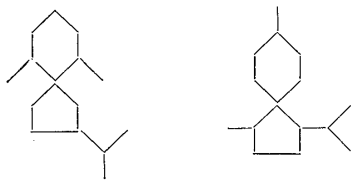
(Received December 26, 1979)

Copper(I) halide-catalyzed decomposition of phenolic α-diazoketones gave spiro[4.5]-deca-6,9-diene-2,8-dione in high yield.

Keywords——spiro-dienone; spiro[4.5]decane; spiro annelation reaction; phenolic α-diazoketone; carbenoid

Sesquiterpenes having a spiro[4.5]decane structure (spirovetivanes, acoranes, alaskanes, *etc.*) are widespread in nature[3] and various syntheses of these compounds continue to be reported.[4] It is well known that intramolecular alkylation of a phenol[5,6] gives a spiro-dienone, but this method has limited synthetic application.[6] Intramolecular reactions between diazoalkanes and benzene rings in the presence of a metal salt give cycloheptatrienes *via* intramolecular carbenoid addition.[7] Recently, Ledon and his co-workers[8] reported that acidic hydrolysis of the cycloheptatriene derivative obtained by copper-catalyzed decomposition of *p*-methoxybenzyl methyl diazomalonate gives the 2-oxaspiro[4.5]decane derivative.



spirovetivanes　　acoranes and alaskanes

Chart 1

We examined the intramolecular cyclization of phenolic α-diazoketones in the presence of cuprous halides and report a novel synthesis of the spiro[4.5]decane carbon framework.

A solution of the 2-(*p*-hydroxyphenyl)ethyl diazomethyl ketone (Ia) in benzene [or tetrahydrofuran (THF)] in the presence of cuprous chloride (or cuprous iodide) was heated under reflux for 4.5—5.5 hr. After removing the insoluble material, preparative thin-layer chromatography (TLC) of the crude product gave spiro[4.5]deca-6,9-diene-2,8-dione (IIa)[5a] in

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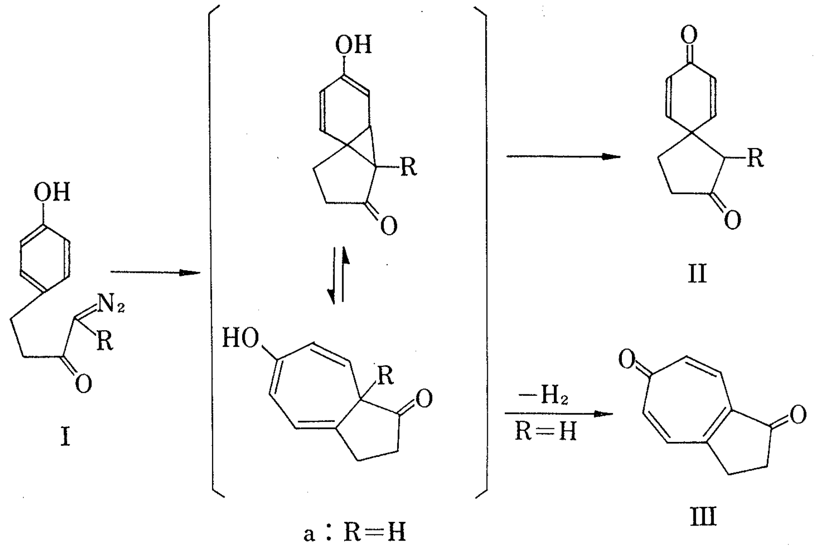

a : R=H
b : R=Me

Chart 2

high yield (Table). Similarly, catalytic decomposition of 2-(*p*-hydroxyphenyl)ethyl α-diazoethyl ketone (Ib), prepared from the corresponding acid chloride and diazoethane, gave 1-methylspiro[4.5]deca-6,9-diene-2,8-dione (IIb) in high yield (Table).

When Ia in benzene was heated under reflux in the presence of cuprous chloride for only 20 min, the starting material completely disappeared, and preparative TLC of the crude product gave IIa (34%), 2,3-dihydroazulene-1,6-dione (III) (8%), and several unidentified products. However, when the above reaction was carried out in a degassed benzene solution under an atmosphere of nitrogen, III was not isolated. Compound (III) is pale brown crystalline material, mp 125—126°, and is very unstable. The structure of III was determined from the following spectral data. The infrared (IR) spectrum ($CHCl_3$) showed absorption bands at 1718, 1637, 1617, and 1583 cm^{-1}. The last strong band is a specific band of tropone.[9] The nuclear magnetic resonance (NMR) spectrum ($CDCl_3$) showed signals at δ 7.43 (1H, d, J=12 Hz,[9] C_8–H), 7.1—7.2 (2H, m, C_5–H and C_4–H), 6.99 (1H, br. d, J=12 Hz, C_7–H), and 3.2—2.8 and 2.8—2.5 (each 2H, m, C_2–H and C_3–H). The ultraviolet (UV) spectrum (EtOH) showed absorption bands at 233 (log ε=4.35), 240 (sh), 309 (sh), and 316 (log ε=3.89) nm.[10,11]

Table I. Catalytic Decomposition of Phenolic α-Diazoketones

Diazoketone	Cuprous halide (mol)	Solvent (concentration, mol)	Time (hr)	Spiro[4.5]decane (yield, %)	
Ia	CuCl (1)	THF (0.3)	4.5	IIa	61
	CuCl (1)	THF (0.16)	4.5		79
	CuCl (1)	C_6H_6 (0.16)	5.5		80
	CuCl (2)	C_6H_6 (0.16)	5.5		72
	CuCl (0.3)	C_6H_6 (0.16)	5.5		67
	CuI (1)	THF (0.16)	4.5		48
	CuI (1)	C_6H_6 (0.16)	5.5		55
Ib	CuCl (1)	THF (0.16)	2	IIb	60
	CuCl (1)	C_6H_6 (0.16)	2		90

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The above results indicate that the catalytic decomposition of phenolic α-diazoketones proceeds *via* norcaradiene derivatives to give the spiro-dienone.

