Carbon Dioxide Activation and Catalytic Lactone Synthesis by Telomerization of Butadiene and CO_2

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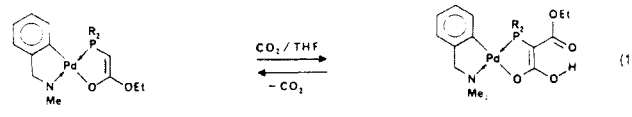
Abstract: Several aspects of the catalytic telomerization of 1,3-butadiene and CO_2 have been examined with the aims of studying the catalytic properties of reversible CO_2-carrier complexes and of selectively producing the δ-lactone 2-ethylidene-6-hepten-5-olide (**3**). When using Pd(II) complexes containing a cyclometalated ligand and a functional phosphine, only the specific CO_2 carriers $[(o\text{-}C_6H_4CH_2NMe_2)Pd\{R_2PC(CO_2Et)=C(O)OH\}]$ (**2a**, R = Ph; **2b**, R = Cy) showed catalytic activity. They represent the first examples of CO_2 carriers having a catalytic activity in CO_2 chemistry. The complex isolated at the end of the reaction was identified as the cyclometalated phosphine carboxylate complex $[(o\text{-}C_6H_4CH_2NMe_2)Pd\{R_2PCH_2C(O)O\}]$ (**8**). Another new catalytic system consisting of $[Pd(MeCN)_4][BF_4]_2$ associated to a phosphine ligand, *p*-hydroquinone, and triethylamine was tested under various conditions. Yield and selectivity of the six-membered ring lactone **3** are functions of the basicity and the bulk of the phosphine ligand. The yield of CO_2 telomers can be increased up to 76% (based on butadiene) by addition of acetophenone to the latter catalytic system containing PPh_3. Furthermore, isomeric telomers of formula $C_9H_{12}O_2$ formed during catalysis can be converted into the δ-lactone **3**, leading to an overall selectivity of 96%.

Despite the large number of reports about CO_2 chemistry, reflecting, inter alia, the considerable interest for this cheap and readily available C_1 molecular building block, there are only a few transition-metal-catalyzed homogeneous reactions which lead to the incorporation of CO_2 into an organic product.[1] The fundamental importance of such reactions is to develop a chemistry based on CO_2 itself and not on its reduction products, e.g., CO, whose formation will require an additional input of energy. In view of the inertness of CO_2, the need for a catalyst is obvious, and an important question is to know whether its function will be to activate CO_2 only, the organic substrate, or both. The CO_2 complexes isolated and characterized so far have not been reported to display any catalytic activity in CO_2 reactions, and, conversely, no CO_2 complex has ever been isolated from catalytically active systems. This stimulated our interest for a catalytic reaction allowing us to evaluate the activity of structurally well characterized palladium complexes previously shown to be reversible CO_2 carriers under ambient conditions (eq 1).[2] The telomerization

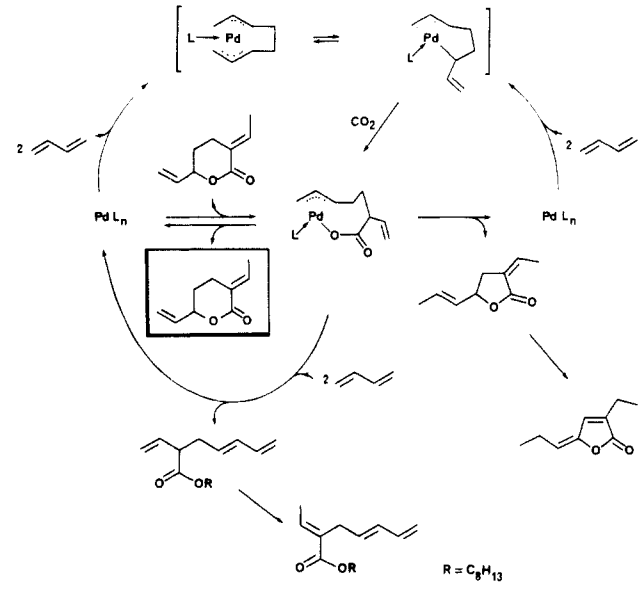


1a, R= Ph
1b, R= Cy

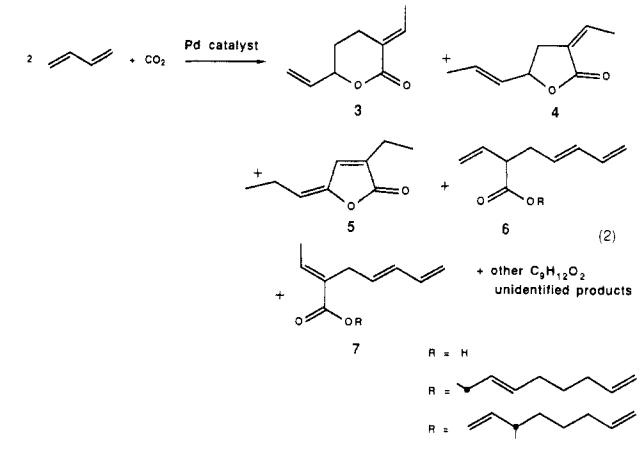
2a, R= Ph
2b, R = Cy

of butadiene and CO_2 appeared to be an interesting objective

Scheme I



involving carbon–carbon and carbon–oxygen bond formation between CO_2 and the organic substrate, leading to lactones and carboxylic acids or esters (eq 2).[3-8] According to numerous



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(2) (a) Braunstein, P.; Matt, D.; Dusausoy, Y.; Fischer, J.; Mitschler, A.; Ricard, L. *J. Am. Chem. Soc.* **1981**, *103*, 5115. (b) Reaction with CO_2 has also been reported for the Pd complex containing the chelating ligands $[Ph_2PCH{=}C(O)OEt]^-$ and 8-mq (where 8-mqH = 8-methylquinoline).[2a] Furthermore, the complex $[(o\text{-}C_6H_4CH_2NMe_2)Pd\{Cy_2PCH{=}C(O)OEt\}]$ was shown by ^1H NMR (in C_6D_6) to react reversibly with CO_2 in a similar manner, affording $[(o\text{-}C_6H_4CH_2NMe_2)Pd\{Cy_2PC(CO_2Et){=}C(O)OH\}]$ in which the enolic OH proton appears at δ 15.10 ppm.

