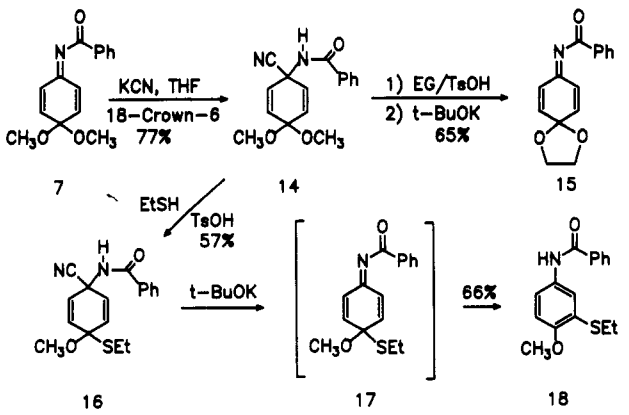

mixed ketal of the acylated quinone imine **17**. Instead, the meta-substituted amide **18**[12] was formed as the exclusive product. Since **15** was cleanly prepared from **14** under these reactions conditions, it appears that **18** results from an extremely rapid 1,2-migration of the ethylthio group in **17**. Thus, if products akin to **4** (Y = S) or **10** (Nu = SR) are formed in metabolic processes of acylated aromatic amines, a 1,2-shift of the alkyl sulfur group to give **5a** or **13** is a viable process.

The results presented herein establish the extremely facile 1,2-shift of an ethylthio group in acylated quinone imine systems. Analogous reactions explain the production of 1- and 3-substituted products from the metabolism of (*N*-acetylamino)fluorene in the rat. These results emphasize the different mechanisms by which oxygen and sulfur nucleophiles may be incorporated into quinone imine type intermediates. In view of the higher nucleophilicity of sulfur relative to oxygen and the presence of sulfur nucleophiles in living systems, the addition of sulfur nucleophiles to the carbon–nitrogen double bond of biologically generated imine systems followed by 1,2-rearrangements may be an important reaction.

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Supplementary Material Available: Experimental procedures and ^{1}H NMR spectra of the compounds reported in this paper (12 pages). Ordering information is given on any current masthead page.

(12) This compound, mp 181–182 °C (lit.[5] mp 185–185.5 °C), showed spectroscopic properties identical with those of an authentic sample.

A Multistep Rearrangement from 2,2-Disubstituted 1,3-Cyclohexanediones to 3-Substituted 2-Cyclohexenones via Phosphonate Anions and Its Application to a Formal Synthesis of (±)-α-Acoradiene

Yoshinori Yamamoto* and Toshiaki Furuta

Department of Chemistry, Faculty of Science, Tohoku University, Sendai 980, Japan

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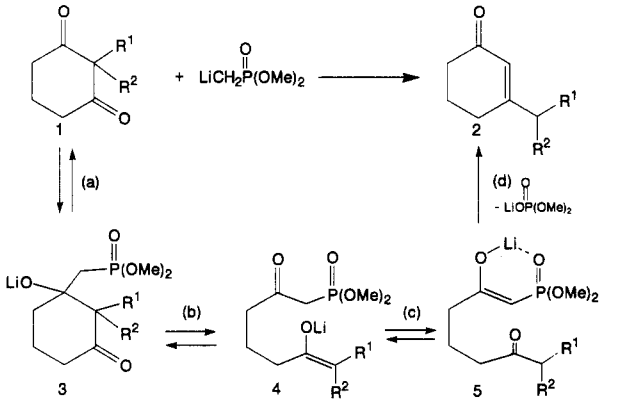
Summary: The reaction of 2,2-disubstituted 1,3-cyclohexanediones (**1**) with dimethyl methylphosphonate anion in the presence of trimethylsilyl chloride produces 3-substituted 2-cyclohexenones (**2**) in moderate to very good yields. This new overall reaction is accounted for by (a) attack of the phosphonate anion on a carbonyl group, (b) retro-aldol cleavage, (c) reorganization of the acidic proton, and (d) an intramolecular Wadsworth–Emmonds condensation. The new rearrangement is applied to a short synthesis of (±)-α-acoradiene.

