24. Note on the Preparation of 1,2-Diketones from Acetylenes

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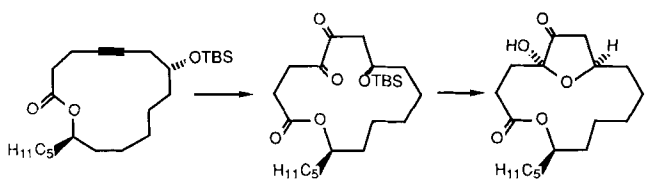
A mild method for the oxidation of acetylenes to 1,2-diketones using $NaIO_4/RuO_2$ is described. An investigation on the compatibility of various functional groups with this oxidizing agent is reported.

In connection with our recent work on the total synthesis of gloeosporone[2]) (*Scheme 1*) [1] [2], we required an efficient method for the oxidation of an acetylene to the corresponding 1,2-diketone in the presence of an ester and a protected alcohol group. A

Scheme 1

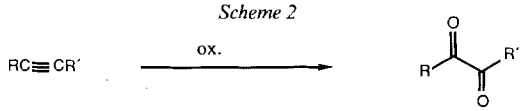


TBS = (*t*-Bu)Me_2Si

search of the literature revealed many reagents for this transformation; however, the substrates in all cases were simple aliphatic or aromatic acetylenes. The known methods are summarized in *Scheme 2*.

Of these reagents, Ru(VIII) appeared to be suitable for our purpose, especially since in the cleavage of olefins with $RuCl_3 \cdot nH_2O/NaIO_4$, *Sharpless* and coworkers had re-

Scheme 2



Oxidant	Ref.	Oxidant	Ref.
$KMnO_4$/aq. acetone	[3]	$RuCl_2(PPh_3)_3$/PhIO	[8]
$KMnO_4$/*Adogen-464*	[4]	RuO_2/NaOCl or $NaIO_4/CCl_4/H_2O$	[9]
$OsO_4/KClO_3$	[5]	$RuO_2 \cdot 2H_2O$/aq. NaCl/CCl_4, 6.1–13.4 F	[10]
N-Bromosuccinimide/DMSO	[6]	$(HMPA)MoO(O_2)_2/Hg(OAc)_2$	[11]
O_3/MeOH/Ph_3P	[7]	$Tl(NO_3)_3/HClO_4$	[12]

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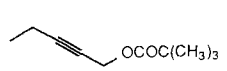
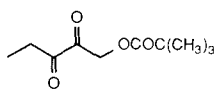
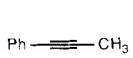
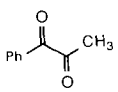
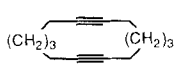
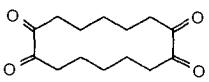
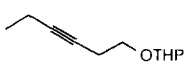
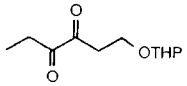
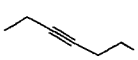
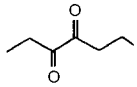
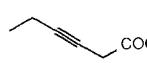
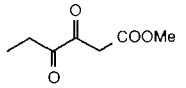
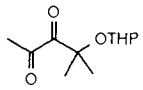
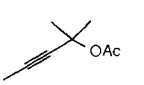
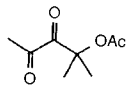
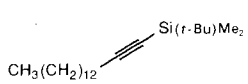
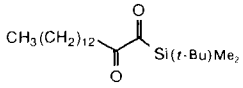
[2]) A full account of this synthesis is being prepared and will be published shortly.

Table. *Oxidations of Acetylenes to 1,2-Diketo Derivatives in the Presence of Various Functional Groups*

Entry	Starting material[a])	Product[a])	Reaction time at r.t. [min]	Yield [%] of purified material
1			30	82
2			60	80
3			180	47
4			20	62
5			15	60
6			30	32
7			15	69[b])
8			20	27[c])
9			240	95
10	$CH_3(CH_2)_{12}CCH$	$CH_3(CH_2)_{12}COOH$	210	47[c])

[a]) THP = 3,4,5,6-tetrahydro-2*H*-pyran-2-yl; Bn = benzyl.
[b]) Diketone product is extremely volatile.
[c]) Yield after filtration through *Celite*.

ported that functional groups such as epoxides and other cyclic ethers were compatible with the reaction conditions [13] [14]. While CCl_4/H_2O was the standard solvent system for RuO_4 oxidations, it was found that acetonitrile serves to greatly accelerate the rate of reaction [13]. Thus, we chose to adopt these conditions[3]) and initiated a study on the use of $RuO_2/NaIO_4$ for the oxidation of acetylenes containing various additional functional groups. It turned out that this reagent is indeed very versatile for the preparation of

