scanning calorimetry. They are air and water stable up to 60 °C. At higher temperatures the phosphonium and arsonium compounds are more stable than the corresponding ammonium compounds. It is worth noting that stable aqueous microemulsions (lasting at least three weeks) with concentrations of up to 10 mg mL^{-1} were obtained with phosphonium and arsonium compounds. Under the same conditions ammonium compounds underwent hydration to yield unstable suspensions and should thus be prepared immediately before use.

Ammonium, phosphonium, and arsonium fatty phosphonates were simultaneously assessed for transfection of a reporter gene β-galactosidase on two adherent cell lines (CFT1, Hela) and one hematopoietic nonadherent cell line (K562), with lipofectine as reference, consistent with previously described protocols.[3b] Figure 1 compares the data for oniums ($A = N, P, As$) in which $R = C_{14}H_{29}$ and $R' = R'' = CH_3$. It is clear from the two first histograms that phosphonium and arsonium salts are more efficient than ammonium compounds, especially for transfection into Hela cells. Cellular toxicity was evaluated as the number of cells surviving the transfection experiment using a chemiluminescent assay (Packard);[9] nontransfected cells served as a control. The third histogram indicates clearly that phosphonium and arsonium compounds are less cytotoxic than the ammonium derivatives, which is consistent with the observations of Stekar et al.[4]

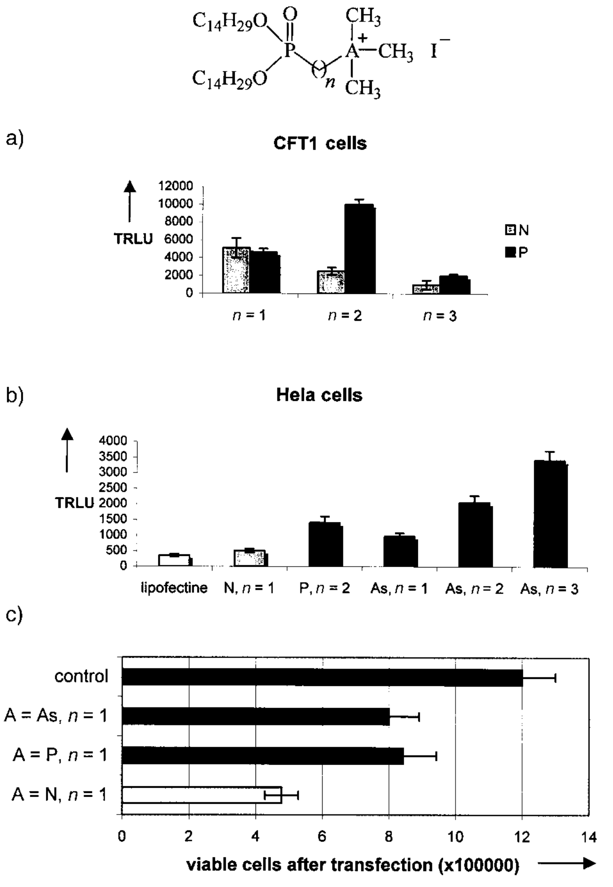
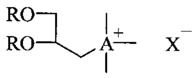


Figure 1. Results of transfection activity on CFT1 (a) and Hela cells (b), and cellular toxicity on K562 cells (c). TRLU = total relative light unit.

A more detailed biological study with a complete biological evaluation of efficiency and toxicity will be published soon elsewhere. Moreover, we have continued with this concept of replacing ammonium in the polar head of cationic lipids and have synthesized the phosphonium and arsonium analogues of DOTMA[1] and DOTAP,[10] (Scheme 6), two well-studied nonviral vectors. These new compounds are currently under biological evaluation.



Scheme 6. Phosphonium and arsonium analogues of DOTAP and DOTMA ($A = P$, As; X = halogen; $R = C_{18}H_{35}$, $C_{17}H_{33}C(O)$, $C_{15}H_{31}C(O)$).

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Phosphane Sulfide/Octacarbonyldicobalt-Catalyzed Pauson–Khand Reaction Under an Atmospheric Pressure of Carbon Monoxide

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Dedicated to Professor Jean-Marie Lehn
on the occasion of his 60th birthday

The Pauson–Khand reaction, a method for constructing the cyclopentenone skeleton from an alkene, an alkyne, and carbon monoxide, has found extensive use in synthetic organic

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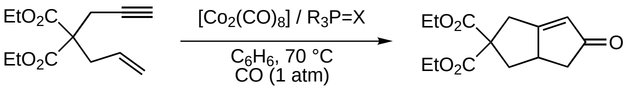
chemistry, including natural product synthesis.[1] Recently there have been dramatic developments in catalytic Pauson–Khand-type reactions with various transition metal catalysts.[2, 3] However, most of these catalytic reactions require drastic conditions such as high pressure, high temperature, and/or irradiation. Only a few catalytic Pauson–Khand reactions under atmospheric pressure are known.[2e, 2i, 2o, 2p]

We recently demonstrated that phosphane sulfides can be used as ligands in the palladium-catalyzed bis-alkoxycarbonylation of olefins.[4] The fact that tributylphosphane oxide promotes the stoichiometric cobalt-mediated Pauson–Khand reaction and gives a greatly improved yield[5] prompted us to attempt the catalytic version of this reaction with a variety of phosphane chalcogenides as ligands. The cobalt-catalyzed reaction proceeded smoothly and in good yield even under an atmospheric pressure of CO, provided that an optimized quantity of a suitable phosphane sulfide was added. Here we report one of the most practical procedures to date for the catalytic Pauson–Khand reaction, achieved by using a phosphane sulfide as an additive.

