Michael Reaction of Stabilized Carbon Nucleophiles Catalyzed by $[RuH_2(PPh_3)_4]$

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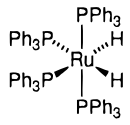
Abstract: The Michael reaction of active methylene compounds lacking cyano groups such as malonates, β-ketoesters, 1,3-diketones, 1,1-disulfones, nitrocompounds, Meldrum acid, and anthrone with common acceptors proceeds in acetonitrile solution in the presence of $[RuH_2(PPh_3)_4]$ as the catalyst. Cyano acetates, more acidic than malonates in organic solvents, are also excellent substrates for this reaction. In a number of cases, intramolecular aldol reactions catalyzed by $[RuH_2(PPh_3)_4]$ were also observed as side reactions. Catalysis by other ruthenium and rhodium complexes has been examined. Selectivity studies performed with malonate and disulfone donors indicate that the catalyst selectively activates Michael donors that can coordinate with ruthenium(II). Additionally, it has been shown that the reaction requires the presence of free phosphine. Therefore, the Michael reaction of stabilized enolates appears to be a ruthenium- and phosphine-catalyzed reaction. From a practical point of view, the use of readily prepared $[RuH_2(PPh_3)_4]$ as the catalyst in acetonitrile provided the best solution for the Michael reaction of active methylene compounds.

Introduction

The Michael addition of stabilized nucleophiles to α,β-unsaturated carbonyl compounds is one of the fundamental processes for the formation of carbon−carbon bonds.[1,2] The reactions is quite general, although in certain cases the Michael adducts suffer further transformations such as retrograde Michael reactions and intramolecular condensations.[1] Additionally, polymerization of the Michael acceptor under the basic conditions is frequently observed.[1] Recently, Murahashi reported on the Michael and Knoevenagel reactions of activated nitriles catalyzed by the ruthenium complex $[RuH_2(PPh_3)_4]$ (**1**).[3,4,5] The Michael reaction also proceeds in the presence of a rhodium(I) hydride,[6] which has led to the development of efficient asymmetric processes by using trans-chelating chiral diphosphines.[7] These ruthenium- or rhodium-catalyzed conjugate additions proceeded readily at room temperature and, more importantly, under neutral conditions.



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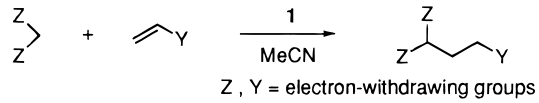
In all these processes, active methylene compounds lacking cyano groups such as 1,3-diketones, β-ketoesters, dialkyl malonates, and nitroalkanes were shown to be unreactive.[3,6] A mechanistic rationale has been advanced by Komiya and Murahashi[3b,8] to explain the selectivity observed for the ruthenium-catalyzed Michael reaction. According to this rationale, which was based on the isolation of an intermediate ruthenium(II) enolate,[8] coordination of the substrate to Ru(II) through the cyano group was a requirement for the conjugate addition.[3]

However, in contradiction to the above findings, we have found that ruthenium complex **1** is an excellent catalyst for the Michael addition of non-cyano nucleophiles when the reactions are performed in acetonitrile instead of THF. Under these reaction conditions the ruthenium-catalyzed Michael reaction is quite general providing the desired adducts in good yields under mild conditions (eq 1). Apparently, we have succeeded



(Eq 1)

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(1) (a) Jung, M. E. In *Comprehensive Organic Synthesis*; Trost, B. M., Fleming, I., Eds.; Pergamon: Oxford, 1991; Vol. 4, Chapter 1.1. (b) Bergmann, E. D.; Ginsburg, D.; Pappo, R. *Org. React.* **1959**, *10*, 179. (c) House, H. O. *Modern Synthetic Reactions*, 2nd ed.; Benjamin: Menlo Park, 1972; pp 595−623. (d) Perlmutter, P. *Conjugate Addition Reactions in Organic Synthesis*; Pergamon: Oxford, 1992. (e) March, J. *Advanced Organic Chemistry*, 4th ed.; Wiley: New York, 1992; pp 795−797. (f) Stowell, J. C. *Carbanions in Organic Synthesis*; Wiley: New York, 1987.

(2) For recent lead references on Michael reactions of activated nucleophiles, see: (a) Arai, T.; Sasai, H.; Aoe, K.; Okamura, K.; Date, T.; Shibasaki, M. *Angew. Chem., Int. Ed. Engl.* **1996**, *35*, 104. (b) Ozaki, Y.; Kubo, A.; Okamura, K.; Kim, S.-W. *Chem. Pharm. Bull.* **1995**, *43*, 734. (c) Sasai, H.; Arai, T.; Shibasaki, M. *J. Am. Chem. Soc.* **1994**, *116*, 1571. (d) Bonadies, F.; Lattanzi, A.; Orelli, L. R.; Pesci, S.; Scettri, A. *Tetrahedron Lett.* **1993**, *34*, 7649. (e) Lubineau, A.; Augé, J. *Tetrahedron Lett.* **1992**, *33*, 8073. (f) Antonioletti, R.; Bonadies, F.; Monteagudo, E. S.; Scettri, A. *Tetrahedron Lett.* **1991**, *32*, 5373. (g) Ranu, B. C.; Bhar, S.; Sarkar, D. C. *Tetrahedron Lett.* **1991**, *32*, 2811. (h) Botteghi, C.; Schianato, A.; Rosini, C.; Salvadori, P. *J. Mol. Catal.* **1990**, *63*, 155. (i) Koerner, M.; Rickborn, B. *J. Org. Chem.* **1990**, *55*, 2662.