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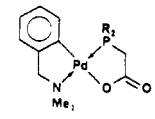
patents, these products may be useful monomers for the synthesis of polyester resins or used as intermediates in the synthesis of fungicides, pesticides, or plasticizers.[4] Furthermore, palladium complexes have been used to catalyze this reaction, which has attracted a considerable interest since its discovery by Inoue et al. in 1976.[5] Many studies have been aimed at gaining a better understanding of the factors governing the selectivity of the reaction. Thus, Musco studied catalysts of the type $Pd(PR_3)_n$ (n = 2, 3) and found that the distribution of the reaction products depends largely on the phosphine ligand bound to palladium.[6] The δ-lactone **3** is preferentially formed with the more basic phosphines [e.g., PCy_3, P-*i*-Pr_3], whereas mainly esters are formed with ligands less basic than P-*t*-Bu_2Ph. These results were interpreted as originating mainly from an electronic control exerted by the phosphorus ligand. Behr et al. reported the highly selective synthesis of **3** by using a $Pd(acac)_2/PR_3$ catalytic system (R = Cy, *i*-Pr).[7] The use of phosphine ligands of high basicity and large cone angle proved necessary in order to optimize yield and selectivity. Various catalytic systems have been reported, which are all multicomponent in that additional ligands (mostly phosphines, with other additives sometimes) are required, besides the transition metal. The general mechanism currently accepted for these reactions is shown in Scheme I. The palladium(II) precursor complex would be reduced in situ to the zerovalent state which is stabilized by coordination of the phosphine. The oxidative coupling of two butadiene units[9] would be followed by insertion of CO_2 into the palladium–carbon σ-bond of the C_8 chain, affording the carboxylate species which reductively eliminates the product and regenerates the active Pd^0L_n complex.[1a-c]

A number of questions immediately arise concerning the function(s) of the catalyst. Is it primarily to activate the diolefin, thus leading to a very reactive organometallic palladium complex capable of readily inserting CO_2, or does a primary metal–CO_2 interaction play a crucial role? This latter consideration might be generalized if extended to a metal complex–CO_2 interaction occurring via a significant participation of a metal–ligand system, whose role would then be to bring the "activated" CO_2 in proximity to the site of its coupling with the organic substrate. These considerations are directly germane (i) to the lack of catalytic activity, at least up to now, of the classical CO_2 complexes in which the metal ions are perhaps unsuitable for activating the organic substrate and (ii) to the fundamental question of whether binding of CO_2 to a metal ion correlates with its chemical activation and the possibility of transferring it onto a suitable organic substrate. With these questions in mind, we studied the catalytic properties of the reversible CO_2 carriers **2a** and **2b** and of new efficient and selective systems for the synthesis of lactone **3**.

Results and Discussion

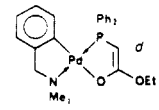
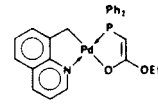
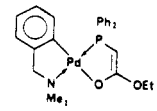
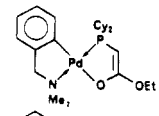
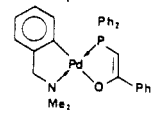
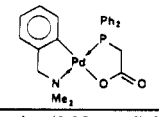
Since the complexes [(*o*-$\overline{C_6H_4CH_2NMe_2}$)$\overline{Pd\{R_2PCH{=}C(O)OEt\}}$] (**1a**, **1b**) immediately react upon bubbling of CO_2 through their solution at atmospheric pressure and room temperature to give [(*o*-$\overline{C_6H_4CH_2NMe_2}$)$\overline{Pd\{R_2PC(CO_2Et){=}C(O)OH\}}$] (**2a**, **2b**),[2] it was not surprising that under the conditions of the catalytic experiments (CH_3CN, 50 bar CO_2, 90 °C), **1** and **2** led to identical results. They were thus used indifferently in the following. These complexes were found to telomerize CO_2 and butadiene in variable yield, without requiring additional ligands (Table I). With the exception of PdL_n systems,[6] there are, to our knowledge, no other transition-metal complexes displaying catalytic activity and reasonable selectivity without needing additional ligands. Furthermore, **2a** and **2b** represent the first examples of CO_2 carriers having catalytic activity in CO_2 chemistry. The improved results with complexes **1b** (or **2b**) versus **1a** (or **2a**) (entries 1 and 4, Table I) parallel the beneficial role of tricyclohexylphosphine versus triphenylphosphine observed in other systems.[6b] The N → Pd bond of the cyclometalated ligand is likely to open during catalysis, providing a coordination site for the organic substrate, while the entropically favored reformation of this bond[10,11] may assist the lactone elimination. This is supported by the observation that the corresponding 8-methylquinoline complex is totally inactive (entry 2, Table I), despite its ability to reversibly bind CO_2 under the same conditions as **1**.[2] Indeed, other work has shown that the five-membered palladacycles involving 8-methylquinoline are more inert than those with dimethylbenzylamine,[12] and we suggest that this is, at least in part, due to a less labile metal–nitrogen bond. However, the lifetime of the catalyst is limited, and at the end of the reaction, the known[13] organometallic complex [(*o*-$\overline{C_6H_4CH_2NMe_2}$)$\overline{Pd\{R_2PCH_2C(O)O\}}$] (**8**) could be isolated. The



8

ester group of **1** has been hydrolyzed during catalysis, leading to

Table I

entry	complex[a]	additives	yield of CO_2 telomers[b] (%)	selectvty[c] (%) for **3**	mol telomers/ mol Pd
1			4.5	12	22
2			0	0	0
3		$2PCy_3$	16	93	211
4			8	80	106
5			0	0	0
6			0	0	0

[a] Complex (0.25 mmol) 0.33 mol of butadiene, CH_3CN 20 mL, CO_2 20 bar, 15 h at 90 °C. [b] Defined as 200 × (mol product)/(mol butadiene engaged). [c] Defined as 100 × (mol **3**)/(mol telomers with mass 152). [d] Complex (0.6 mmol), 0.29 mol of butadiene, CH_3CN 20 mL, CO_2 0.479 mol (ca. 20 bar), 9.5 h at 90 °C.

