Ring-enlargement reaction of alkylidenecarbenes bearing a cyclic ether or acetal group. Formation of medium-sized cyclic enol ethers or dienol ethers *via* bicycloalkenyloxonium ylides

Takashi Mori, Masahiko Taniguchi, Fumito Suzuki, Hisashi Doi and Akira Oku *

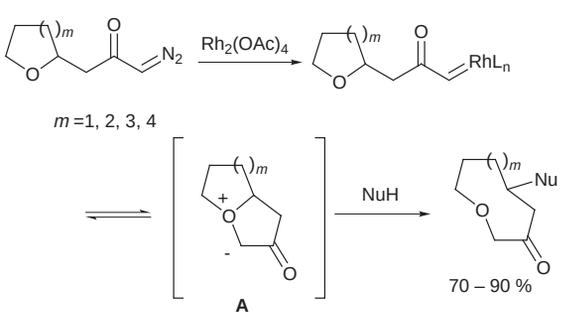
Department of Chemistry and Materials Technology, Kyoto Institute of Technology, Matsugasaki, Sakyo-ku, Kyoto 606 Japan

Received (in Cambridge) 24th April 1998, Accepted 9th September 1998

The reaction of 2-acetonyltetrahydrofuran **1a** and 2-acetonyltetrahydropyran **1b** with the potassium salt of dimethyl diazomethylphosphonate (DAMP) in the presence of MeOH produced ring enlargement product 1-methyl-3-oxacyclooctene **6a** (22%) and 1-methyl-3-oxacyclononene **6b** (28%), respectively, in addition to nonrearranged products. When the side-chain was elongated by one carbon unit (**1c**), ring enlargement did not take place. Analogous reactions of 2-acetonyl-substituted 1,3-dioxolane **9a**, 1,3-dioxane **9b** and 1,3-dioxepane **9c** also produced, respectively, 3,5-dimethyl-1,6-dioxacycloocta-2,4-diene (**16a**, 58%), a mixture (combined yield 83%) of 3,5-dimethyl-1,6-dioxacyclonona-2,4-diene (**16b**) and 5-*exo*-methylene-3-methyl-1,6-dioxacyclonon-2-ene (**17b**), and a mixture (combined yield 54%) of 3,5-dimethyl-1,6-dioxacyclodeca-2,4-diene (**16e**) and 5-*exo*-methylene-3-methyl-1,6-dioxacyclodec-2-ene (**17e**). Side-chain-elongated dioxolane **9d** did not undergo enlargement and, instead, ring-switched product 3,6-dimethyl-6-[2-(*tert*-butyloxy)ethoxy]-5,6-dihydropyran **22** was formed. The formation of products **6**, **16**, **17** and **22** can be explained in terms of the intermediacy of bicyclooxonium ylides, which are formed in an intramolecular manner between the alkylidenecarbene and a cyclic ether or cyclic acetal unit. In most reactions of acetonyl-substituted cyclic acetals, the major products were di(enol ether)s **16** and **17** even in the presence of a protic nucleophile such as MeOH. A reversible intramolecular process between alkylidenecarbenes and ylides is also proposed.

Ethereal oxonium ylides are highly reactive and short-lived intermediates compared to other onium ylides such as sulfonium, phosphonium and ammonium ylides.[1] While their extremely short lifetimes have made spectroscopic identification difficult,[2] their intermediacy has been proposed in several carbene reactions in which ethereal oxygen atoms take part as nucleophiles *via* both inter-[3] and intramolecular routes.[4] From a synthetic perspective, ethereal oxonium ylides are useful tools for substituting one of the two ethereal ligands for another which can be derived from a carbene, and this type of ligand exchange seems useful for the reassembly of ethereal frameworks.[5] However, the systematic use of ethereal oxonium ylides for synthetic purposes has been limited,[3,4] whereas other types of oxonium ylides, such as carbonyl ylides[6] and hydroxonium ylides,[7] have been extensively studied. This limited application may be due to the lability of these ylides, which exist as extremely short-lived compounds in equilibrium with carbenes or carbenoids.[2] To overcome this disadvantage, we recently designed an intramolecular pathway for the formation of oxonium ylides, in which a cyclic ether or acetal is tethered to a diazocarbonyl group by a suitably extended side-chain. In this system, a constrained bicyclooxonium ylide is formed as a transient intermediate, resulting in the efficient construction of medium-sized cyclic keto ethers or keto diethers (Scheme 1).[8] Although this method was efficient, it was limited in that only keto carbenoids could be used as the precursor. This raised the question of whether a similar intramolecular strategy could be extended to the use of free carbenes such as alkylidenecarbenes.

This report deals not only with the reversible intramolecular formation of bicyclic oxonium ylides but also with the synthesis of unsaturated medium-sized cyclic enol ethers or di(enol ether)s, based on a method analogous to that which we adopted for the synthesis of medium-sized keto ethers.[8] In the present study, we have assembled an alkylidenecarbene side-chain and a cyclic acetal or ether in a single molecule (**3** in Scheme 2 and **11** in Scheme 3). Another goal was to compare keto carbenoids and free alkylidenecarbenes with regard to the reversible formation of oxonium ylides. In this regard, Sueda and Ochiai *et al.* recently reported the kinetics and equilibrium of free alkylidenecarbene-derived oxonium ylides for bimolecular processes.[2b]

