Chem. Pharm. Bull.
33(2) 853—855 (1985)

A Modified Procedure for the Synthesis of Spirodienones from Phenolic α-Diazoketones[1a)]

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(Received June 29, 1984)

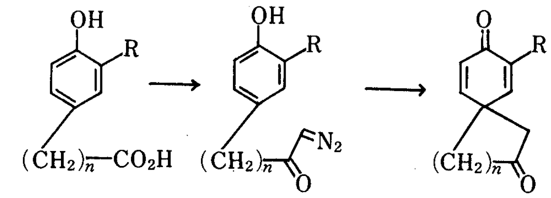
Rhodium(II) pivalate, rhodium(II) acetate, and palladium(II) acetate were found to be effective catalysts for the synthesis of spirodienones from phenolic α-diazoketones.

Keywords——spirodienone; spiro[5.5]undecane; spiro[4.5]decane; spiroannulation; phenolic α-diazoketone; metal catalyst

It has been shown that the intramolecular cyclization of a phenolic α-diazoketone (**2a**) in the presence of copper (I) halide provides a novel route to the spiro[4.5]decane carbon framework (**3a**).[1b)] In our continuing studies on spirocyclic sesquiterpenoids synthesis,[2)] we tried to extend the scope of this reaction to a homologous spiro[5.5]undecane system, but found that the analogous spiroannulation reaction of the diazoketone (**2c**) derived from 4-(4-hydroxyphenyl)butanoic acid (**1c**) occurred in low yield.[3)]

Recently, there has been increasing interest in the use of transition metal complexes in the catalytic decomposition of diazocarbonyl compounds. For example, it has been reported that rhodium (II) derivatives were highly effective for the cyclopropanation of olefins with alkyl diazoacetates[4a)] and for the synthesis of bicyclo[5.3.0]decatrienones from 1-diazo-4-aryl-2-butanones.[4b)] Therefore, we examined the spiroannulation reaction of diazoketones (2a—d) in the presence of rhodium (II) pivalate, rhodium (II) acetate or palladium (II) acetate as a catalyst. In this paper, we describe a modified procedure for the synthesis of spirodienones (3a—d) from phenolic α-diazoketones (2a—d).

	n	R
a	2	H
b	2	OCH_3
c	3	H
d	3	OCH_3



1 2 3

Chart 1

Diazoketones (2b—d) were prepared from the corresponding carboxylic acids (1b—d)[5)] in good yields by the conventional method[6)] with some modifications.[1b)] The structures of 2b—d were supported by their spectral data (Experimental).

The results of the spiroannulation reaction are summarized in Table I. In the cases of unsubstituted phenolic α-diazoketones (**2a** and **2c**), the best yields of the resultant spirodienones (**3a** and **3c**) were obtained in the presence of rhodium (II) catalysts (methods B-1 and A-1). In particular, rhodium (II) pivalate gave a great improvement (7→73%) in the yield of

TABLE I. Spiroannulation Reaction of Diazoketones (**2a**—**d**)

Substrate	Method[a]	Temperature	Time (min)	Yield (%) of **3**[b]
2a	A-1	r.t.	20	63
	A-2	r.t.	20	43
	B-1	r.t.	20	70
	B-2	r.t.	60	25
	C-1	r.t.	600	c)
	C-2	Reflux	240	c)
	D	Reflux	330	80[d]
2b	A-1	r.t.	60	22
	A-2	r.t.	60	17
	B-1	r.t.	60	12
	B-2	r.t.	60	13
	C-1	Reflux	240	13 (21)[e]
	C-2	Reflux	30	21 (47)[e]
	C-3	Reflux	30	48
	D	Reflux	360	31
2c	A-1	r.t.	20	73
	A-2	r.t.	60	19
	B-1	r.t.	20	57
	B-2	r.t.	20	34
	C-1	Reflux	240	c)
	C-2	Reflux	240	c)
	D	Reflux	180	7[f]
2d	A-1	r.t.	60	33
	A-2	r.t.	60	26
	B-1	r.t.	60	19
	B-2	r.t.	60	22
	C-1	Reflux	360	22 (33)[e]
	C-2	Reflux	30	31 (65)[e]
	C-3	Reflux	50	8
	D	Reflux	120	34