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Table II. Influence of the Phosphine Ligands on the $[Pd(MeCN)_4][BF_4]_2$-Based Catalytic Lactone Synthesis[a]

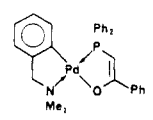
entry	phosphine	yield of δ-lactone **3** (%) (selectvty %)	yield of other CO_2 telomers[b] (%)	total yield of CO_2 telomers
1		0	0	0
2	PPh_3	22.2 (40)	33.7	55.9
3	PMe_2Ph	2.2 (45)	2.5	4.7
4	PEt_3	5.3 (36)	9.6	14.9
5	PCy_3[c]	traces		
6	PCy_3	19 (88)	2.6	21.6
7	$Cy_2PCH_2CH_2PCy_2$[d]	0	0	0
8	$P(CH_2CN)_3$	1.5	traces	1.5
9	Ph_2PCH_2CN	32.4 (73)	12.1	44.5
10	$Ph_2PCH_2C(O)Ph$	0	0	0
11	$Ph_2PCH_2C(O)Ph$[e]	1.7 (68)	0.8	2.5
12	$Ph_2PCH_2CO_2C_2H_5$	17.4 (54)	15.8	33.2
13	$P(OPh)_3$	0	0	0

[a] The following general conditions were used for these systems: $[Pd(MeCN)_4][BF_4]_2$; 0.071 g (0.16 mmol); phosphine, 0.64 mmol; butadiene, 0.28 mol; *p*-HOC_6H_4OH, 0.80 mmol; NEt_3, 0.4 mL; CH_3CN, 20 mL; 90 °C, 15 h, except in entry 1 in which $[Pd(MeCN)_4][BF_4]_2$ was used without any additional ligand, CO_2 20 bar. [b] Consisting of **4**, **5**, and other butadiene–CO_2 telomers with mass 152. Yields (%) are defined as 200 (mol product)/(mol butadiene engaged); selectivity (%): 100 (mol δ-lactone **3**)/(mol telomers with mass 152). [c] Without NEt_3 and without *p*-HOC_6H_4OH. [d] Phosphine (0.32 mmol). [e] Phosphine (0.16 mmol).

this phosphine carboxylate complex **8**, independently shown to be totally inactive in catalysis. Even though the solvent and butadiene had been carefully dried, minute amounts of water are of course sufficient to hydrolyze the catalyst. (This reaction was independently performed on a larger scale and shown to be very facile.[13]

The fact that the cyclometalated ligand is still coordinated to palladium in **8** rules out that formation of the latter results from a Pd(0) intermediate generated during the catalytic cycle. Indeed, rupture of the Pd–C bond, leading to $C_6H_5CH_2NMe_2$, could not be reversible in the presence of Pd(0) since the required ortho-metalation reaction is known to proceed by electrophilic and not by nucleophilic attack of the ortho C–H bond.[14] Although a high percentage (ca. 80%) of the palladium involved in the form of **1** is recovered as **8**, it is impossible to rule out that a very small fraction of **1** was transformed into a catalytically active species (perhaps even Pd(0)) present in too small a concentration to be characterized. But assuming that the cyclometalated ligand remains attached to the active species, the lowest possible oxidation state of palladium during the catalytic cycle would be +1, corresponding to the binding of this uninegative, three-electron donor ligand. Thus, formation of the C_8 chain could occur by electrophilic coupling reactions, shown by Sen et al., in a different context, to account for the dimerization of alkenes.[15] A possible catalytic cycle operating with nonzerovalent palladium catalysts is represented in Scheme II. Coupling of two butadiene units is expected to be a rapid process, which would be followed by CO_2 insertion and reductive elimination of the lactone. Catalytic C–C bond formation has been reported recently to involve the ortho carbon atom of a cyclometalated ruthenium phosphite ligand,[16] a situation not encountered in this work.

Because of the transformation during catalysis of the functional phosphine ligand in **1**, we tested complexes **9–11** containing the phosphine–enolate ligand $[Ph_2PCH{=}C(O)Ph]^-$, which are not water-sensitive. Unfortunately, these complexes are totally in-



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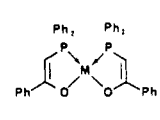
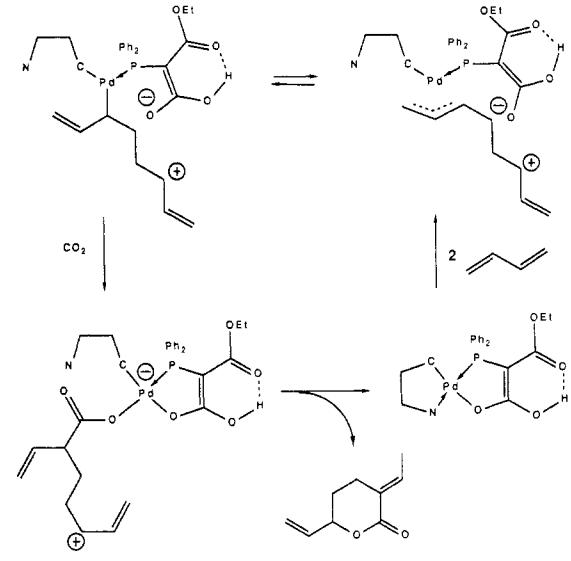