[3]) While this work was in progress, *Carling* and *Holmes* reported an application of these oxidizing conditions for the synthesis of a 1,2-diketone also containing additional functional groups (*e.g.* ether, carboxylic acid) [15]. Incidentally, the target of that synthesis was presumed to be gloeosporone [16].

various 1,2-diketones. This is illustrated by the examples shown in the *Table*. It is important to note that esters are stable to the reaction conditions, as well as ethers (*i.e.* benzyl, 3,4,5,6-tetrahydro-2*H*-pyran-2-yl (THP), and (*tert*-butyl)dimethylsilyl). In the case of a terminal acetylene, a cleavage reaction occurs. However, a silyl acetylene (*Entry 9*) is oxidized to the purple acyl-silane. Incompatible functional groups include primary and secondary alcohols and propargylic tertiary alcohols. Also, olefins are oxidized at a rate similar to that of acetylenes so that these two functional groups are not successfully distinguished by the reagent.

The reaction times range from 15 min to 3 h with the yields moderate to excellent. The oxidizing agent, RuO_4, is generated by the action of $NaIO_4$ on RuO_2 which is used in catalytic amounts making the reaction applicable on preparative scale. A general procedure is described in the *Exper. Part.*

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Experimental Part

General. CCl_4 and MeCN were obtained from *Fluka* (*puriss.*) and used without further purification. Flash column chromatography (FC): *Merck* silica gel *60* (230–400 mesh). IR spectra: *Perkin-Elmer 297* spectrometer (film of $CHCl_3$): ^{1}H-NMR spectra: *Varian EM-390* spectrometer (90 MHz); with reference to TMS signal at (= 0 ppm). MS spectra: *Hitachi-Perkin-Elmer* spectrometer *RMU-6M*; *m/z* (intensity in %).

General Procedure. To a soln. of the acetylene (3 mmol) in $CCl_4/CH_3CN/H_2O$ (14 ml:14 ml:21 ml) was added solid $NaIO_4$ (4.1 equiv.). The mixture was stirred vigorously at r.t. After 2 clear phases resulted, $RuO_2 \cdot H_2O$ (0.022 equiv.) was added. The mixture turned black within min followed by bright yellow with the formation of a white precipitate. All reactions were monitored by TLC. After the starting material had been consumed, the mixture was poured into a separatory funnel, and 75 ml of H_2O added. The phases were separated, the aq. phase was extracted with 2 × 50 ml of CH_2Cl_2. The combined org. phases were dried ($MgSO_4$), and filtered through a column of *Celite* (6 cm high, ∅ 2 cm). The solvent was evaporated and the yellow dicarbonyl compound purified by distillation or FC.

Entry 1: 2,3-Dioxopentyl Pivalate. IR ($CHCl_3$): 2980*s*, 1730 (br.), 1480*m*, 1280*m*, 1150*s*, 890*m*. ^{1}H-NMR (90 MHz, $CDCl_3$): 5.0 (*s*, 2H–C(1)); 2.75 (*q*, *J* = 10, 2H–C(4)); 1.25 (s, *t*-Bu); 1.10 (*t*, *J* = 10, 3H–C(5)); MS: 143 (17.7, $M^+ - t$-Bu), 132 (2.0), 115 (1.1), 105 (2.1), 83 (25.8). Anal. calc. for $C_{10}H_{16}O_4$: C 59.98, H 8.05; found: C 59.32, H 8.14.

Entry 2: 1-Phenyl-1,2-propanedione [6]. IR ($CHCl_3$): 3120*w*, 1715*s*, 1680*s*, 1600*m*, 1300*m*, 1290*m*, 1160*s*, 900*s*, 700*s*, 570*s*. ^{1}H-NMR (90 MHz, $CDCl_3$): 8.0 (*m*, 2 arom. H); 7.5 (*m*, 3 arom. H); 2.50 (*s*, 3H–C(3)). MS: 148 (0.9, M^+), 121 (5.9), 104 (100), 76 (68).

Entry 3: 1,2,8,9-Cyclododecanetetrone. M. p. 97–99°. IR ($CHCl_3$): 2940*m*, 1710*s*, 1460*w*, 930*w*. ^{1}H-NMR (90 MHz, $CDCl_3$): 2.68 (*m*, 2H–C(3), 2H–C(7), 2H–C(10), 2H–C(14)); 1.60 (*m*, 2H–C(4), 2H–C(6), 2H–C(11), 2H–C(13)); 1.12 (*m*, 2H–C(5), 2H–C(12)). MS: 252 (3.6, M^+), 209 (8.7), 168 (7.7), 125 (18.5), 111 (27.3). Anal. calc. for $C_{14}H_{20}O_4$: C 66.65, H 7.99; found: C 66.26, H 8.20.