a) A-1: $Rh_2(O_2C\text{-}t\text{-}C_4H_9)_4$–$CH_2Cl_2$; A-2: $Rh_2(O_2C\text{-}t\text{-}C_4H_9)_4$–$C_6H_6$; B-1: $Rh_2(OAc)_4$–CH_2Cl_2; B-2: $Rh_2(OAc)_4$–C_6H_6; C-1: $Pd(OAc)_2$–CH_2Cl_2; C-2: $Pd(OAc)_2$–C_6H_6; C-3: $Pd(OAc)_2$–toluene; D: $CuCl$–C_6H_6.
b) Yields correspond to isolated products, and no starting materials were recovered unless otherwise noted.
c) The starting materials remained unreacted.
d) See ref. 1*b*.
e) Some of the starting materials were recovered and numbers in parentheses are corrected yields based on the consumed starting materials.
f) See ref. 3.
r.t. = room temperature.

[5.5]spirodienone (**3c**) compared with copper (I) catalyst. Application of this catalytic reaction to methoxy-substituted phenolic α-diazoketones (**2b** and **2d**) produced the corresponding spirodienones (**3b** and **3d**) in all runs. Although the yields were unsatisfactory, palladium (II) acetate (methods C-3 and C-2) was somewhat more effective than rhodium (II) catalysts. The structural assignments of 3b—d were based upon both elemental and spectral analyses (Experimental).

Further extensions and applications of this method to natural products synthesis are in progress.

Experimental

All melting points were measured on a Yanagimoto micromelting point apparatus and are uncorrected. Infrared

(IR) and ultraviolet (UV) spectra were taken on Hitachi EPI-G3 and Hitachi 124 spectrophotometers, respectively. Proton nuclear magnetic resonance (^{1}H-NMR) spectra were taken in $CDCl_3$ solution with tetramethylsilane as an internal standard on a Hitachi R-22 (90 MHz) spectrometer. Mass spectra (MS) and high-resolution mass spectra (High-MS) were taken on a JEOL JMS-D300 mass spectrometer. Preparative thin layer chromatography (PTLC) was performed on silica gel (Merck, Kieselgel 60, PF_{254}).

Palladium (II) acetate was obtained commercially (Wako Pure Chem. Ind., Ltd.) and rhodium(II) pivalate was prepared according to the method described for the preparation of rhodium(II) acetate.[7]

Synthesis of Diazoketones (2b—d)——Diazoketones (2b—d) were prepared in the same manner as described in our previous paper.[1b]

1-Diazo-4-(4-hydroxy-3-methoxyphenyl)-2-butanone (2b)——Pale yellow oil. IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 3680, 3540 (OH), 2100 (N≡N), 1638 (C=O). ^{1}H-NMR δ: 2.43—3.02 (4H, m, C_3- and C_4-H), 3.80 (3H, s, OCH_3), 5.17 (1H, s, C_1-H), 5.90 (1H, br s, OH), 6.50—6.82 (3H, m, aromatic H). MS *m/z* (%): 220 (M^+, 4.6), 192 (42.0), 137 (100). High-MS *m/z*: Calcd for $C_{11}H_{12}N_2O_3$: 220.085 (M^+). Found: 220.085.

1-Diazo-5-(4-hydroxyphenyl)-2-pentanone (2c)——Pale yellow oil. IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 3590, 3320 (OH), 2110 (N≡N), 1632 (C=O). ^{1}H-NMR δ: 1.68—2.70 (6H, m, C_3-, C_4- and C_5-H), 5.21 (1H, s, C_1-H), 6.63—7.00 (4H, AA′BB′ type, aromatic H), 7.02 (1H, br s, OH). MS *m/z* (%): 204 (M^+, 1.0), 176 (44.2), 120 (100). High-MS *m/z*: Calcd for $C_{11}H_{12}N_2O_2$: 204.090 (M^+). Found: 204.090.