10 M = Ni

11 M = Pd

active for butadiene–CO_2 telomerization reaction and even for butadiene dimerization. It is however interesting to relate these

Scheme II



results to the fact that **9–11** do not lead to CO_2 complexes either,[17] even after exposure to 60 bar CO_2, suggesting but not implying that binding of CO_2 could be necessary (but not sufficient, see above the case of the 8-methylquinoline analogue of **2**) in order to observe catalytic telomerization reactions. The specific property of complexes **2a** and **2b** would be to assist coupling of the activated CO_2 with the coordinated C_8 chain, with the crucial participation of a metal–ligand system capable of achieving a triple function: nucleophilic attack on the carbon atom of CO_2 and electrophilic stabilization of each of its oxygen atoms via Pd(II) and H^+. Following the observation that in palladium-based catalytic systems, additional phosphines possessing CHR_2 groups bound to phosphorus (e.g., P-*i*-Pr_3) have been found to lead to excellent results, Behr et al. have suggested that a related activation of CO_2, via its insertion into the PC–H bond, might be responsible for the specific catalytic performance of these systems.[3a]

Catalytic Systems Involving Additional Ligands. Addition of PCy_3 to the previous catalysts (**1a** or **2a**) resulted in an increased yield of lactone (entry 3, Table I). Since the system remained sensitive to hydrolysis, we examined the activity of other phosphine-modified catalytic systems. The phosphine-to-palladium ratio was generally chosen as 4:1 in order to facilitate comparisons with previous systems for which the best results were found for a ratio between 3:1 and 4:1.[4b,7a] We found that $[Pd(MeCN)_4][BF_4]_2$ (**12**) is a suitable precursor for the telomerization

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Table III. Influence of Additional Ligands in the Pd/PPh_3 System[a]

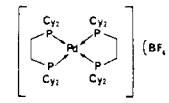
entry	ligands added[b]	yield of δ-lactone **3** (selectvty)	yield of other CO_2 telomers	total yield of CO_2 telomers
1		2.3 (16)	11.9	14.2
2	PhC(O)Ph	3.4 (33)	6.9	10.3
3	*i*-PrC(O)Pr-*i*	4.6 (30)	10.6	15.2
4	PhC(O)Me	5.5 (32)	11.9	17.4
5	$Ph_3PCHC(O)Ph$[c]	0	0	0
6	$Ph_3PCHC(O)Ph$	19.9 (56)	15.6	35.5
7	$Ph_3PCHC(O)Ph$ + *p*-HOC_6H_4OH	26.5 (55)	21.4	47.9
8	NEt_3 + *p*-HOC_6H_4OH	22.2 (40)	33.7	55.9
9	NEt_3 + *p*-HOC_6H_4OH + $Ph_3PCHC(O)Ph$	39.4 (62)	24.1	63.5
10	NEt_3 + *p*-HOC_6H_4OH + PhC(O)Ph	33 (48)	35.7	68.7
11	NEt_3 + *p*-HOC_6H_4OH + PhC(O)Me	35 (46)	41	76.0
12	NEt_3[d] + *p*-HOC_6H_4OH	28 (50)	28	56.0
13	NEt_3[e] + *p*-HOC_6H_4OH + PhC(O)Me	47 (96)	2	49.0

[a] For entries 1–12: $[Pd(MeCN)_4][BF_4]_2$, 0.071 g (0.16 mmol); PPh_3, 0.168 g (0.64 mmol); butadiene, ca. 15 g (0.28 mol); CH_3CN, 20 mL; 90 °C, 15 h. Yields and selectivity defined as in Table II. [b] NEt_3, 0.4 mL; *p*-HOC_6H_4OH, 0.088 g (0.80 mmol); $Ph_3PCHC(O)Ph$, 0.122 g (0.32 mmol); ketone, 0.80 mmol. [c] Without PPh_3. [d] Catalyst prepared from $[PdCl_2(PPh_3)_2]$, 0.098 g (0.14 mmol) and $AgBF_4$, 0.054 g (0.28 mmol); PPh_3, 0.079 g (0.30 mmol); *p*-HOC_6H_4OH, 0.088 g (0.80 mmol) and NEt_3, 0.4 mL; CO_2 20 bar. [e] Details are given in the Experimental Section.

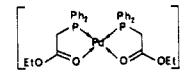
reaction when reacted in the presence of a phosphine ligand, triethylamine, and *p*-hydroquinone (Table II).[18] These additives were reported in an ICI patent to provide an optimal catalytic system, when associated with Pd(0) complexes.[4b] Addition of NEt_3 and hydroquinone results in increased conversions (see entry 8, Table III), whereas the phosphine ligand appears necessary in order to observe a catalytic reaction (entries 1 and 5, Table II; entry 5, Table III). Yield and selectivity for the formation of **3** depend largely on the nature of the phosphine ligand (see Table II). The best selectivity (88%) was reached with PCy_3. Use of other basic phosphine ligands with smaller cone angles led to lower selectivity in **3** as well as decreased yield of telomers. Triphenylphosphite prevents formation of telomers (entry 13, Table II). With PPh_3, the reaction was less selective than with PCy_3, but telomers, including unidentified ones, are formed in higher yields (55.9% for PPh_3 versus 21.6% for PCy_3, entries 2 and 6, Table II). These results contrast with those found by other authors for Pd/PPh_3 systems where the yields of telomers were always found to be lower than for the corresponding Pd/PCy_3 systems.[6,7] Furthermore, we never detected more than traces of esters **6** and **7** although they were usually the main products observed with these other Pd/PPh_3 systems.