Further studies on the extension of this reaction to the synthesis of sesquiterpenes are in progress.

Experimental[12]

Cyclization of 2-(*p*-Hydroxyphenyl)ethyl Diazomethyl Ketone (Ia)——A) A solution of Ia (95 mg) in dry benzene (30 ml) in the presence of cuprous chloride (50 mg) was refluxed for 5.5 hr. After cooling, the reaction mixture was filtered and the residue was washed with $CHCl_3$. The filtrate and the $CHCl_3$ washings were combined, washed with water, dried, and concentrated *in vacuo*. Purification of the residue by preparative TLC on silica gel with Et_2O–petr. ether (1: 1) gave spiro[4.5]deca-6,9-diene-2,8-dione (IIa) in 80% yield, mp 72—74° (from Et_2O–petr. ether).

B) The above reaction mixture was refluxed for only 20 min, and the reaction mixture, when worked up as described in A, gave a red-brown oil. Preparative TLC gave IIa (34%), crude 2,3-dihydroazulene-1,6-dione (III) (8%), and several unidentified products. Further purification of the above III on silica gel with AcOEt gave III, mp 125—126°. MS *m/e*: 160 (M^+), 132 (M^+-CO), 104 (M^+-2CO). High resolution MS: Calcd for $C_{10}H_8O_2$ (M^+), 160.052. Found: 160.053.

2-(*p*-Hydroxyphenyl)ethyl α-Diazoethyl Ketone (Ib)——A solution of 3-(*p*-acetoxyphenyl)propionic acid[5a] (3.1 g) and thionyl chloride (5 ml) in dry benzene (20 ml) was refluxed for 4 hr. The solvent and excess thionyl chloride were removed *in vacuo*. The oily acid chloride was dissolved in dry Et_2O and added to an ice-cold solution of ethereal diazoethane (large excess). After 2 hr, the solvent was removed *in vacuo* to give the crude acetoxy α-diazoketone. A solution of the crude product in MeOH (60 ml) was mixed with a mixture of $NaHCO_3$ (2.1 g), Na_2CO_3 (3.5 g), and water (35 ml). The whole was stirred for 2 hr at room temperature, then poured into ice-water (450 ml). The cold solution was adjusted to pH 7—8 bythe careful addition of cold dilute oxalic acid, then the mixture was extracted with Et_2O. The Et_2O extracts were washed with water and dried. The solvent was removed *in vacuo* to give the phenolic α-diazoketone as a yellow solid (1.4 g, 70%). Recrystallization from Et_2O gave Ib, mp 109—110° (dec.). IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 3300 (OH), 2050 (N≡N), 1620 (C=O). NMR ($CDCl_3$) δ: 1.95 (3H, s, CH_3), 6.68—7.04 (4H, AA′BB′ type, aromatic ring H). *Anal.* Calcd for $C_{11}H_{12}N_2O_2$: C, 64.69; H, 5.97. Found: C, 64.68; H, 5.97.

Cyclization of 2-(*p*-Hydroxyphenyl)ethyl α-Diazoethyl Ketone (Ib)——A solution of Ib (102 mg) in dry benzene (30 ml) in the presence of cuprous chloride (50 mg) was refluxed for 2 hr. The reaction mixture, when worked up as described above for Ia, gave 1-methylspiro[3.5]deca-6,9-diene-2,8-dione (IIb) in 90% yield, mp 93—94° (from Et_2O–petr. ether). IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 1738 (C=O), 1660 and 1625 (C=C–C=O). NMR ($CDCl_3$) δ: 6.20—7.00 (4H, m, $2\times CH$–CH), 0.84 (3H, d, $J=7$ Hz, CH_3). UV λ_{max}^{EtOH} nm (log ε): 242 (4.07), 242 (sh). *Anal.* Calcd for $C_{11}H_{12}O_2$: C, 74.97; H, 6.86. Found: C, 75.08; H, 6.88.

Acknowledgement The authors are grateful to Miss K. Saiki of Kobe Women's College of Pharmacy for measuring the high resolution mass spectra.

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[12] All melting points are uncorrected. The following instruments were used to obtain physical data. NMR spectra: Hitachi Perkin Elmer R-22 machine; IR spectra: Hitachi EPI-G3 spectrometer; mass (MS) spectra: Hitachi RMU-6 spectrometer; UV spectra: Hitachi 124 spectrometer. Organic extracts were dried over anhydrous Na_2SO_4. Preparative TLC was performed on silica gel (Merck, silica gel 60, PF 254).