We first examined the reaction with a catalytic amount of octacarbonyldicobalt in the presence of a variety of phosphane chalcogenides (Table 1). Enyne **1a** was treated with octacarbonyldicobalt (3 mol%) in the presence of a phosphane chalcogenide in benzene at 70 °C for 7 h under a CO atmosphere (1 atm). In the absence of ligand the $[Co_2(CO)_8]$ catalyst decomposed before completion of the reaction; hence, the yield of product was low (entry 1). Belanger et al. recently reported an 83% yield for the same reaction under almost identical reaction conditions, except that a very high purity cobalt complex was used to obtain reproducible results.[2i, 6] Since tributylphosphane oxide is a good promoter of the stoichiometric reaction[5] we tried triphenylphosphane oxide in our catalytic version. However, this resulted in the formation of by-products and no improvement in the yield of the desired compound (entry 2). Only traces of the product were obtained with triphenylphosphane selenide (entry 4) as a result of a rapid decomposition of the cobalt complex. In contrast, the reaction proceeded catalytically under an atmospheric pressure of CO upon addition of a monodentate phosphane sulfide (entries 5–14), and the yield of product was moderately to greatly improved, even with unpurified $[Co_2(CO)_8]$.[6] Bidentate diphosphane disulfides such as $dppeS_2$ slowed the reaction (entry 15), whereas monodentate phosphane sulfides, especially those with electron-donating substituents on the phosphorus atom, effectively promoted the catalytic reaction to afford the product in good yields (entries 5–14). Both the ratio of phosphane sulfide to $[Co_2(CO)_8]$ and the concentration of the catalyst were critical (entries 6–14), probably because a ligand-exchange equilibrium exists between the phosphane sulfide, CO, and the olefin.[7] A ratio of six equivalents of tributylphosphane sulfide to cobalt complex gave the best results (entry 12). Careful control of the reaction temperature was essential, as in other similar reactions; the reaction did not proceed below 50 °C, while the catalyst decomposed above 70 °C.[2i] Although 1,2-dimethoxyethane (DME) is usually used as solvent in the catalytic Pauson–Khand reaction,[8] phosphane sulfide ligands were more effective in benzene.

Table 1. Effect of phosphane chalcogenides on the cobalt-catalyzed Pauson–Khand reaction.[a]

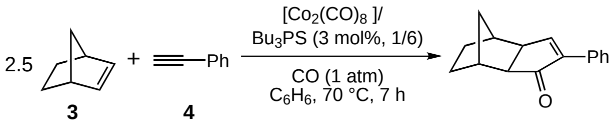


1a **2a**

Entry	Additive	Ratio[b]	Yield [%][c]
1	none	–	50
2	Ph_3PO	4	48
3	Ph_3PS	4	55
4	Ph_3PSe	4	trace
5	An_3PS[d]	4	70
6	$(Me_2N)_3PS$	2	67
7	$(Me_2N)_3PS$	4	79
8	$(Me_2N)_3PS$	6	79
9	$(Me_2N)_3PS$	8	77
10	Bu_3PS	2	74
11	Bu_3PS	4	72
12	Bu_3PS	6	90[e]
13	Bu_3PS	8	75
14	Bu_3PS	6	84[f]
15	$dppeS_2$[g]	2	34

[a] The reaction was performed in the presence of 3 mol% of $[Co_2(CO)_8]$ for 7 h in benzene (0.14 M substrate) under 1 atm of CO. [b] Ratio of phosphane sulfide to $[Co_2(CO)_8]$. [c] Yield of isolated product. [d] An = *p*-anisyl group. [e] The reaction was complete within 5 h. [f] Under the same conditions as entry 12 except for the concentration (0.079 M). [g] $dppeS_2$ = bis(diphenylthiophosphanyl)ethane.