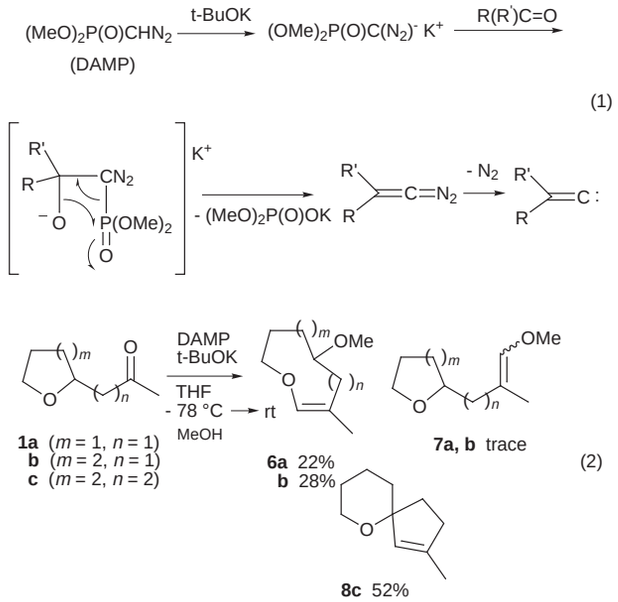


Scheme 1

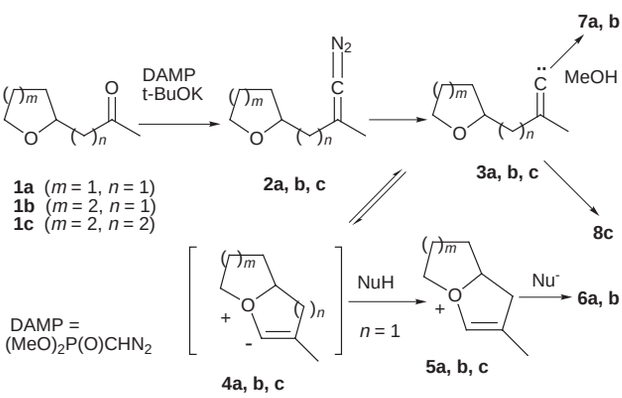
Results and discussion

Generation and reaction of THF-substituted alkylidenecarbene 3a

As a precursor for alkylidenecarbene **3a**, we chose the corresponding diazoalkene **2a**, which can be prepared *in situ* at −78 °C by the diazomethyl transfer reaction of dimethyl diazomethylphosphonate (DAMP)[9] to 2-acetonyltetrahydrofuran **1a** in the presence of potassium 1,1-dimethylethoxide (t-BuOK) [eqn. (1)].[10] This reaction was carried out in tetrahydrofuran (THF) in the presence of methanol (MeOH, 10 equiv.)[11] to yield ring enlarged product **6a** (22%) together with a small



amount of OH insertion product **7a** [2%, eqn. (2)].[12] Although the yield of **6a** could not be improved by varying the reaction conditions, its formation clearly supports the notion that bicycloalkenyl oxonium ylide **4a** is a key intermediate (Scheme 2).



Scheme 2

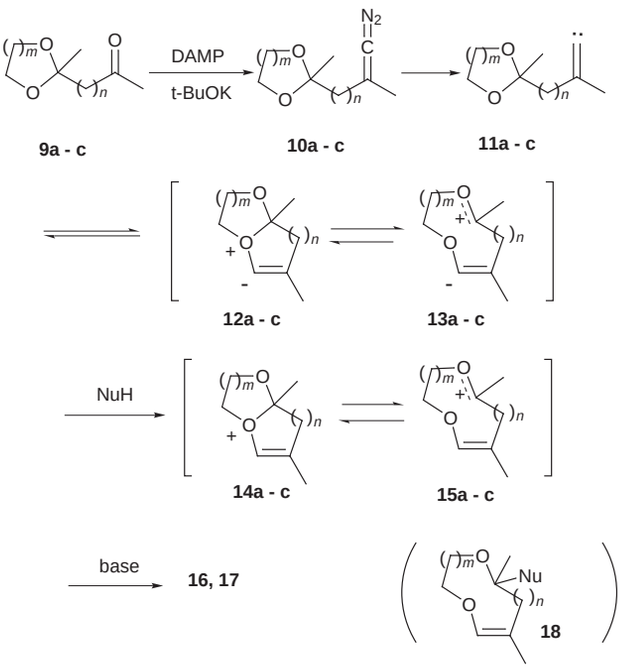
Generation and reaction of THP-substituted alkylidenecarbenes 3b and 3c

When alkylidenecarbene **3b**, which has a tetrahydropyran (THP) ring, was generated from **1b** in a THF solution under conditions analogous to those for **1a**, similar products **6b** and **7b** were obtained in low yields (28 and 2%, respectively) [eqn. (2)]. However, elongation of the side-chain to two methylene units disfavored this enlargement. Thus, the reaction of **1c** only yielded intramolecular C–H insertion product **8c** (52%) instead of the enlargement products [eqn. (2)].

Based on the above results for the reactions of **1a**–**c**, we can deduce that most alkylidenecarbenes, which are tethered to the α-position of a cyclic ether ring by one- or two-carbon bridging,[13] may form the corresponding bicyclooxonium ylide **12**. However, ring enlargement takes place only for bicyclo-[(*m* + 2).3.0]alkenyl-1-oxonium ylides **4a** and **4b** (*n* = 1). This size selective enlargement is attributable mainly to the constrained structure of bicyclic ylides; this strain can be released most efficiently by cleaving the central bridging bond (Scheme 2). In addition to enlargement, however, ylides **4** may also undergo a reversible back-reaction to carbenes **3** and a fraction of this equilibrium can be converted to the intermolecular OH insertion product **7** or intramolecular CH insertion product **8**.

Reactions of 1,3-dioxolane-, 1,3-dioxane- and 1,3-dioxepane-substituted alkylidenecarbenes 11a, 11b and 11c

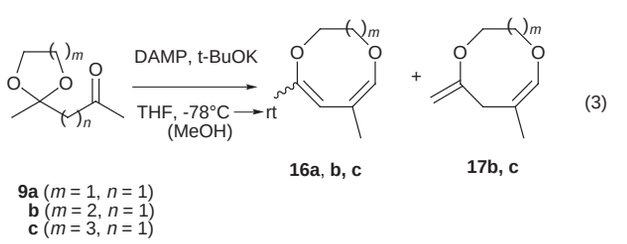
While the initially designed ring enlargement of cyclic ethers has been more or less realized as described above, the efficacy of this ring enlargement was far below that needed for practical use. To overcome this problem, we designed similar alkylidenecarbenes **11** tethered to a cyclic acetal instead of a cyclic ether. In these systems, we can expect that the two ethereal oxygen atoms in the dioxolane, dioxane and dioxepane rings should stabilize the initially formed bicyclic ylide intermediates **12** with ring-opened zwitterion structures **13** and, by analogy, also with the corresponding protonated oxonium ion structures **14** and **15** (Scheme 3).[8b] Another consequence of ylide-stabilization



Scheme 3

should be suppression of the reversible back-reaction to carbenes **11** which disfavors the insertion reactions.

Indeed, the reaction of dioxolanylacetone **9a** with DAMP (2.2 equiv.) by treatment with t-BuOK (2.2 equiv.), in the absence of MeOH, produced the expected ring enlargement product 3,5-dimethyldioxacycloocta-2,4-diene (**16a**) in 61% yield [eqn. (3)].[14] The same product **16a** was isolated as a sole



product (58%) even in the presence of MeOH (3 equiv.), but the other expected dioxocane product **18** (Nu = OMe) was not formed. In comparison with the reactions of ylides **4** and keto oxonium ylides **A** (Scheme 1), the exclusive formation of **16**, regardless of the presence of MeOH, indicates that an intramolecular proton shift in ylide **12a** is facilitated more than protonation and subsequent nucleophilic attack by a nucleophile NuH, resulting in the formation of diene **16a**.