Functional phosphines are also suitable additional ligands for the reaction. Thus, with the phosphine–ester $Ph_2PCH_2C(O)OC_2H_5$ (**13**), 33.2% of telomers are obtained, whereas with the phosphine–nitrile Ph_2PCH_2CN (**14**), 44.5% telomers are formed with increased selectivity in lactone **3** (73%). Although these two phosphines should display a similar behavior due to their comparable steric and electronic properties,[2,19] both selectivity and total yield of telomers were found to be better with **14**. These results may be related to their different coordination properties: whereas **13**, when acting as a bidentate ligand, easily leads to mononuclear chelate complexes, **14** forms preferentially binuclear complexes with a μ(P, N) coordination mode.[2a] Intermolecular linkage by the phosphine–nitrile may stabilize the system and/or allow storage of reactive coordination sites, as nitrile ligands can subsequently be displaced easily by olefins.

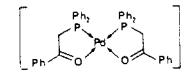
With the ketophosphine $Ph_2PCH_2C(O)Ph$ (**15**), no telomers are formed (entry 10, Table II), owing to formation of **11** which is totally inactive under these conditions. With the diphosphine $Cy_2PCH_2CH_2PCy_2$ possible formation of **16** (entry 7, Table II) may also prevent catalysis.



16



17



18

The bis-phosphine–ester complex **17** was found to be a selective catalyst, affording 10.7% telomers containing 82% lactone **3**.[20] In contrast to **17**, the related ketophosphine complex **18** was totally inactive. The difference of behavior between **17** and **18** may be explained by a more facile Pd–O bond dissociation in **17**. Indeed, easier M–O(ester) versus M–O(ketone) bond cleavage has been shown to occur, for instance, in complexes of formula *mer,cis*-$[RhCl_3\{Ph_2PCH_2C(O)R\}\{Ph_2PCH_2C(O)R\}]$ (R = Ph, OEt), in which phosphine exchange is observed on the NMR time scale.[19,21]

In order to improve our Pd/PPh_3 system, we studied the influence of supplementary additives. Thus, addition of the phosphorus ylide $Ph_3PCHC(O)Ph$ resulted in an increased yield of telomers (63.5%) (entries 6, 7, and 9, Table III). A similar effect was observed in Behr's $Pd/P\text{-}i\text{-}Pr_3$ system upon addition of phosphorus or arsenic ylides, and it was suggested to originate from a CO_2 activation by means of the ylide ligand.[3a] Although no such complex could be isolated, this CO_2 activation was inspired by the situation observed in eq 1, which involves well-characterized complexes.

The results obtained with this functional ylide led us to consider the possible influence of ketones upon the course of this catalysis. We thus found that addition of ketones to the PPh_3-based system resulted also in an increased yield of telomers, which reached 76% in the case of acetophenone (entry 11, Table III). This represents the best yield reported so far for butadiene–CO_2 coupling reactions performed in batch reactors with Pd(II) precursors, although higher selectivities were obtained by Behr et al. with systems leading to lower conversions.[7] The role of the ylide or of the ketone would be to increase the rate of the elimination step of the $C_8H_{12}CO_2$ unit from the palladium center. Gollaszewski and Schwartz observed a similar effect in the palladium-catalyzed cyclodimerization of butadiene in which maleic anhydride induces rapid elimination of the cyclic dimer,[22a] and this acidic olefin is also known to accelerate reductive elimination of η^3-allyl aryl Pd(II) complexes.[22b]

It is noteworthy that each component in these systems enhances the yield of telomers (see Table III) when compared to the simple Pd/PPh_3 system (entry 1). The system of entry 12 was operated on a larger scale in a 2-L autoclave, affording 55.8% telomers containing 64% lactone **3** (see Experimental Section). We found that refluxing the crude reaction mixture of entry 11 at atmospheric pressure for 3 days resulted in the conversion of the unidentified CO_2 telomers of mass 152, mentioned in eq 2, into **3** which was then formed with a selectivity of 96% (see Experimental

(18) For other organic transformations catalyzed by $[Pd(MeCN)_4][BF_4]_2$, see: Nugent, W. A.; Hobbs, F. W. *J. Org. Chem.* **1983**, *48*, 5364, and ref 15.

(19) Braunstein, P.; Matt, D.; Mathey, F.; Thavard, D. *J. Chem. Res., Synop.* **1978**, 232. *J. Chem. Res., Miniprint* **1978**, 3041.

(20) Reaction conditions: $[Pd\{Ph_2PCH_2C(O)OEt\}_2][BF_4]_2$, 0.14 mmol; PPh_3, 0.27 mmol; *p*-HOC_6H_4OH, 0.73 mmol; *N*-ethylpiperidine, 3.6 mmol; butadiene, 0.31 mol; CO_2 (17.3 g – 50 bar); CH_3CN, 20 mL; 90 °C for 19 h.

(21) Braunstein, P.; Matt, D.; Nobel, D., unpublished results.

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Table IV. Catalytic Systems with Dinuclear Palladium Complexes[a]

entry	complex[b]	ligands[c]	yield of δ-lactone **3** (selectvty)	total yield of CO_2 telomers
1	$[Pd(dppm)(CH_3CN)]_2[BF_4]_2$	PPh_3 p-HOC_6H_4OH	22.3 (62)	35.9
2	$[Pd(dppm)(CH_3CN)]_2[CF_3SO_3]_2$	PPh_3 p-HOC_6H_4OH $C_5H_{10}NC_2H_5$	6.8 (68)	10
3	$[Pd(dppm)(CH_3CN)]_2[BF_4]_2$	PPh_3	2.9 (73)	4

[a] CO_2 20 bar, 90 °C, 15 h. [b] Complex 0.080 mmol. [c] Phosphine, 0.64 mmol; hydroquinone, 0.80 mmol; $C_5H_{10}NC_2H_5$ (*N*-ethylpiperidine), 0.4 mL.