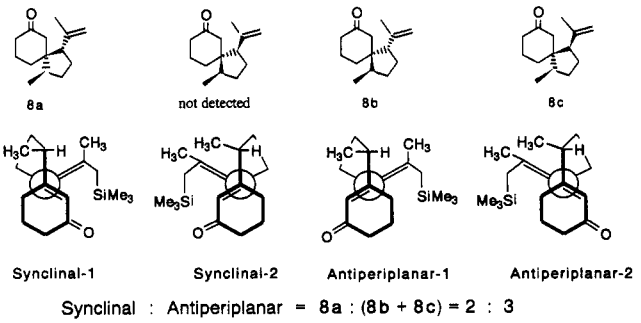
3-Substituted 2-cyclohexenones are versatile building blocks for the synthesis of complex cyclic natural products such as spirocyclic and fused ring sesquiterpenes. The synthetic method most commonly used is based either on the 1,4-addition of organocopper reagents to 3-halogenated(or acetoxy)-2-cyclohexenones[1] or on the 1,2-addition of organolithium or magnesium reagents to 3-alkoxy-2-cyclohexenones.[2] These organometallic-based procedures are subject to inherent drawbacks involved in the use of organometallic reagents; introduction of secondary alkyl groups or of functional groups often causes difficulties.

We report herein a new approach for the synthesis of 3-substituted 2-cyclohexenones via phosphonate anions. The reaction of 2,2-disubstituted 1,3-cyclohexanediones (**1**) with dimethyl methylphosphonate anion produces **2** in moderate to very good yields.

Scheme I



Scheme II



Synclinal : Antiperiplanar = 8a : (8b + 8c) = 2 : 3

(1) (a) Casey, C. P.; Marten, D. F.; Boggs, R. A. *Tetrahedron Lett.* **1973**, 2071. (b) Piers, E.; Nagakura, I. *J. Org. Chem.* **1975**, *40*, 2694.

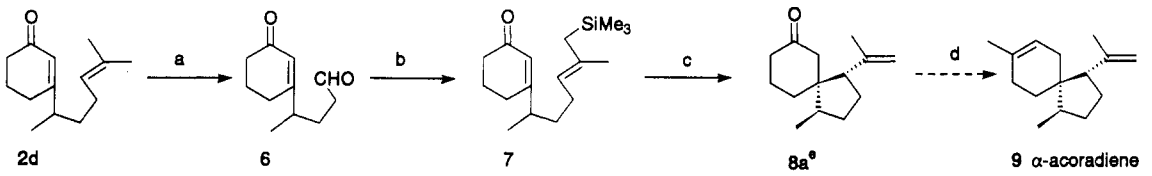
(2) (a) Woods, G. F.; Griswold, P. H.; Armbrecht, B. H.; Blumenthal, D. I.; Plapinger, R. *J. Am. Chem. Soc.* **1949**, *71*, 2028. (b) Frank, R. L.; Hall, H. K., Jr. *J. Am. Chem. Soc.* **1950**, *72*, 1645.

Table I. Synthesis of 2 from 1

entry	substrate 1	R^1	R^2	method[a]	product (2a–g) isolated yield, %
1	**1a**	Me	$PhCH_2$	A	93 (**2a**)
2	**1a**	Me	$PhCH_2$	B	65 (**2a**)
3	**1a**	Me	$PhCH_2$	C	47 (**2a**)
4	**1b**	Me	CH_2=$CHCH_2$	A	89 (**2b**)
5	**1c**	Me	Me	C[b]	58 (**2c**)
6	**1d**	Me	Me_2C=$CHCH_2CH_2$	A	61 (**2d**)
7	**1e**	Me	*n*-Bu	A	65 (**2e**)
8	**1e**	Me	*n*-Bu	B	61 (**2e**)
9	**1f**	Me	$MeO_2CCH_2CH_2$	C[b]	33 (**2f**)[c]
10	**1g**	Et	Et	A	22 (**2g**)[c]

[a] Method A: see text. Method B: same as method A except for absence of TMSCl. Method C: same as method B except for use of *n*-BuLi instead of LDA. [b] Instead of methyl dimethylphosphonate, 2,4,6-trimethyl-2-oxo-1,3,2-dioxaphosphorinane was used as a phosphonate. [c] Unidentified polar products, presumably phosphonate-containing compounds, were produced along with the desired product.

Scheme III[a]



[a] (a) O_3, CH_2Cl_2, then Zn, AcOH; (b) Ph_3P=$C(CH_3)CH_2SiMe_3$, THF; (c) $EtAlCl_2$, toluene, −75 °C; (d) Reference 8; (e) see Scheme II.