In the analogous reaction with DAMP, 1,3-dioxan-2-ylacetone **9b** behaved similarly to efficiently give a mixture of ring enlarged diene products 3,5-dimethyl-1,6-dioxacyclonona-2,4-

Table 1 Reaction of DMAP with ketones bearing a cyclic acetal

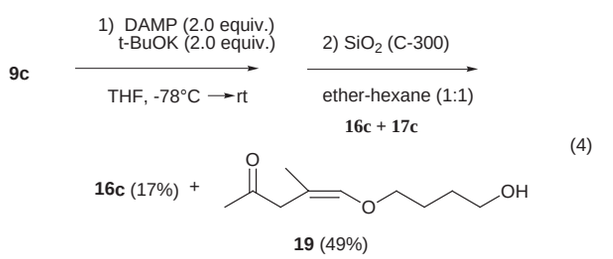
Substrate	*m*, *n*	Products and yield (%)
9a	*m* = 1, *n* = 1	**16a** (61)[a]
9b	*m* = 2, *n* = 1	**16b** (74),[a] **17a** (7)[a]
9c	*m* = 3, *n* = 1	**16c** (18),[a] **17c** (36)[a]
9d	*m* = 1, *n* = 2	**20** (24),[b,c] **21** (17),[b] **22** (7)[b]

[a] GC yield. [b] NMR yield. [c] Calculated on the molar basis of **9d**.

diene (**16b**) and 5-methylene-4-methyl-1,6-dioxacyclonon-2-ene (**17b**) in a combined yield of 81% [eqn. (3), Table 1].

The analogous reaction of 1,3-dioxepan-2-ylacetone **9c** with DAMP gave two ring enlargement products **16c** and **17c** in combined yields of 54–66% [eqn. (3)]. Taken together, these results indicate that the size of the cyclic acetal does not impair the expected enlargement reaction.

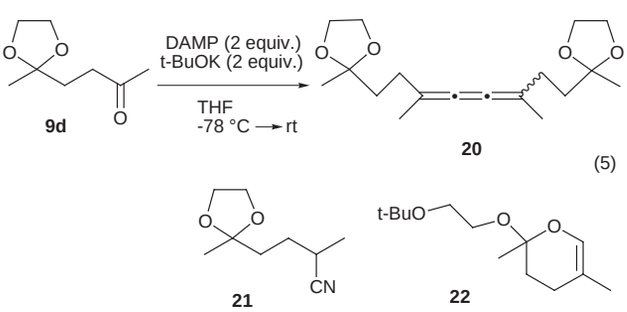
1,3-Diene **16c** and 1,4-diene **17c** are considered to have *cis*,*cis* and *cis* configurations, respectively, based on the structure of the corresponding ylide precursor **12c** (*m* = 3, *n* = 1) in which the double bond should have a *cis* configuration.[15] Since product **17c** was found to be unstable under the isolating conditions, a mixture of **16c** and **17c** was hydrolyzed on moistened silica gel to give a mixture of ring opened alcohol **19** (49%) and unreacted **16c** (17%) [eqn. (4)]. Evidently, the formation of **19** supports the structure of **17c**.



(4)

Reaction of dioxolane-substituted alkylidenecarbene 11d

4-(2-Methyl-1,3-dioxolan-2-yl)butan-2-one (**9d**), which has a longer side-chain than **9a** by one methylene unit, behaved differently under analogous reaction conditions to give ring-switched product **22** (7%), carbene dimer **20** (30%) and cyanobutyldioxolane **21** (17%) [eqn. (5)]. The formation of **22** indi-

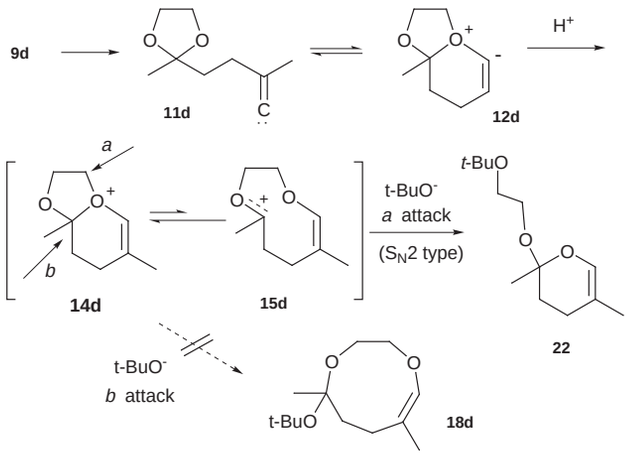


(5)

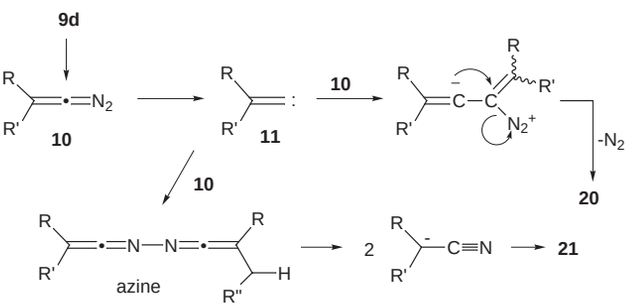
cates that it was produced from bicyclooxonium ylide **12d** or its protonated oxonium ion **14d**, whose weakly strained bicyclic structures underwent an S_N2-type attack by t-BuO$^-$ ion at the a-position of the oxonium atom (Scheme 4).[8a] The formation of **21** may be explained by analogy to the diazomethylation of pyruvate reported by Ohira and co-workers.[16] We presume that either a homolysis or base-catalyzed cleavage of an intermediate azine will lead to nitrile **21** (Scheme 5).

Reaction mechanism for diene formation

For the formation of enlargement product dienol ethers **16** and **17**, three routes are possible. (1) Elimination *via* primary product **18**: this product is formed by trapping bicyclooxonium ylide

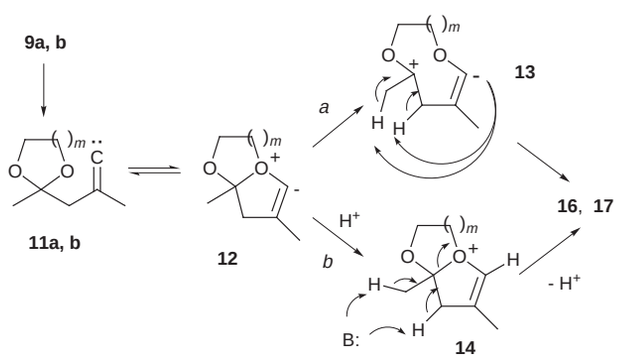


Scheme 4



Scheme 5

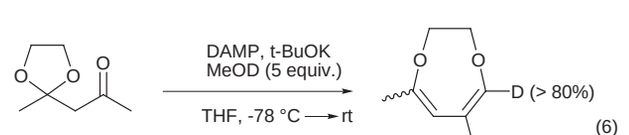
12 or its ring-opened zwitterion **13** with a protic nucleophile MeOH. However, acetals **18** seem stable under the standard workup conditions. Additional evidence against this elimination route was provided by the reaction of **9a** in the absence of MeOH, which gave the same product **16a** in a comparable yield. Therefore, this route is unlikely. (2) Intramolecular proton shift in ylide **12** or zwitterion **13**: a proton shift may take place in **13** from the position adjacent to the carbocation to the anionic center to form **16** or a mixture of **16** + **17** (Scheme 6, route *a*).