Section). We also found that prolonged (3 days) heating at 90 °C of the reaction mixture of entry 11, at atmospheric pressure and after evaporation of CH_3CN, resulted in the precipitation of palladium metal and in the slow conversion of **3** into **5**, the latter existing as two isomers, *Z* and *E* (*Z*:*E* ratio ca. 4:1). It is known that isomerization of **3** into the fully conjugated **5** requires a higher palladium concentration than the butadiene–CO_2 telomerization reaction.[7a] This isomerization most probably involves the formation of a metallocyclic intermediate.[23]

Other catalytic systems were also examined. The precursor prepared in situ from $[PdCl_2(PPh_3)_2]$ and $AgBF_4$ (in a 1:2 ratio) in CH_3CN was also found to be efficient (entry 12, Table III), affording telomers in 56% yield (containing 50% of **3**) when reacted under the same conditions.[24] Other cationic complexes also displayed catalytic activity in the butadiene–CO_2 reaction. Thus, for example, the dimeric complex $[Pd(\mu\text{-dppm})(CH_3CN)]_2[BF_4]_2$ (dppm = $Ph_2PCH_2PPh_2$), prepared and isolated from $[Pd(\mu\text{-dppm})Cl]_2$ and $AgBF_4$ (in a 1:2 ratio) in CH_3CN, led to 35.9% of telomers (yield obtained after rapid distillation under reduced pressure) containing 62% of **3** (entry 1, Table IV). Important changes in conversion were observed with use of $[Pd(\mu\text{-dppm})(CH_3CN)]_2[CF_3SO_3]_2$, prepared in situ, since only 10% of telomers were produced (entry 2, Table IV). This could be related to the greater coordinating ability of the $[CF_3SO_3]^-$ anion compared to $[BF_4]^-$, resulting in a modification of the coordination sphere of the metal ion and therefore limiting the access of the organic substrate.[25] In the absence of hydroquinone, the yield of telomers dropped to 4% (entry 3, Table IV).

In conclusion, we have shown that Pd/PPh_3-based systems obtained from cationic Pd(II) precursor complexes constitute original and efficient catalysts for the telomerization of butadiene and CO_2. This contrasts with the situations previously encountered with other Pd(II) systems for which the best yields and selectivities were always obtained with basic and sterically demanding phosphines, e.g., P-*i*-Pr_3 and PCy_3, which are also more expensive than PPh_3. Although the palladium oxidation state in the active species is not known in our case, we believe that other mechanisms than those proposed for Pd(0) systems by Inoue et al.,[5] Musco,[6] or Behr et al.[3] could be operative. As suggested by the results obtained with complexes **1** or **2**, which constitute the first examples of CO_2 carriers displaying catalytic activity in CO_2 chemistry and which telomerize butadiene and CO_2 into the δ-lactone **3** without needing additional ligands, catalysis may be operative with palladium in an oxidation state superior or equal to +1.

Experimental Section

The general techniques used throughout this work have been described in previous papers from this laboratory.[2a,17] The complexes used in this work, $[(o\text{-}C_6H_4CH_2NMe_2)Pd\{Ph_2PCH{=}C(O)OEt\}]$,[2a] $[(C_{10}H_8N)Pd\{Ph_2PCH{=}C(O)OEt\}]$,[2a] $[(o\text{-}C_6H_4CH_2NMe_2)Pd\{Cy_2PCH{=}C(O)OEt\}]$,[13] $[(o\text{-}C_6H_4CH_2NMe_2)Pd\{Ph_2PCH{=}C(O)Ph\}]$,[17] *cis*-$[Pd\{Ph_2PCH{=}C(O)Ph\}_2]$,[17] $[(o\text{-}C_6H_4CH_2NMe_2)Pd\{Ph_2PCH_2C(O)O\}]$,[13] *cis*-$[Pd\{Ph_2PCH_2C(O)Ph\}_2][BF_4]_2$,[26] $[Pd(MeCN)_4][BF_4]_2$,[27] and $[PdCl_2(PPh_3)_2]$[28] were prepared according to literature methods. $[Pd_2(\mu\text{-dppm})_2(CH_3CN)_2][BF_4]_2$ was prepared from $[PdCl(\mu\text{-dppm})]_2$[29] and $AgBF_4$ in CH_3CN in quantitative yield: IR (Nujol) ν (C≡N) 2285 w cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.48 (s, 6 H, CH_3), 4.34 (m, 4 H, PCH_2); $^{31}P\{^1H\}$ (CH_2Cl_2/D_2O_{ext}) δ −5.25 (s).[30] The complex *cis*-$[Pd\{Ph_2PCH_2C(O)OEt\}_2][BF_4]_2$ was prepared quantitatively from *trans*-$[PdCl_2\{Ph_2PCH_2C(O)OEt\}_2]$[19] and $AgBF_4$ (2 equiv) in CH_2Cl_2: IR (CH_2Cl_2): ν (C=O) 1607 s cm^{-1}; ^1H NMR (CD_2Cl_2) δ 1.26 (t, 6 H, CH_3, ^3J = 7.1 Hz), 4.08 (d, 4 H, PCH_2, ^2J (PH) = 11.9 Hz), 4.35 (q, 4 H, OCH_2, ^3J = 7.1 Hz), 7.34–7.54 (20 H, aromatic H). Anal. Calcd for $C_{32}H_{34}B_2F_8O_4P_2Pd$ (M = 824.6): C, 46.62; H, 4.16. Found: C, 46.85; H, 4.18.