Entry 4: 1-(3',4',5',6'-Tetrahydro-2'H-pyranyl-2'-oxy)-3,4-hexanedione. IR ($CHCl_3$): 2940 (br.), 1720 (br.), 1200*s*, 1030*s*, 970*m*. MS: 214 (0.1, M^+), 157 (3.7), 119 (2.4), 101 (19.8). ^{1}H-NMR (90 MHz, $CDCl_3$): 4.55 (*m*, H–C(2')); 3.5–4.1 (*m*, 2H–C(1), 2H–C(6')); 3.0 (*t*, *J* = 10, 2H–C(2)); 2.80 (*q*, *J* = 10, 2H–C(5)); 1.4–1.7 (*m*, 2H–C(3'), 2H–C(4'), 2H–C(5')); 1.08 (*t*, *J* = 10, 3H–C(6)). Anal. calc. for $C_{11}H_{18}O_4$: C 61.66, H 8.47; found: C 61.41, H 8.53.

Entry 5: 1-Benzyloxy-3,4-hexanedione. IR ($CHCl_3$): 2980*w*, 2880*w*, 1715*s*, 1500*w*, 1450*m*, 1100*s*, 900*s*, 740*s*, 700*s*. ^{1}H-NMR (90 MHz, $CDCl_3$): 7.3 (*s*, 5 arom. H); 4.5 (*s*, PhCH_2); 3.82 (*t*, *J* = 10, 2H–C(1)); 3.0 (*t*, *J* = 10, 2H–C(2)); 2.71 (*q*, *J* = 10, 2H–C(5)); 1.05 (*t*, *J* = 10, 3H–C(6)). MS: 163 (2.3, $M^+ - C_3H_5O$), 114 (7.8), 107 (5.6), 91 (100). Anal. calc. for $C_{13}H_{16}O_3$: C 70.89, H 7.32; found: C 71.01, H 7.43.

Entry 6: Methyl 3,4-Dioxohexanoate. IR ($CHCl_3$): 2950*w*, 2870*w*, 1740–1710 (br.), 1360*m*, 1160*m*, 1120*m*. ^{1}H-NMR (90 MHz, $CDCl_3$): 5.9 (*s*, 2H–C(2)); 3.75 (*s*, CH_3O); 3.4 (*s*, 2H–C(2)); 2.4 (*q*, *J* = 10, 2H–C(5)); 1.15 (*t*,

J = 10, 3H–C(6)). This compound was unstable when exposed to rigorous purification by distillation or chromatography.

*Entry 7: 4-Methyl-4-(3',4',5',6'-tetrahydro-2'*H*-pyranyl-2-oxy)-2,3-pentanedione.* M.p. 79–81°. IR ($CHCl_3$): 2940*s*, 2860*m*, 1715*s*, 1390*m*, 1350*s*, 1160*s*, 1130*s*, 1060*s*, 1030*s*, 910*m*. ^{1}H-NMR (90 MHz, $CDCl_3$): 4.6 (*m*, H–C(2')); 4.0 (*m*, H–C(6')); 3.4 (*m*, H–C(6')); 2.3 (*s*, 3H–C(5)); 1.8–1.3 (*m*, 2H–C(3'), 2H–C(4'), 2H–C(5')); 1.60 (*s*, CH_3–C(4)); 1.50 (*s*, 3H–C(5)). MS: 143 (6.4, $M^{+\cdot} - C_3H_3O_2$), 113 (2.0), 101 (1.4), 85 (100).

Entry 8: 3,4-Dioxo-2-methylpentan-2-yl Acetate. ^{1}H-NMR (90 MHz, $CDCl_3$): 2.3 (*s*, CH_3COO); 2.05 (*s*, 3H–C(5)); 1.6 (*s*, 3H–C(1), CH_3–C(2)).

*Entry 9: 1-[(*tert*-Butyl)dimethylsilyl]-1,2-pentadecanedione.* IR ($CHCl_3$): 2960–2920 (br.), 2840*s*, 1850 (br.), 1700 (br.), 1460*m*, 1250*m*, 1000*w*. ^{1}H-NMR (90 MHz, $CDCl_3$): 2.3 (*m*, 2H–C(3)); 1.2–1.35 (*m*, 22H); 0.1–0.3 (*m*, $(CH_3)_2Si$); 0.95 (*s*, *t*-Bu); 0.90 ('*t*', 3H–C(15)). MS: 325 (6.2, $M^{+\cdot} - C_2H_5$), 267 (9.8), 228 (12.8), 211 (6.8), 147 (12.1). This compound was unstable when exposed to rigorous purification by distillation or chromatography.

Entry 10: Myristic Acid. Identical in all respects (NMR, IR, MS, m.p.) to the commercially available material.

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