Scheme 6

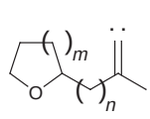
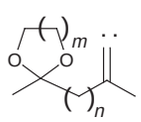
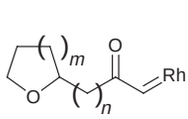
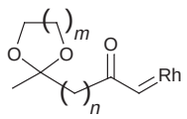
(3) Deprotonation of oxonium ions **14** and/or **15**: this route seems plausible in the presence of a protic substrate (Scheme 6, route *b*). Deprotonation must be more facile than nucleophilic attack by a conjugate base Nu$^-$ because only dienol diethers **16** and **17** were produced.

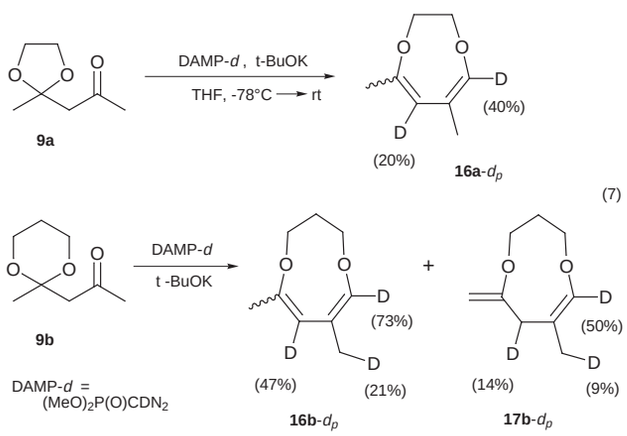
To differentiate between routes (2) and (3), some isotope-labeling experiments with **9a** and **9b** were investigated [eqns. (6)



(6)

Table 2 Applicable range of the ring-expansion reaction

	Alkylidenecarbene		Rhodium keto-carbenoid	
	Ether	Acetal	Ether	Acetal
n				
n-1	Yes	Yes	Yes	Yes
n-2	No	No	No	Yes



and (7)]. First, the reaction of **9a** with DAMP was carried out in the presence of deuterated methanol (MeOD) [eqn. (6)]. ^{1}H NMR analysis of product **16a** proved that deuterium was incorporated at the 5-position (>80%) but not significantly in other positions. This implies that, in the presence of methanol, the major proton source is provided intermolecularly, thus supporting route (3).

Second, deuterated DAMP, $(MeO)_2P(O)CDN_2$, was used as the diazomethylating reagent for both **9a** and **9b** in the absence of a proton source, *e.g.* MeOH [eqn. (7)]. The primary reason for using this deuterated reagent was to determine the destination of the label. In the middle stage of this reaction system, a mixture of the potassium salt of DAMP, t-BuOD, t-BuOK and DAMP-d_1 must be present. After the reaction was complete, products **16** and **17** were isolated to analyze isotope scrambling. This scrambling was observed at more than two positions in the product structures. If route (2) was the sole process, deuterium could not be incorporated in concentrations as high as 40–73% at the position of **16** originating from the carbene centre. Even without MeOH, ylide **12** can be deuterated by t-BuOD (route 3), which is formed by the reaction of t-BuOK with DAMP-d_1, thus incorporating deuterium at the position of **16** and **17** originating from the carbene centre. To rule out the possibility of the deuteration of **16a**, we carried out an independent treatment of **16a**-d_0 with DAMP-d_1 under the same conditions, and found that the H/D exchange did not take place at the same position. Therefore, we can conclude that in the reactions with DAMP-d_1 but without MeOH, both routes (2) and (3) are followed, albeit the latter seems to be the faster of the two.

Isotope scrambling in other positions can be explained in terms of H/D exchange reactions which take place before the diazomethyl-transfer reaction.

Summary

The major structural requisite for the ring enlargement of cyclic ether- and acetal-substituted alkylidenecarbenes is the length of the side-chain which tethers both the carbene center and a cyclic ether functional group: it should be one methylene unit ($n = 1$), since relieving the internal strain of the intermediate bicyclo[3.3.0]- or [m + 2.3.0]oxonium ylide **12** plays a key role in the enlargement process. Thus, with $n = 1$, ring-opened zwitterion structure **13** is preferred to the bicyclic ylide form **12**, whereas with $n = 2$ or larger, the bicyclic form **12** is preferred, and undergoes an S_N2-type ring-switching substitution reaction. As long as the length of the tethering side chain is fixed at $n = 1$, the size of the ethereal rings does not impair the enlargement, albeit acetals are favored more than ethers. Another major requisite is stabilization of the carbocation in the ylides and/or oxonium ions, as was exemplified by the efficient enlargement of cyclic acetal systems **12** in comparison with cyclic ether systems **4**.

Table 2 summarizes the scope and limitations of the present ring enlargement reaction in comparison with rhodium keto carbenoid systems,[8a,b] where *yes* or *no* means the enlargement is possible or impossible, respectively. In summary, the present ring-enlargement reaction meets our initial expectation that cyclic ethereal oxonium ylides, which are formed from cyclic acetal-substituted alkylidenecarbenes, may be used for the synthesis of cyclic dienol diethers and dioxacycloalkane derivatives of medium ring-sizes.

Experimental

General

^{1}H NMR spectra (300 MHz, in $CDCl_3$) were expressed in ppm (δ) using residual $CHCl_3$ (δ 7.26) as the internal standard, and ^{13}C NMR spectra (75.6 MHz, in $CDCl_3$) were expressed in δ values using $CDCl_3$ (δ 77.00) unless otherwise noted. Flash column chromatography was performed using silica gel (Wakogel C-300) or alumina (Merck aluminium oxide 90 active basic). Solvents were dried and distilled before use. High resolution mass spectra (HRMS) (EI, unless otherwise stated) were taken for most of the key liquid products together with, or in place of, elemental analyses.

