Nickel catalyzed Grob fragmentation: ω-dienyl aldehydes synthesis†

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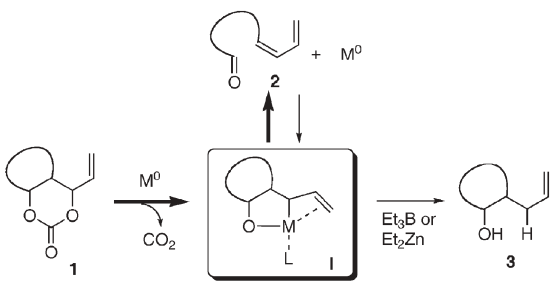
With a proper choice of phosphane ligands, a $Ni(cod)_2$–phosphane catalyst promotes decarboxylative ring-opening reaction of a wide structural variety of cyclic carbonates 1 to give ω-dienyl aldehydes 2 in good yields.

The Grob fragmentation reaction is a very powerful tool for the construction of desired molecules.[1] However, harsh reaction conditions, either strongly basic or acidic and/or high temperatures, have limited its wide use.

In the last decade, C–C bond cleavage reactions catalyzed or mediated by transition metals have gained significant attention,[2,3] because they can be performed under much milder reaction conditions and provide new organic transformations that are otherwise difficult to achieve.

In 1997, we revealed that many palladium species, especially $Pd_2[(dba)_3]_2{\cdot}CHCl_3$ [dba = dibenzylideneacetone] in acetonitrile, catalytically promoted the Grob type decarboxylative ring-opening reaction of cyclic carbonates **1** into ω-dienyl aldehydes **2** (Scheme 1).[4] The reaction proceeds at room temperature and is rationalized by a facile β-C elimination of an oxapalladacyclopentane intermediate **I** (M = Pd^{2+}). On the other hand, we have demonstrated that, $Ni(acac)_2$ in the presence of triethylborane[5] or diethylzinc[6] catalytically promotes the reductive cyclization (homoallylation) of **2** and provides bis-homoallyl alcohols **3** in good yields (Scheme 1).[7] This formally reverse reaction was supposed to proceed through oxidative addition of a nickel(0) species across the diene and aldehyde moieties of **2**, followed by the reduction of an oxanickellacyclopentane intermediate **I** (M = Ni^{2+}) with Et_3B or Et_2Zn. Recently, the intermediacy of **I** (M = Ni^{2+}) was supported by Ogoshi and Kurosawa, who have succeeded in the isolation and X-ray structure characterization of **I** (without a tether) prepared by the stoichiometric reaction of $Ni(cod)_2$ [cod = 1,5-cyclooctadiene], a diene and an aldehyde in the presence of a monodentate phosphane ligand.[8]



Scheme 1 Nickel (or palladium) catalyzed fragmentation of **1** to **2** and cyclization of **2** to **3** *via* a common intermediate **I** (M = Ni or Pd).

These observations suggest that the equilibrium between **I** and **2** and M^0 is strongly affected by the nature of the transition metal; nickel tends to shift the equilibrium to the side of **I**, while palladium works oppositely to drive the equilibrium to the side of **2** and Pd^0. This contrasting behaviour between nickel and palladium might be rationalized in part by the fact that nickel forms a stronger metal–oxygen bond than palladium, *e.g.*, $DH°$(Ni–O) = 60.5 kcal mol^{-1} and $DH°$(Pd–O) = 58.9 kcal mol^{-1} for *cis*-$(PH_3)_2M(OMe)Me$.[9]

Here we disclose that $Ni(cod)_2$, despite the above-mentioned unfavorable reaction features, nicely catalyzes the decarboxylative fragmentation reaction of a wide structural variety of **1** and furnishes ω-dienyl aldehydes **2** in comparable or better yields than palladium species. However, unlike the palladium catalysis, which worked equally well irrespective of the structure types of **1**,[4] a nickel species required a fine tuning of the reaction conditions, especially an appropriate choice of phosphane ligands, depending on the structure types of **1**.

As summarized in Table 1, carbonates characterized by their ring strain (**1a–c**) and/or torsional strain (**1d,e**) smoothly underwent the fragmentation reaction in the presence of $Ni(cod)_2$ (10 mol%) and PPh_3 (40 mol%) in acetonitrile at room temperature and furnished **2** in comparable yields or even in better yields than those obtained by $Pd_2(dba)_3{\cdot}CHCl_3$.