Phosphine ligands were commercially available except $Ph_2PCH_2C(O)OEt$,[19] $P(CH_2CN)_3$,[31] Ph_2PCH_2CN,[19] and $Ph_2PCH_2C(O)Ph$[17] which were prepared as described in the literature. Butadiene (Air Liquide, N 25) was used as received or dried over molecular sieves (experiments involving complexes **1** and **2**), and CO_2 (Air Liquide, N 45) was used without further purification. The catalytic reactions were carried out in 100-mL steel autoclaves, fitted with a manometer and a magnetic stirrer. The products were analyzed by GC by using an SE 30 (10% on chromosorb W AW DMCS 100–200 Mesh) column and a temperature program from 60 to 220 °C. For the GLC analyses, γ-butyrolactone was used as an internal standard. For the preparative chromatography, silica gel 60F-254 plates were used, the elution being performed with ethyl acetate–hexane mixtures.

General Procedure. (a) Reaction in a 100-mL Autoclave. A mixture of 0.071 g (0.16 mmol) of $[Pd(MeCN)_4][BF_4]_2$, 0.64 mmol of phosphine ligand, 0.088 g (0.80 mmol) of *p*-hydroquinone, 0.4 mL of triethylamine, and 10 mL of acetonitrile were introduced into a steel autoclave. Then, 15 g of butadiene (0.28 mol), condensed at −20 °C in 10 mL of acetonitrile, was added, and the autoclave was pressurized with 30 bar CO_2 (≈ 15 g) and heated for 15 h at 90 °C. After cooling, the unreacted CO_2 and butadiene as well as the solvent were removed in vacuo. Analysis of the product mixtures was performed by GLC or by preparative chromatography. Alternatively, rapid distillation under reduced pressure of the reaction mixture, after solvent evaporation, afforded lactone **3** and its isomers in a ratio similar to that found by GC analysis of the crude reaction mixture. It indicates that this operation is not accompanied by lactone isomerization.

(b) Reaction in a 2-L Autoclave. A mixture of butadiene (301.6 g, 5.58 mol), carbon dioxide (363 g, 8.25 mol), PPh_3 (1.38 g, 5.26 mmol), p-HOC_6H_4OH (1.38 g, 12.59 mmol), NEt_3 (7 mL), and $[Pd(CH_3CN)_2(PPh_3)_2][BF_4]_2$ (2.15 g, 2.43 mmol) in CH_3CN (344 mL) was reacted at 77 °C for 16 h. After cooling, the unreacted CO_2 and butadiene as well as the solvent were removed in vacuo. Preparative chromatography of portions of the residual oil using ethyl acetate/hexane showed that 151.8 g of lactone **3** (1 mol, yield 35.8%), 84.8 g (0.56 mol, yield 20%) of other telomers of mass 152, and 9.8 g of octatrienes (0.09 mol, 2%) were present in the reaction mixture.

Selective Synthesis of Lactone 3. A mixture of 0.071 g (0.16 mmol) of $[Pd(MeCN)_4][BF_4]_2$, 0.168 g (0.64 mmol) of triphenylphosphine, 0.088 g (0.80 mmol) of *p*-hydroquinone, 0.4 mL of triethylamine, 0.1 mL of acetophenone, and 10 mL of acetonitrile was introduced into a steel autoclave. Then, 14 g of butadiene (0.26 mol), condensed at −20 °C in 10 mL of acetonitrile, was added, and the autoclave was pressurized with 30 bar CO_2 and heated for 15 h at 90 °C. After cooling, the unreacted CO_2 and butadiene were released, and the reaction mixture was refluxed

(23) See, for example, the ring contraction reactions described in the following: Yamamoto, T.; Sano, K.; Yamamoto, A. *J. Am. Chem. Soc.* **1987**, *109*, 1092.

(24) These systems have been recently found to be efficient catalysts for the linear dimerization of acrylic acid esters, see: Oehme, G.; Pracejus, H. *J. Organomet. Chem.* **1987**, *320*, C56.

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for 60 h. Analysis of the reaction mixture gave 9.7 g (yield 49%) of telomers (M = 152) containing 96% lactone **3**.

2-Ethylidene-6-hepten-5-olide (3): IR (Nujol) ν (C=O) 1710 s cm^{-1}; bp 76 °C/10^{-2} Torr; ^1H NMR ($CDCl_3$) δ 1.73 (dd, 3 H, Me, $^5J \approx 1$ Hz and ^3J = 7.2 Hz), 1.95-2.07 (m, 2 H, CH_2CH), 2.30-2.60 (m, 2 H, $=CCH_2CH_2$), 4.72 (m, 1 H, CH_2CH), 5.17 (dd, 1 H, CH = CH_2, cis, $^3J_{cis}$ = 10.6 and ^2J = 1.1 Hz), 5.29 (dd, 1 H, CH = CH_2, trans, $^3J_{trans}$ = 17.2 and ^2J = 1.1 Hz), 5.83 (m, 1 H, CH = CH_2), 7.14 (q of t, 1 H, CH_3CH, ^3J = 7.2, $^4J \approx 2$ Hz); $^{13}C\{^1H\}$ NMR ($CDCl_3$) δ 13.05 (Me), 21.16 ($=CCH_2-$), 26.86 ($-CH_2CHO$), 77.89 (-CHO), 115.53 ($=CH_2$), 125.64 ($C=CHMe$), 135.51 ($CHCH_2$), 139.46 ($CHMe$), 164.80 (C=O); MS, m/e 152 (37), 137 (12), 124 (27), 96 (100), 81 (28), 68 (75), 67 (48), 55 (29), 54 (40), 53 (37), 41 (34), 39 (60). Anal. Calcd for $C_9H_{12}O_2$ (M = 152.19): C, 71.03; H, 7.95. Found: C, 70.84; H, 7.98.