Preparation of ketones

(Tetrahydrofuran-2-yl)acetone **1a** was prepared from 2-chlorotetrahydrofuran,[17] (tetrahydropyran-2-yl)acetone **1b** from 2-chlorotetrahydropyran[17] and (tetrahydropyran-2-yl)butan-3-one **1c** from tetrahydropyran-2-ylmethyl bromide. Acetonyl-substituted cyclic acetals **9a**–**d** were prepared by acetalyzation of the corresponding diketones as reported elsewhere (*vide infra*). Spectroscopic data of cyclic ether- and cyclic acetal-substituted alkanones are as follows. Product yields are calculated on the basis of isolated products and are shown in the main text.

(Tetrahydrofuran-2-yl)acetone (1a).[17–19] ^{1}H NMR 1.40–1.52 (m, 1H), 1.84–1.94 (m, 2H), 2.04–2.19 (m, 1H), 2.19 (s, 3H), 2.55 (dd, J = 15.9, 5.7 Hz, 1H), 2.74 (dd, J = 15.9, 7.5 Hz, 1H), 3.67–3.76 (m, 1H), 3.82–3.90 (m, 1H), 4.17–4.26 (m, including J = 7.5 Hz, 1H); IR (liquid film) 1715 (s), 1075 (s) cm^{-1}.

(Tetrahydropyran-2-yl)acetone (1b).[18–20] ^{1}H NMR 1.17–1.30 (m, 1H), 1.40–1.61 (m, 4H), 1.73–1.85 (m, 1H), 2.14 (s, 3H), 2.38 (dd, J = 15.6, 4.8 Hz, 1H), 2.62 (dd, J = 15.6, 8.1 Hz, 1H), 3.36–3.44 (m, 1H), 3.67–3.76 (m, 1H), 3.87–3.92 (m, 1H); ^{13}C NMR 23.3, 25.7, 30.9, 31.7, 50.3, 68.5, 74.1, 207.4; IR (liquid film) 1710 (s), 1085 (s) cm^{-1}. HRMS: Calc. for $C_8H_{14}O_2$ 142.0994. Found 142.0993. Anal. Calc. for $C_8H_{14}O_2$: C, 67.57; H, 9.92. Found: C, 67.65; H, 10.11.

4-(Tetrahydropyran-2-yl)-2-butanone (1c).[21] ^{1}H NMR 1.15–1.81 (m, 8H), 2.11 (s, 3H), 2.42–2.62 (m, 2H), 3.14–3.23 (m, 1H), 3.30–3.39 (m, 1H, including J = 11.1 Hz), 3.88–3.94 (m, 1H, including J = 11.1 Hz); IR (liquid film) 1715(s), 1090 (s) cm^{-1}.

(2-Methyl-1,3-dioxolan-2-yl)acetone (9a).[22] ^{1}H NMR 1.40 (s, 3H), 2.21 (s, 3H), 2.76 (s, 2H), 3.97 (m, 4H); ^{13}C NMR 24.2, 31.5 52.4, 64.5, 107.7, 205.8; IR (liquid film) 1710 (s), 1120 (s), 1100 (s) cm^{-1}.

(2-Methyl-1,3-dioxan-2-yl)acetone (9b).[23] ^{1}H NMR 1.49 (s, 3H), 1.57–1.61 (m, 1H), 1.80–1.94 (m, 1H), 2.25 (s, 3H), 2.79 (s, 2H), 3.85–4.02 (m, 4H); ^{13}C NMR 20.4, 25.1, 31.7, 53.0, 59.7, 97.6, 206.3; IR (liquid film) 1710 (s), 1140 (s), 1115 (s), 1085 (s) cm^{-1}.

(2-Methyl-1,3-dioxepan-2-yl)acetone (9c). ^{1}H NMR 1.35 (s, 3H), 1.59–1.62 (m, 4H), 2.19 (s, 3H), 2.70 (s, 2H), 3.67–3.70 (m, 4H); ^{13}C NMR 22.9, 29.5, 31.6, 51.8, 62.3, 100.7, 206.4; IR (liquid film) 1705 (s), 1215 (s), 1130 (s), 1060 (s), 1035 (s) cm^{-1}.

General experimental procedure for the reaction of acetonyl-substituted cyclic ethers (1) and acetals (9) with potassium salt of DAMP

Dimethyl diazomethylphosphonate (DAMP, $(MeO)_2P(O)$-CHN_2) was prepared from dimethyl phthalimidomethylphosphonate according to the method reported by Seyferth and co-workers.[10a] DAMP-d_1 was prepared by the H/D exchange reaction of DAMP with an excess of methanol-d_1 in the presence of t-BuOK, followed by distillation *in vacuo*; *d*-content of DAMP-d_1 >96%.

In an argon-flushed flask were placed t-BuOK (2.0 equiv.) and THF (an amount necessary to prepare approximately 0.1 M ketone solution), and the flask was cooled to −78 °C. DAMP, which was dissolved in a small amount of THF, was slowly added to the cold solution, followed by the addition of the ketone (**1a**–**c** and **9a**–**d**, 1.0 equiv.) dissolved in a small amount of THF. After stirring for 5 min at −78 °C, the cold-bath was removed and the reaction mixture was slowly warmed to ambient temperature, while the evolution of N_2 gas was observed. After 1 h, the solution was condensed under a moderately reduced pressure to remove THF, and the residue was washed and extracted with a mixture of aq. $NaHCO_3$ and either pentane or diethyl ether. The extracted organic layer was dried over anhydrous $MgSO_4$, condensed, and submitted to analyses.

Yields of products obtained from the reactions of **1a**–**c** and **9a**–**c** were mainly determined by quantitative gas-chromatographic analysis using *m*-dimethoxybenzene or *n*-tetradecane as the internal standard. Product yields from **9d** were determined by ^{1}H NMR analysis.

Spectroscopic data of key products obtained in the reactions of cyclic ether- and cyclic acetal-substituted alkanones with the potassium salt of DAMP are as follows.

3-Methyl-5-methoxy-5,6,7,8-tetrahydro-4*H*-oxocine (6a)

^{1}H NMR 1.45–2.00 (m, 4H), 1.62 (d, J = 1.2 Hz, 3H), 2.29 (dd, J = 13.8, 3.0 Hz, 1H), 2.39 (dd, J = 13.8, 8.7 Hz, 1H), 3.35 (s, 3H), 3.44–3.54 (m, including J = 8.7 and 3.0 Hz, 1H), 3.69–3.78 (m, 2H), 5.92 (narrow m, including J = 1.2 Hz, 1H); ^{13}C NMR 18.7, 23.5, 31.8, 34.5, 56.1, 71.5, 79.7, 124.9, 138.9; IR (liquid film) 1675 (w), 1130 (s), 1090 (s) cm^{-1}. HRMS: Calc. for $C_9H_{16}O_2$ 156.1151. Found 156.1140. Anal. Calc. for $C_9H_{16}O_2$: C, 69.20; H, 10.32. Found: C, 69.32; H, 10.17.