In sharp contrast to these, as shown in run 1, Table 2, a strain-free six-membered carbonate **1f** was robust and remained unchanged under usual conditions (at 25 °C) and even under forcing conditions undertaken at a higher temperature (81 °C). This was rather surprising in view of a smooth fragmentation of **1f** with $Pd_2[(dba)_3]_2{\cdot}CHCl_3$ at room temperature yielding **2f** in 77% isolated yield (E : Z = 10 : 1, footnote b, Table 2). Neither the monodentate trialkyl- nor triarylphosphane ligands were effective (runs 1–3). Among bidentate phosphane ligands, only those with bite angles of *ca.* 95–105° effectively promoted the fragmentation reaction (runs 6 and 7, Table 2).

Similar results were obtained for other cyclohexane derivatives **1j** (runs 7 and 8, Table 3) and **1k** (runs 9 and 10); with $Ni(cod)_2$/PPh_3, they remained intact even after long heating at the refluxing temperature of acetonitrile, while with $Ni(cod)_2$/DPPF, they smoothly underwent the ring-opening reaction at room temperature and provided **2j** and **2k** in much better yields than those with $Pd_2[(dba)_3]_2{\cdot}CHCl_3$.

The large bite angle of DPPF (99–105°) might be suited to the tetrahedral geometry of a Ni^0 species **III** and not to a square planer geometry of a Ni^{2+} species **II** (Scheme 2).[10] This destabilization of

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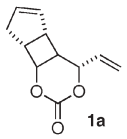
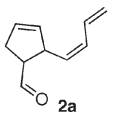
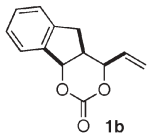
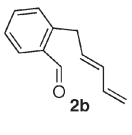
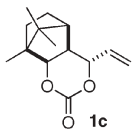
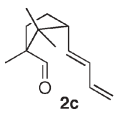
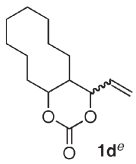
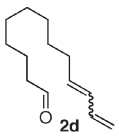
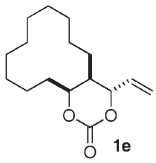
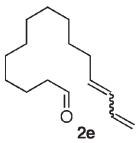
† Electronic supplementary information (ESI) available: Experimental procedures and analytical and spectroscopic data for **1a–m**[13] and **2a–m**. See DOI: 10.1039/b610164j

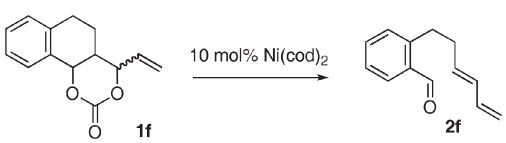
Table 1 Synthesis of ω-dienyl aldehydes **2** by Ni-catalyzed decarboxylative ring-opening reaction of **1**[a]

Run	**1**	*t*/h	Product **2**	Yield[b] (%) Ni	Pd
1	 **1a**	2	 **2a**	75 (1 : 2.4)	65 (1 : 4.4)[c]
2	 **1b**	6	 **2b**	78 (2 : 1)	87 (1.7 : 1)[c]
3	 **1c**	0.5	 **2c**	96 (only *E*)	70 (only *E*)[d]
4	 **1d**[e]	24	 **2d**	97 (1 : 1)	91 (1 : 1)[c]
5	 **1e**	24	 **2e**	85 (1 : 1)	85 (1 : 3)[d]

[a] *Reaction conditions*: **1** (1 mmol), $Ni(cod)_2$ (0.1 mmol) and PPh_3 (0.4 mmol) in acetonitrile (5 mL) at room temperature under N_2. [b] *E*/*Z* Ratio of products in parenthesis. [c] Yield obtained using $Pd_2(dba)_3{\cdot}CHCl_3$.[4a,d] [d] Ref. 4*a*. [e] A mixture of stereoisomers (see ESI).

II and stabilization of **III** by bidentate ligands with wide bite angles might cooperate to facilitate the fragmentation of **II** and shift the equilibrium to the side of a mixture of **2** and **III**. The complex **III**, however, might be reactive enough toward oxidative addition to allylic carbonates **1** and might be able to supply **II**, hence accomplishing the catalytic cycle.

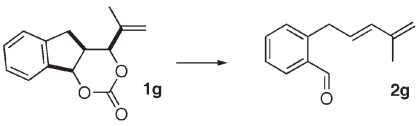
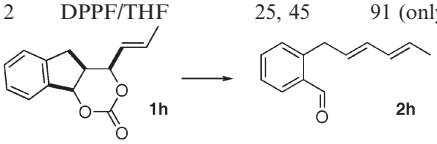
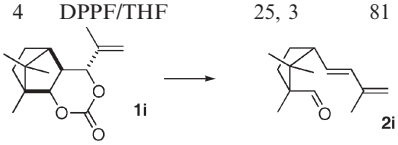
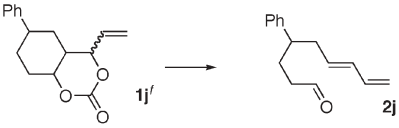
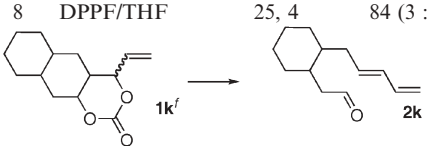
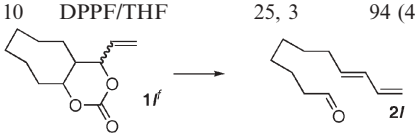
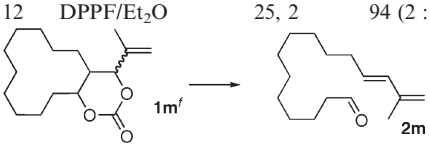
Table 2 Effects of phosphanes on the fragmentation of **1f**