2-Ethyl-2,4-heptadien-4-olide (5): ^1H NMR ($CDCl_3$) δ Z isomer (E isomer in square brackets) 1.08 [$\approx$ 1.08] (t, $CH_3CH_2C=$, ^3J = 7.5 Hz), 1.19 [1.18] (t, $CH_3CH_2CH=$, ^3J = 7.5 Hz), 2.39 [2.32] (m, CH_2), 5.16 [5.64] (t, $-CH_2CH=C$, ^3J = 7.8 Hz), 6.97 [7.27] (t, $C=CHC=$, ^4J = 1.4 Hz); $^{13}C\{^1H\}$ NMR ($CDCl_3$) δ 11.7 ($CH_3CH_2C=$, E and Z isomers) 13.5 ($CH_3CH_2CH=$, E + Z), 14.35 (CH_2CH, E), 18.40 ($CH_2C=$, E + Z), 19.45 ($-CH_2CH$, Z), 115.04 ($-CH_2CH=C$, E), 115.78 ($-CH_2CH=C$, Z), 131.86 ($OC=C$, Z), 134.88 ($=CCH=C$, E), 136.16 ($C=CHC=$, Z), 147.97 ($=CC_2H_5$, E + Z), 170.4 (C = O, E + Z); MS for Z, m/e 152 (23), 137 (12), 110 (66), 109 (11), 82 (85), 81 (36), 77 (17), 69 (19), 67 (17), 55 (100); MS for E, m/e 152 (10), 137 (9), 110 (67), 82 (84), 81 (34), 77 (16), 69 (17), 67 (15), 55 (100).

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Registry No. 1a, 79110-94-4; **1b**, 105813-68-1; **2a**, 79079-77-9; **2b**, 113379-49-0; **3**, 67693-94-1; (*Z*)-**5**, 74888-98-5; (*E*)-**5**, 74888-97-4; **8** (R = Ph), 105784-57-4; **8** (R = Cy), 105813-67-0; **9**, 111287-12-8; **10**, 97954-27-3; **11**, 113379-50-3; **12**, 21797-13-7; *cis*-**17**, 113379-43-4; *trans*-**17**, 113472-62-1; **18**, 113379-45-6; CO_2, 124-38-9; $[(\overline{C_{10}H_8N})Pd\{Ph_2PCH{=}C(O)OEt\}]$, 79110-93-3; $[(o\text{-}\overline{C_6H_4CH_2NMe_2})Pd\{Ph_2PCH_2C(O){=}O\}]$, 105784-57-4; $PdCl_2(PPh_3)_2$, 13965-03-2; $[Pd(dppm)(CH_3CN)_2][BF_4]_2$, 113379-47-8; $[Pd(dppm)(CH_3CN)_2][CF_3SO_3]_2$, 113379-48-9; 1,3-butadiene, 106-99-0.

Biologically Useful Chelators That Release Ca^{2+} upon Illumination†

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Abstract: A series of Ca^{2+}-selective chelators incorporating a photosensitive *o*-nitrobenzhydryl ether, alcohol, or ester (λ_{max} 350-360 nm, $\epsilon \approx 5500$ M^{-1} cm^{-1}) were synthesized. The key step of the syntheses required the novel and mild trimethylsilyl triflate catalyzed Friedel-Crafts alkylation of a *N*,*N*-dialkylaniline by a nitrobenzaldehyde or its acetal. Before photolysis, the chelators show dissociation constants for Ca^{2+} of about 10^{-7} M, roughly matching the typical free [Ca^{2+}] inside unstimulated cells. Considerable adjustment of the affinities is possible by subtle variations in the stereochemistry of the linkage between the two halves of the binding site. Irradiation around 365 nm smoothly converts the chelators into *o*-nitrosobenzophenones whose Ca^{2+} affinity is 10-30-fold weaker than the unphotolyzed compounds. The photolyses have quantum efficiencies of 0.01-0.04 and release Ca^{2+} with rate constants of 5-3000 s^{-1} after a flash, with free benzhydrols remarkably faster than their ethers. Therefore, these chelators can be used to generate controlled fast jumps in intracellular free [Ca^{2+}] to mimic and analyze a host of important cellular responses, especially in nerve and muscle.

Brief, localized fluctuations of intracellular free Ca^{2+} concentrations are believed to control neurosynaptic transmission, hormone secretion, muscle contraction, and a myriad of other physiological functions.[1,2] The ability to generate similarly fast and localized rises in free [Ca^{2+}] would be a powerful tool both in studying the physiology of intact cells and the biochemistry of their many Ca^{2+}-sensitive proteins. Recently, flash photolysis has been used in biological systems to generate sudden jumps in the concentration of adenosine triphosphate, cyclic nucleotides, cholinergic agonists, and protons.[3-9] The resulting concentration jumps cause cellular or biochemical responses whose kinetics can give valuable insights into the molecular sensing mechanisms. Photochemistry in principle can generate concentration changes that are much faster and spatially more controllable than possible with rapid mixing techniques; photolysis is also applicable to the inside of intact cells, where turbulent mixing would not be possible or desirable. Perhaps the main current limitation is the need to design and synthesize compounds that "cage" active natural trigger substances. The "caged" substance should itself be biologically inert yet readily and rapidly release the active agent once illuminated.

† BAPTA, 1,2-bis(*o*-aminophenoxy)ethane-*N*,*N*,*N*′,*N*′-tetraacetic acid; EDTA, ethylenediaminetetraacetic acid; EGTA, ethylenebis(oxyethylenenitrilo)tetraacetic acid, or ethylene glycol bis(2-aminoethyl ether)-*N*,*N*,*N*′,*N*′-tetraacetic acid; HEEDTA, *N*-(2-hydroxyethyl)ethylenediamine-*N*,*N*′,*N*′-triacetic acid; MOPS, 3-morpholinopropanesulfonic acid; OTf, trifluoromethanesulfonate, CF_3SO_2-; TMS, trimethylsilyl, Me_3Si-; Tris, tris(hydroxymethyl)aminomethane.

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