2-(2′-Methyl-3′-methoxyprop-2′-enyl)tetrahydrofuran (7a) (*E* or *Z*)

^{1}H NMR 1.63 (d, J = 1.2 Hz, 3H), 1.80–2.25 (m, 6H), 3.56 (s, 3H), 3.68–3.75 (m, 1H), 3.83–3.96 (m, 2H), 5.83 (narrow m, including J = 1.2 Hz, 1H).

3-Methyl-5-methoxy-4,5,6,7,8,9-hexahydrooxonine (6b)[24]

^{1}H NMR (C_6D_6) 1.27–1.36 (m, 3H), 1.42 (d, J = 1.2 Hz, 3H), 1.52–1.65 (m, 2H), 1.71–1.81 (m, 1H), 2.28 (dd, J = 14.4, 9.0 Hz, 1H), 2.50 (dd, J = 14.4, 3.6 Hz, 1H), 3.10 (s, 3H), 3.33–3.48 (m, 2H), 3.57–3.64 (m, including J = 9.0, 3.6 Hz, 1H), 5.61 (narrow m, J = 1.2 Hz, 1H); ^{13}C NMR (C_6D_6) 19.3, 22.3, 29.8, 34.4, 36.1, 55.9, 70.4, 80.8, 119.3, 140.6; IR (liquid film) 1680 (m), 1140 (s), 1090 (s) cm^{-1}. HRMS: Calc. for $C_{10}H_{18}O_2$ 170.1307. Found 170.1313. Anal. Calc. for $C_{10}H_{18}O_2$: C, 70.55; H, 10.66. Found: C, 70.62; H, 10.88.

2-(2′-Methyl-3′-methoxyprop-2′-enyl)tetrahydropyran (7b) (*E* or *Z*)

^{1}H NMR 1.13–1.57 (m, 5H), 1.59 (s, 3H), 1.75–1.84 (m, 1H), 1.89 (dd, J = 14.0, 6.3 Hz, 1H), 2.10 (dd, J = 14.0, 6.5 Hz, 1H), 3.28–3.44 (m, 2H), 3.54 (s, 3H), 3.93–4.00 (m, 1H), 5.77–5.81 (narrow m, 1H).

Another isomer of 7b (*Z* or *E*)

^{1}H NMR 1.20–1.52 (m, 5H), 1.55 (s, 3H), 1.75–1.83 (m, 1H), 2.16 (dd, J = 13.5, 6.3 Hz, 1H), 2.27 (dd, J = 13.5, 7.2 Hz, 1H), 3.32–3.44 (m, 2H), 3.50 (s, 3H), 3.93–4.00 (m, 1H), 5.82 (narrow m, including J = 0.6 Hz, 1H).

2-Methyl-1-oxaspiro[5,4]dec-9-ene (8c). ^{1}H NMR 1.50–1.73 (m, 6H), 1.75–1.76 (m, including J = 1.2 Hz, 3H), 1.85–2.06 (m, 2H), 2.12–2.23 (m, 1H), 2.35–2.46 (m, 1H), 3.61–3.76 (m, 2H), 5.55 (q, J = 1.2 Hz, 1H); ^{13}C NMR 16.8, 20.9, 25.9, 34.9, 35.3, 35.4, 63.3, 87.4, 128.5, 144.2; IR (liquid film) 1655 (w), 1080 (s), 820 (w) cm^{-1}. HRMS: Calc. for $C_{10}H_{16}O$ 152.1202. Found 152.1193. Anal. Calc. for $C_{10}H_{16}O$: C, 78.89; H, 10.59. Found: C, 78.68; H, 10.68.

5,7-Dimethyl-2,3-dihydro-1,4-dioxocine (16a). ^{1}H NMR 1.61 (d, J = 1.5 Hz, 3H), 1.84 (d, J = 0.6 Hz, 3H), 3.80–3.83 (m, including J = 7.5 Hz, 2H), 4.26–4.29 (m, including J = 7.5 Hz, 2H), 4.35 (q, J = 0.6 Hz, 1H), 5.76 (narrow m, including J = 1.5 Hz, 1H); ^{13}C NMR (C_6D_6) 18.4, 22.0, 63.8, 64.0, 99.0, 122.7; IR (liquid film) 1645 (s), 1205 (s), 1185 (s), 1035 (w) cm^{-1}. HRMS: Calc. for $C_8H_{12}O_2$ 140.0837. Found 140.0844. Anal. Calc. for $C_8H_{12}O_2$: C, 68.55; H, 8.63. Found: C, 68.28; H, 8.81.

8-Methyl-6-methylene-2,3-dihydro-1*H*,7*H*-1,5-dioxonine (17b). ^{1}H NMR (C_6D_6) 1.35–1.36 (m, including J = 1.5, 0.6 Hz, 3H), 1.38–1.45 (m, 2H), 2.67–2.68 (m, including J = 0.6 Hz, 2H), 3.35–3.39 (m, 2H), 3.80–3.83 (m, 2H), 4.21 (d, J = 0.9 Hz, 1H), 4.30 (narrow m, including J = 0.9 Hz, 1H), 5.68–5.71 (m, including J = 1.5 Hz, 1H); ^{13}C NMR (C_6D_6) 18.67, 28.80, 37.91, 68.42, 69.31, 87.93, 117.36, 139.66, 162.80.

6,8-Dimethyl-2,3-dihydro-1*H*-1,5-dioxonine (16b). ^{1}H NMR (C_6D_6) 1.56 (dd, J = 1.5, 0.6 Hz, 3H), 1.60–1.66 (m, 2H), 1.67 (d, J = 0.9 Hz, 3H), 3.55–359 (m, 2H), 3.70–3.73 (m, 2H), 4.66 (br, 1H), 5.91–5.94 (q, J = 1.5 Hz, 1H).

A mixture of 16b and 8-methyl-6-methylene-2,3-dihydro-1*H*,7*H*-1,5-dioxonine (17b). IR (liquid film) 1650 (s), 1210 (s), 1060 (s), 1045 (s) cm^{-1}. HRMS: Calc. for $C_9H_{14}O_2$ 154.0994. Found 154.1000. Anal. Calc. for $C_9H_{14}O_2$: C, 70.15; H, 9.16. Found: C, 70.01; H, 9.35.