The procedure for the synthesis of **2b** is representative (method A). To a stirring cold solution of 76 mg (0.61 mmol) of dimethyl methylphosphonate in 6 mL of dry THF at −70 °C was added 0.3 mL of lithium diisopropylamide (2.1 M in cyclohexane) under an Ar atmosphere. After the mixture was stirred for 45 min, a solution consisting of 83 mg (0.50 mmol) of diketone **1b** in 2 mL of THF was added, and stirring was then continued for 10 h at −70 °C. A solution of 65 mg (0.60 mmol) of TMSCl in 2 mL of dry THF was then added at −70 °C. The reaction mixture was allowed to warm to room temperature, and stirring was continued for an additional 36 h. The reaction was quenched with 2 mL of dilute NH_4Cl solution. Ether extraction, followed by drying over $MgSO_4$, concentration in vacuo, and silica gel chromatography (5 g) with 20:1 hexane–ethyl acetate as an eluent gave 73 mg (89%) of **2b** as a colorless oil.

The use of TMSCl as an additive enhanced the product yield (entry 1 vs 2), while use of *n*-BuLi as a base resulted in low yields (entries 3, 5, and 9); LDA was superior to *n*-BuLi. Phosphonate-containing compounds were detected when the desired cyclohexenones were obtained in low yields (entries 9 and 10). Presumably, the sequential enolizations are arrested on the way to the final product (see Scheme I).

The observed rearrangement can be explained by the sequence shown in Scheme I: (a) the phosphonate anion attacks one of the two carbonyl groups of **1** to give **3**; (b) retro-aldol cleavage of **3** produces the keto phosphonate anion **4**; (c) reorganization of the acidic protons affords **5**. (d) An intramolecular Wadsworth–Emmonds reaction of **5** gives the final product **2**. TMSCl may shift the equilibrium in the forward direction. When the reaction was quenched after a short period, the protonated product of **5** was isolated along with **2**. Furthermore, the following observations in regard to related systems support the above mechanism. A similar retro-aldol cleavage is observed in the reaction of 2,2-disubstituted 1,3-cyclohexanedione (**1**) with alcoholic sodium hydroxide,[3] and the bond reorganization in enol lactones has been reported previously.[4]

The present method was applied to a short formal synthesis of (±)-α-acoradiene **9**. Selective ozonolysis[5] of **2d** followed by reductive workup with Zn/AcOH gave the enone–aldehyde **6** in quantitative yield. Allylsilane **7** was prepared in 50% yield using the Seyferth–Fleming method.[6] The intramolecular Sakurai–Hosomi type condensation in the presence of $EtAlCl_2$[7] gave the corresponding spiroketones **8** as a mixture of three diastereomers in 53% yield (**8a**:**8b**:**8c** = 2:2:1). The desired diastereomer **8a**[8] results from the *synclinal-1* transition state, while the other two diastereomers **8b** and **8c** are produced via the antiperiplanar transition states (Scheme II). Accordingly, the ratio of the synclinal versus antiperiplanar products is 2:3. Schinzer has reported that a synclinal transition state is involved in a related system.[7] However, the cyclization of **7** proceeds predominantly through the antiperiplanar transition state, indicating that the transition-state geometry of the intramolecular cyclization is highly dependent on the substrate structures. Synthesis of **9** from **8a** can be performed according to the procedure reported by Oppolzer and co-workers[8] (Scheme III).

Supplementary Material Available: Experimental procedure for synthesis of **8a** and spectral data for compounds **1d**, **2d**, **7**, and **8a–c** (7 pages). Ordering information is given on any current masthead page.

(3) Stetter, H. In *Newer Methods of Preparative Organic Chemistry*; Foerst, W., Ed.; Academic Press: New York, 1963, Vol. 2, p 51.
(4) Henrick, C. A.; Boehme, E.; Edwards, J. A.; Fried, J. H. *J. Am. Chem. Soc.* **1968**, *90*, 5926.
(5) Veysoglu, T.; Mitcher, L. A.; Swayze, J. K. *Synthesis* **1980**, 808.
(6) (a) Seyferth, D.; Wursthorn, K. R.; Mammarella, R. E. *J. Org. Chem.* **1977**, *42*, 3104. (b) Fleming, I.; Paterson, I. *Synthesis* **1979**, 446.
(7) Schinzer, D. *Angew. Chem., Int. Ed. Engl.* **1984**, *23*, 308.
(8) The ^1H NMR spectrum was identical to that of an authentic sample. We thank Prof. Oppolzer for providing us with the ^1H NMR spectra. Oppolzer, W.; Zutterman, F.; Baettig, K. *Helv. Chim. Acta* **1983**, *66*, 522.