Run	Phosphane/solvent[c]	*T*/°C, *t*/h	Yield (*E* : *Z*)[d] (%)	Bite angle/°
1	PPh_3/AN	81, 24	NR	—
2	*n*-Bu_3P/AN	81, 24	NR	—
3	Cy_3P/AN	81, 24	NR	—
4	DPPE/THF	25, 48	NR	85
5	DPPP/THF	25, 48	NR	90–95
6	DPPB/THF	25, 4	76 (>20 : 1)	94–99
7	DPPF/THF	25, 4	78 (18 : 1)	99–105

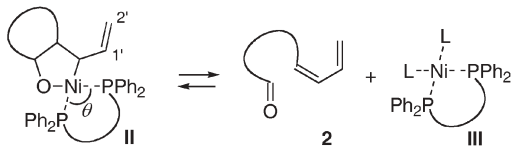
[a] *Reaction conditions*: **1f** (1 mmol, a mixture of stereoisomers, see ESI), $Ni(cod)_2$ (0.1 mmol) and a phosphane (0.4 mmol for a monodentate and 0.2 mmol for a bidentate ligand) in a solvent (5 mL) under N_2. [b] **2f** in 77% (*E* : *Z* = 10 : 1) using $Pd_2(dba)_3{\cdot}CHCl_3$ as a catalyst.[4a] [c] AN = acetonitrile, THF = tetrahydrofuran, Cy = cyclohexyl, DPPE = 1,2-bis(diphenylphosphino)ethane, DPPP = 1,3-bis(diphenylphosphino)propane, DPPB = 1,4-bis(diphenylphosphino)butane, DPPF = 1,1′-bis(diphenylphosphino)ferrocene. [d] Yields refer to the isolated spectroscopically homogeneous **2f**.

Table 3 Acceleration of the Ni-catalyzed fragmentation of **1** with bidentate phosphane ligands with wide bite angles[a]

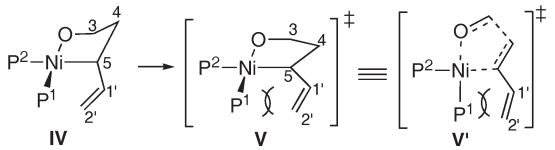
Run	Phosphane/solvent[b]	*T*/°C, *t*/h	Yield (*E*/*Z*) (%) Ni	Pd
	 **1g** → **2g**			
1	PPh_3/AN	81, 24	NR	
2	DPPF/THF	25, 45	91 (only *E*)	82 (only *E*)[c]
	 **1h** → **2h**			
3	PPh_3/AN	81, 24	NR	
4	DPPF/THF	25, 3	81 (only *E*,*E*)	93 (only *E*,*E*)[c]
	 **1i** → **2i**			
5	PPh_3/AN	81, 24	24 (only *E*)[e]	
6	DPPF/ether	25, 9	98 (only *E*)	55 (only *E*)[d]
	 **1j**[f] → **2j**			
7	PPh_3/AN	81, 24	NR	
8	DPPF/THF	25, 4	84 (3 : 1)	42 (2 : 1)[d]
	 **1k**[f] → **2k**			
9	PPh_3/AN	81, 30	NR	
10	DPPF/THF	25, 3	94 (4 : 1)	60 (1 : 1)[d]
	 **1l**[f] → **2l**			
11	PPh_3/AN	81, 15	40 (1 : 5)	
12	$DPPF/Et_2O$	25, 2	94 (2 : 1)	54 (1 : 4)[c]
	 **1m**[f] → **2m**			
13	PPh_3/AN	81, 40	NR	
14	DPPF/THF	25, 72	43 (only *E*)	
15	DPPPent/THF	25, 30	100 (only *E*)	63 (only *E*)[c]

[a] *Reaction conditions*: **1** (1 mmol), $Ni(cod)_2$ (0.1 mmol) and a phosphane (0.4 mmol for a monodentate and 0.2 mmol for a bidentate ligand) in a solvent (5 mL) under N_2. [b] DPPPent = 1,5-bis(diphenylphosphino)pentane. [c] Ref. 4*a*. [d] Yield obtained using $Pd_2(dba)_3{\cdot}CHCl_3$.[4a] [e] 59% conversion (59% isolated yield based on conversion). [f] A mixture of stereoisomers (see ESI).