7,9-Dimethyl-2,3,4,5-tetrahydro-1,6-dioxecine (16c). ^{1}H NMR (C_6D_6) 1.42–1.53 (m, 4H), 1.54 (d, J = 1.5 Hz, 3H), 1.67 (d, J = 1.2 Hz, 3H), 3.53–3.56 (m, 2H), 3.62–3.65 (m, 2H), 4.66 (s, 1H), 5.68–5.70 (m, including J = 1.5, 1.2 Hz, 1H); ^{13}C NMR (C_6D_6) 17.9, 18.2, 25.1, 28.2, 66.9, 71.2, 108.0, 112.4, 140.9, 151.3; IR (liquid film) 1655 (s), 1200 (s), 1075 (s), 1015 (s) cm^{-1}. HRMS: Calc. for $C_{10}H_{16}O_2$ 168.1150. Found 168.1147.

9-Methyl-7-methylene-2,3,4,5-tetrahydro-7*H*-1,6-dioxecine (17c). ^{1}H NMR (C_6D_6) 1.29 (s, 3H), 1.38–1.54 (m, 4H), 2.72–2.73 (m, including J = 1.2 Hz, 2H), 3.37–3.40 (m, 2H), 3.79–3.83 (m, 2H), 4.15 (overlapping two d, J = 2.1 Hz, 2H), 5.51–5.54 (m, including J = 1.2 Hz, 1H).

10-Hydroxy-4-methyl-6-oxadec-4-ene-2-one (19). ^{1}H NMR 1.54 (d, J = 1.2 Hz, 3H), 1.57–1.74 (m, including J = 6.0 Hz, 4H), 1.77 (br s, 1H), 2.12 (s, 3H), 3.11 (s, 2H), 3.63–3.67 (m, including J = 6.0 Hz, 2H), 3.71–3.76 (m, including J = 6.0 Hz, 2H), 5.97–5.98 (narrow m, including J = 1.2 Hz, 1H); ^{13}C NMR 10.0, 17.6, 26.2, 28.9, 29.2, 44.8, 62.3, 71.7, 107.1, 142.7; IR (liquid film) 3420 (br), 1705 (s), 1170 (s), 1140 (s) cm^{-1}. HRMS: Calc. for $C_{10}H_{18}O_3$ 186.1255. Found 186.1253.

1,8-Bis(2′-methyl-1′,3′-dioxolan-2′-yl)-3,6-dimethylocta-3,4,5-triene (20). ^{1}H NMR 1.33 (s, 6H), 1.85–1.91 (m, 4H), 1.89 (s, 6H), 2.17–2.23 (m, 4H), 3.91–3.95 (m, 8H). ^{13}C NMR 22.9, 23.9, 31.4, 37.2, 64.6, 109.7, 112.1, 214.8. HRMS: Calc. for $C_{18}H_{28}O_4$ 308.1987. Found 308.1981.

2-Methyl-2-(3′-cyanobutyl)-1,3-dioxolane (21). ^{1}H NMR 1.31 (d, J = 7.2 Hz, 3H), 1.31 (s, 3H), 1.61–1.92 (m, including J = 6.6 Hz, 4H), 2.59–2.71 (m, including J = 6.6, 7.2 Hz, 1H), 3.88–3.99 (m, 4H). ^{13}C NMR 18.0, 23.8, 25.4, 28.4, 36.2, 64.6, 64.7, 109.2, 122.8. IR (liquid film) 2240, 1065 cm^{-1}. HRMS (CI): Calc. for $C_{10}H_{18}O_3$ (MH^+) 170.1180. Found 170.1189.

2-[2′-(*tert*-Butoxy)ethoxy]-2,5-dimethyl-3,4-dihydro-2*H*-pyran (22). ^{1}H NMR 1.17 (s, 9H, t-Bu), 1.37 (s, 3H), 1.54 (narrow m, 3H), 1.54–1.74 (m, 2H), 1.88–1.95 (m, 1H), 2.11–2.23 (m, including J = 1.2 Hz, 1H), 3.40–3.44 (m, including J = 5.7, 6.0 Hz, t-BuOCH_2CH$_2$O-), 3.52–3.63 (m, including J = 5.7, 6.0 Hz, 2H, -CH$_2$CH_2O-ring), 5.99 (narrow m, including J = 1.2 Hz, 1H); ^{13}C NMR 18.2, 22.6, 23.5, 27.4, 31.7, 60.4, 61.4, 72.8, 96.9, 109.3, 134.7. HRMS: Calc. for $C_{13}H_{24}O_3$ 228.1725. Found 228.1735.

1-Oxocan-3-ylidenemethyl 5,6,7,8-tetrahydro-4*H*-1-oxocin-3-yl ether (24). ^{1}H NMR one isomer (*E* or *Z*) 1.50–1.75 (br m, 12H), 2.25–2.40 (br m, 4H), 3.61 (m, 2H), 3.77 (m, 2H), 3.96 (d, J = 0.6 Hz, 2H), 5.85 (s, 1H), 6.10 (s, 1H). HRMS: Calc. for $C_{15}H_{24}O_{13}$ 252. 1726. Found 252.1719. ^{1}H NMR of another isomer of **24** (*Z* or *E*) 1.50–1.75 (br m, 12H), 2.13 (br t, 2H), 2.25–2.35 (br m, 2H), 3.59 (br t, 2H), 3.76 (br t, 2H), 4.21 (d, J = 1.5 Hz, 2H), 5.82 (s, 1H), 6.10 (br s, 1H).

References

1 K. Kondo, I. Tabushi, R. Noyori and S. Fujita, *Carbenes*, *Ylides*, *Nitrenes and Benzynes*, ed. T. Goto, Hirokawa, Tokyo, 1976.

2 The lifetimes of ethereal oxonium ylides are too short for them to be identified by spectroscopic methods. Therefore, their intermediacy has been demonstrated indirectly: (*a*) I. Naito, A. Oku, N. Ohtani, H. Tanimoto and H. Fujiwara, *J. Chem. Soc.*, *Perkin Trans. 2*, 1996, 725; (*b*) T. Sueda, T. Nagaoka, S. Goto and M. Ochiai, *J. Am. Chem. Soc.*, 1996, **118**, 10141.