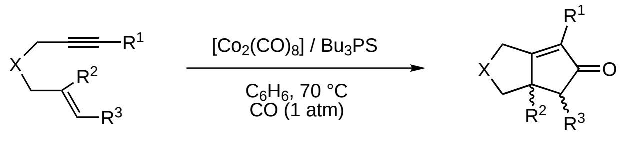
The scope of this reaction was then investigated with $[Co_2(CO)_8]/Bu_3PS$ (Table 2). Intramolecular reactions proceeded smoothly to give the corresponding bicyclic cyclopentenones in good yields. A substituent on the alkyne or alkene moiety did not prevent the reaction from proceeding. Although an enyne containing a 1,2-disubstituted alkene group required a longer reaction time, the corresponding cyclopentenone was formed in good yield (entry 2), and the isomer ratio of the substrate ($E/Z = 90/10$) was almost maintained in the product (*trans*/*cis* = 85/15). Enynes connected by a heteroatom also gave the corresponding cyclopentenones in good yields when increased ratios of catalyst to substrate were used (entries 4, 5).[9] In many cobalt-catalyzed Pauson–Khand reactions oxaenyne-type substrates, such as allyl propargyl ethers, demonstrate low reactivity. In contrast, **1e** gave a satisfactory result with 10 mol% of catalyst under our conditions. Without phosphane sulfide the reaction stopped at its initial stage to afford **2e** in only 25% yield. By using the same conditions and the reactive olefin norbornene (**3**) an intermolecular version of the catalytic Pauson–Khand reaction was achieved [Eq. (1)].



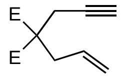
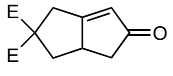
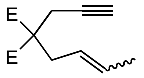
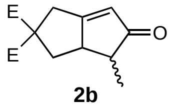
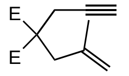
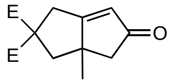
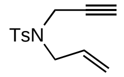
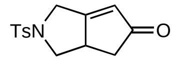
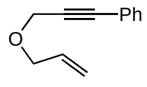
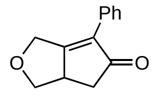
3 **4** **5** (92%) (1)

Although the role of the phosphane sulfide is still not clear, the following are plausible explanations for its effectiveness: 1) Lewis bases such as amines[10] and phosphane oxides[5] are known to promote the stoichiometric Pauson–Khand

Table 2. Catalytic Pauson–Khand reaction in the presence of $[Co_2(CO)_8]$/Bu_3PS under an ambient pressure of CO.[a]



1a–e **2a–e**

Entry	Substrate[b]	Product	Time [h]	Yield[c] [%]
1	 **1a**	 **2a**	5	90 (50)
2	 **1b** (*E/Z* = 90/10)	 **2b** (*trans/cis* = 85/15)	8	86
3	 **1c**	 **2c**	5	90
4	 **1d**	 **2d**	4	87[d]
5	 **1e**	 **2e**	24	83[e] (25)

[a] The reaction was performed on a 0.4-mmol scale. A mixture of substrate, $[Co_2(CO)_8]$, and Bu_3PS in benzene (0.14 M substrate) was stirred under CO (1 atm) at 70 °C. [b] E = CO_2Et. [c] Yield of isolated product. The yields in parentheses are those obtained without phosphane sulfide. [d] 5 mol % of the cobalt complex and 30 mol % of the phosphane sulfide were employed, since the reaction was slow when only 3 mol % of the catalyst was used. [e] 10 mol % of the cobalt complex and 40 mol % of the phosphane sulfide were used, since the reaction did not go to completion when only 3–5 mol % of the catalyst was used.

reaction, and since dissociation of coordinated CO must take place before olefin coordination can occur, this effect presumably arises from acceleration of this ligand-exchange reaction. The reaction is faster in the presence of phosphane sulfide and this suggests that the phosphane sulfide may promote the catalytic cycle by means of its favorable basicity and coordinative lability. 2) In the stoichiometric, thermal Pauson–Khand reaction, the $[Co_2(CO)_8]$ complex is transformed into a $[Co_4(CO)_{12}]$ cluster, which requires CO pressure for reconversion to the active species $[Co_2(CO)_8]$.[2k] In our case, a coordinatively unsaturated species formed by elimination of the product could be trapped as a phosphane sulfide complex before it can decompose; the reaction would then proceed in a catalytic manner under only 1 atm of CO. This mechanism is in accord with the fact that the reaction at a lower concentration required a higher ratio of tributylphosphane sulfide to catalyst; occupation of the vacant ligand site and/or promotion of ligand exchange is suppressed by dilution.

Experimental Section

Typical procedure: A solution of enyne **1a** (99 mg, 0.42 mmol), $[Co_2(CO)_8]$ (4.3 mg, 0.013 mmol), and tributylphosphane sulfide (17.7 mg, 0.077 mmol) in dry benzene (3 mL, 0.14 M solution of substrate) was vigorously stirred at 70 °C under a CO atmosphere (supplied from a balloon, 1 atm) until the substrate was consumed. When the substrate could no longer be detected by thin-layer chromatography, the reaction mixture was heated under reflux for 20 min to ensure complete reaction. The reaction mixture was then evaporated to dryness, and the residue was purified by preparative TLC on silica gel.

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[9] In the case of entry 5, reaction with a catalyst to additive ratio of 1:4 gave a better result than with a ratio of 1:6, but the reason for this is unclear.

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