1-Diazo-5-(4-hydroxy-3-methoxyphenyl)-2-pentanone (2d)——Pale yellow oil. IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 3552 (OH), 2105 (N≡N), 1640 (C=O). ^{1}H-NMR δ: 1.68—2.69 (6H, m, C_3-, C_4- and C_5-H), 3.83 (3H, s, OCH_3), 5.17 (1H, s, C_1-H), 5.75 (1H, br s, OH), 6.46—6.86 (3H, m, aromatic H). MS *m/z* (%): 234 (M^+, 20.3), 206 (28.6), 150 (100). High-MS *m/z*: Calcd for $C_{12}H_{14}N_2O_3$: 234.101 (M^+). Found: 234.101.

General Procedure for Metal-Catalyzed Spiroannulation of 2a—d——The diazoketone (100 mg) in dry CH_2Cl_2, C_6H_6 or toluene (10 ml) was added dropwise over a period of 20 min to a stirred solution of rhodium (II) or palladium (II) catalyst (2 mg) in dry CH_2Cl_2, C_6H_6 or toluene (100 ml) at room temperature under an argon atmosphere. When the addition was complete, the reaction mixture was stirred for the period indicated in Table I. The catalyst was filtered off, the solvent was removed under reduced pressure, and the spirodienone was separated by PTLC on silica gel with ether–petr.ether (3 : 2).

7-Methoxy-spiro[4.5]deca-6,9-diene-2,8-dione (3b)——Colorless plates (from ethyl acetate–petr. ether), mp 96.5—97.0 °C. IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 1751 (C=O), 1671, 1646, and 1615 (C=C–C=O). UV λ_{max}^{EtOH} nm (ε): 243 (10400), 285 (4660). ^{1}H-NMR δ: 2.00—2.75 (6H, m, C_1-, C_3- and C_4-H), 3.67 (3H, s, OCH_3), 5.79 (1H, d, J=3 Hz, C_6-H), 6.27 (1H, d, J=10 Hz, C_9-H), 6.89 (1H, dd, J=10, 3 Hz, C_{10}-H). MS *m/z* (%): 192 (M^+, 100). *Anal.* Calcd for $C_{11}H_{12}O_3$: C, 68.73; H, 6.29. Found: C, 68.61; H, 6.29.

Spiro[5.5]undeca-7,10-diene-2,9-dione (3c)——Colorless needles (from ethyl acetate), mp 98.5—102.0 °C. IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 1722 (C=O), 1673 and 1632 (C=C–C=O). UV $\lambda_{max}^{CH_3CN}$ nm (ε): 232 (13200). ^{1}H-NMR δ: 1.78—2.60 (8H, m, C_1-, C_3-, C_4- and C_5-H), 6.10—6.97 (4H, AA′BB′ type, olefinic H). MS *m/z* (%): 176 (M^+, 100). *Anal.* Calcd for $C_{11}H_{12}O_2$: C, 74.97; H, 6.86. Found: C, 74.69; H, 6.92.

8-Methoxy-spiro[5.5]undeca-7,10-diene-2,9-dione (3d)——Colorless needles (from ethyl acetate–pert. ether), mp 114.5—115.5 °C. IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 1720 (C=O), 1674, 1645, and 1617 (C=C–C=O). UV λ_{max}^{EtOH} nm (ε): 240 (9950), 285 (3470). ^{1}H-NMR δ: 1.75—2.65 (8H, m, C_1-, C_3-, C_4- and C_5-H), 3.66 (3H, s, OCH_3), 5.81 (1H, d, J=3 Hz, C_7-H), 6.23 (1H, d, J=10 Hz, C_{10}-H), 6.92 (1H, dd, J=10, 3 Hz, C_{11}-H). MS *m/z* (%): 206 (M^+, 100). *Anal.* Calcd for $C_{12}H_{14}O_3$: C, 69.88; H, 6.84. Found: C, 69.58; H, 6.93.

References and Notes

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