3 For examples of intermolecular oxonium ylide formation, see: (*a*) H. Nozaki, H. Takaya and R. Noyori, *Tetrahedron Lett.*, 1966, **7**, 2563; (*b*) K. Friedrich, U. Jansen and W. Kirmse, *Tetrahedron Lett.*, 1985, **26**, 193; (*c*) H. Iwamura and Y. Imahasi, *Tetrahedron Lett.*, 1975, 1401; (*d*) G. A. Olah, H. Doggweiler and J. D. Felberg, *J. Org. Chem.*, 1984, **49**, 2116; (*e*) M. S. Baird, A. G. W. Baxter, A. Hoorter and I. Jefferson, *J. Chem. Soc.*, *Perkin Trans. 1*, 1991, 2575; (*f*) F. G. West, T. H. Eberlein and R. W. Tester, *J. Org. Chem.*, 1992, **57**, 3479; (*g*) M. P. Doyle, J. H. Griffin, M. S. Chinn and D van Leusen, *J. Org. Chem.*, 1984, **49**, 1917; (*h*) M. C. Pirrung, W. L. Brown, S. Rege and P. Laughton, *J. Am. Chem. Soc.*, 1991, **113**, 8561; (*i*) J. C. Gilbert and U. Weerasooriya, *Tetrahedron Lett.*, 1980, **21**, 2041.

4 For examples of intramolecular oxonium ylide formation, see: (*a*) J. S. Clark, A. G. Dossetter and W. G. Whittingham, *Tetrahedron Lett.*, 1996, **37**, 5603; (*b*) J. S. Clark and G. A. Whitlock, *Tetrahedron Lett.*, 1994, **35**, 6381; (*c*) M. C. Pirrung and J. A. Werner, *J. Am. Chem. Soc.*, 1986, **108**, 6060.

5 A. Oku, S. Ohwaki and K. Kimura, *Acta Chem. Scand.*, 1993, **47**, 391.

6 (*a*) A. Padwa and S. F. Hornbuckle, *Chem. Rev.*, 1991, **91**, 263; (*b*) A. Padwa and K. E. Krumpe, *Tetrahedron*, 1992, **48**, 5385.

7 (*a*) C. J. Moody and R. J. Taylor, *J. Chem. Soc.*, *Perkin Trans. 1*, 1989, 721; (*b*) M. J. Davies, C. J. Heslin and C. J. Moody, *J. Chem. Soc.*, *Perkin Trans. 1*, 1989, 2473; (*c*) M. J. Davies, C. J. Moody and R. J. Taylor, *Synlett*, 1990, 93.

8 (*a*) A. Oku, S. Ohki, T. Yoshida and K. Kimura, *Chem. Commun.*, 1996, 1077; (*b*) A. Oku, N. Murai and J. Baird, *J. Org. Chem.*, 1997, **62**, 2123; (*c*) T. Kamada, Ge-Quin, M. Abe and A. Oku, *J. Chem. Soc.*, *Perkin Trans. 1*, 1996, 413.

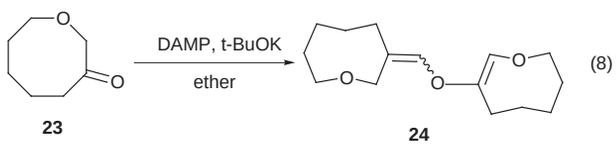
9 Other diazomethylation reagents such as diazomethyl(trimethyl)-silane in combination with n-BuLi were not successful for this purpose.

10 For the standard procedure of diazomethylation, see: (*a*) D. Seyferth, R. S. Marmor and P. Hilbert, *J. Org. Chem.*, 1971, **36**, 1379; (*b*) E. W. Colvin and B. Hamill, *J. Chem. Soc.*, *Perkin Trans. 1*, 1977, 869; (*c*) J. C. Gilbert and U. Weerasooriya, *J. Org. Chem.*, 1979, **44**, 4997; (*d*) J. C. Gilbert, D. H. Giamalva and U. Weerasooriya, *J. Org. Chem.*, 1983, **48**, 5251; (*e*) J. C. Gilbert and B. K. Blackburn, *J. Org. Chem.*, 1986, **51**, 3656 and 4087; (*f*) S. Ohira, K. Okai and T. Moritani, *J. Chem. Soc.*, *Chem. Commun.*, 1992, 721.

11 MeOH was used as a protic nucleophile to trap the ylide.

12 (*a*) The amount of isolated **7** (R = Me, both **a** and **b**) were scanty. Therefore, their structures were determined simply on the basis of ^{1}H NMR spectra. See the Experimental section; (*b*) when diethyl ether was used as the solvent in place of THF, **7a** (R = C_2H_5O, 3%) was obtained, which was presumed to be formed from oxonium ylide of **3a** with diethyl ether.

13 When oxocan-3-one **23**[8a] was treated with DAMP and t-BuOK in diethyl ether under similar reaction conditions, an isomeric mix of ethereal products **24** (isomer ratio = 2.5) was isolated in 78% yield. For spectral data of **24**, see the Experimental section.

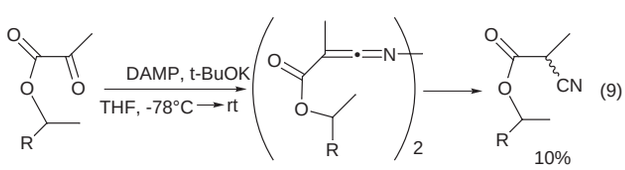


23 **24**

14 Isolated diene **16a** was treated independently over silica gel and was shown to be intact under the same conditions.

15 Two configurations, *cis*,*cis* and *cis*,*trans*, have been reported for cycloocta-1,3-diene and cyclodeca-1,3-diene, respectively. (*a*) W. J. Leigh, K. Zheng, N. Nguyen, N. H. Werstiuk and J. Ma, *J. Am. Chem. Soc.*, 1991, **113**, 4993; (*b*) A. T. Blomquist and A. Goldstein, *J. Am. Chem. Soc.*, 1954, **77**, 998.

16 S. Ohira, I. Noda, T. Mizobata and M. Yamato, *Tetrahedron Lett.*, 1995, **36**, 3375. They presumed that 2-cyanopropionate could be formed from pyruvate *via* the corresponding azines of diazoalkene [eqn. (9)].



17 T. Shono, Y. Matsumura, O. Onomura and Y. Yamada, *Synthesis*, 1987, 1099.

18 R. Bihovsky, M. U. Kumar, S. Ding and A. Goyal, *J. Org. Chem.*, 1989, **54**, 4291.

19 A. P. Krapcho and A. J. Lovey, *Tetrahedron Lett.*, 1973, 957.

20 V. Berens and H. D. Scharf, *J. Org. Chem.*, 1995, **60**, 5127.

21 C. S. Marvel and F. D. Hager, *Org. Synth.*, 1932, **Coll. Vol. 9**, 248.

22 M. Bertrand, G. Leandri and A. Meou, *Tetrahedron*, 1981, **37**, 1703.

23 J. A. Hyatt, *J. Org. Chem.*, 1983, **48**, 129.

24 J. C. Gilbert and B. K. Blackburn, *J. Org. Chem.*, 1986, **51**, 656.

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