In Table 3 are summarized the carbonates **1** that are either unreactive (NR) or provide **2** albeit in low yields with the catalyst $Ni(cod)_2/PPh_3$. Comparison of the data in Tables 1 and 3 clearly



Scheme 2 Acceleration of β-C elimination by bidentate ligands with wide bite angles (θ).



Scheme 3 Increase in steric repulsion between P1 and vinyl moiety in a transition state **V**, placing all the P1, P2, Ni, C5, C4, C3 and O atoms in the same plane.

indicates that both the C1′- and C2′-substituents on the vinyl group of **1** seriously retard the reaction. For example, while **1b** undergoes fragmentation at room temperature with $Ni(cod)_2/PPh_3$ (run 2, Table 1), the C1′-Me and C2′-Me derivatives, **1g** and **1h**, remain unchanged under the same or even under forcing conditions (runs 1 and 3, Table 3). The fragmentation of **1g** and **1h** was successfully achieved by making use of the $Ni(cod)_2$/DPPF catalytic system (runs 2 and 4). More contrasting results were observed between the reactions of **1e** (run 5, Table 1) and **1m** (runs 13–15). For the latter substrate, even the $Ni(cod)_2$/DPPF catalytic system was not effective enough, and $Ni(cod)_2$/DPPPent [1,5-bis(diphenylphosphino)pentane] turned out to work much better.[11]

The retardation of the reaction by the C1′ and C2′ substituents, especially by the one on C1′ (cf, the reaction times in runs 2 and 4, Table 3), might be ascribed to the increase in the steric repulsion between P1 and the vinyl group moiety that arises when **IV** approaches a transition state **V** (Scheme 3), since this process is accompanied by the decrease in the absolute value of the dihedral angle Ni–C5–C4–C3, and hence the decrease in the dihedral angle P1–Ni–C5–C1′. That is, there seems to exist an interesting dichotomy in the role of bidentate phosphane ligands with wide bite angles; electronically they accelerate the fragmentation reaction by stabilizing **III** and destabilizing **II** (Scheme 2),[12] while sterically they retard the reaction preventing the Ni–C5 bond from taking coplanar conformation with the C3–C4 bond.

Cyclic carbonates **1a–m** were prepared readily according to the following three-step procedures (see, ESI†): (1) cross-aldol of α,β-unsaturated aldehyde with lithium enolate of cyclic ketone, (2) $LiAlH_4$ reduction to diol, (3) cyclic carbonation with methyl chloroformate/triethylamine.

Finally, it may be worth noting that the present nickel catalyzed degradation not only records better yields, but also shows higher (*E*)-selectivity than the palladium catalyzed reaction. For example, a mixture of (*E*)- and (*Z*)-**2k** was obtained in a ratio of 1 : 1 in 60% isolated yield under the palladium catalysis, while under the nickel catalysis the same product was obtained in a ratio of 4 : 1 in 94% yield (run 10, Table 3). More contrasting results were observed for the reaction of **1*l***, where the yield was doubled and the stereoselectivity was reversed from the (*Z*)-selective one to the (*E*)-selective one (run 12, Table 3).

In summary, the $Ni(cod)_2/PPh_3$ or $Ni(cod)_2$/DPPF catalytic system promotes a novel decarboxylative fragmentation of a wide structural variety of cyclic carbonates **1** to furnish ω-dienyl aldehydes **2**, where the phosphane ligands play a pivotal role to shift the equilibrium between an intermediate **I** and an ω-dienyl aldehyde **2** to the product side. The reaction shows better yields and higher (*E*)-selectivity than the original palladium-catalyzed reaction reported previously by the authors.[4a] The ready availability of the starting materials **1** and the importance of the products **2** as strategic intermediates for natural product synthesis may augment the utility of the present reaction as a synthetic method. Furthermore, the reaction provides examples that explicitly demonstrate the salient difference in catalytic reactivity between a nickel(0) and a palladium(0) species.

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13 *Crystal data* for **1c**: $C_{14}H_{20}O_3$, M = 236.31, orthorhombic, space group $P2_12_12_1$, a = 7.5620(4), b = 10.2674(8), c = 16.5730(11) Å, U = 1286.76(15) Å^3, T = 296.1 K, Z = 4, μ(Mo-Kα) = 0.7107 mm^{-1}, 1551 reflections measured, 985 unique (R_{int} = 0.025), $wR(F^2)$ = 0.1596 (all data). For crystallographic data in CIF or other electronic format see DOI: 10.1039/b610164j.