(3) (a) Naota, T.; Taki, H.; Mizuno, M.; Murahashi, S.-I. *J. Am. Chem. Soc.* **1989**, *111*, 5954. (b) Murahashi, S.-I.; Naota, T.; Taki, H.; Mizuno, M.; Takaya, H.; Komiya, S.; Mizuho, Y.; Oyasato, N.; Hiraoka, M.; Hirano, M.; Fukuoka, A. *J. Am. Chem. Soc.* **1995**, *117*, 12436.

(4) (a) Knoevenagel condensation of activated nitriles catalyzed by Ir and Ru hydrides: Lin, Y.; Zhu, X.; Xiang, M. *J. Organomet. Chem.* **1993**, *448*, 215. (b) Knoevenagel condensation of activated nitriles catalyzed by a Re hydride: Hirano, M.; Ito, Y.; Hirai, M.; Fukuoka, A.; Komiya, S. *Chem. Lett.* **1993**, 2057.

(5) (a) The related reaction of activated nitriles with imine derivatives is catalyzed by a variety of metal complexes: Yamamoto, Y.; Kubota, Y.; Honda, Y.; Fukui, H.; Asao, N.; Nemoto, H. *J. Am. Chem. Soc.* **1994**, *116*, 3161. (b) For the reaction of activated nitriles with allenes catalyzed by Pd(0) complexes, see: Yamamoto, Y.; Al-Masum, M.; Asao, N. *J. Am. Chem. Soc.* **1994**, *116*, 6019.

(6) Paganelli, S.; Schionato, A.; Botteghi, C. *Tetrahedron Lett.* **1991**, *32*, 2807.

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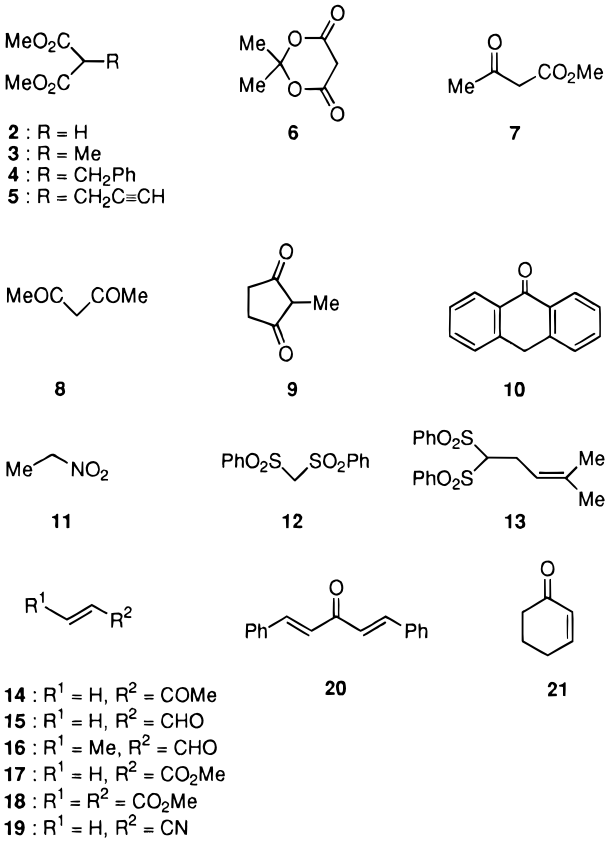
Chart 1

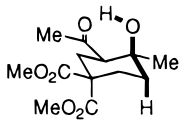


in increasing substantially the reactivity of the parent ruthenium complex **1** by substitution of one or more triphenylphosphine ligands by acetonitrile. Herein we report the scope of this reaction. We also address in this paper the nature of the catalytic species and the essential role played by the phosphine in the reaction system.[9,10]

Results and Discussion

Reaction Scope. The reactions of Michael donors **2**−**13** with acceptors **14**−**21** proceeded very cleanly in the presence of ruthenium dihydride **1** (3 mol %) in acetonitrile at 23 °C (Table 1).[11] Dimethyl malonate (**2**) reacted smoothly with 1 equiv of methyl vinyl ketone (**14**), acrolein (**15**), crotonaldehyde (**16**),[12] and dimethyl fumarate (**18**) to give monoalkylated products **22**,[13] **25**,[12] **26**,[12,14] and **28**,[15] respectively, in 54−96% yields. Methyl acrylate (**17**) led to dialkylated malonate **27**[9] in quantitative yield. Substituted malonates **3** and **4** also reacted with **14** to give adducts **29**[16] and **30**, respectively, in excellent yields. The presence of a terminal alkyne does not interfere with the ruthenium dihydride[17] as shown in the uneventful formation of adducts **31** and **32** from donor **5** and acceptors **14** and **19**. With dibenzylideneacetone (**20**) as the acceptor, malonate **2** led to the formation of cyclohexanone **44**[18] by a double Michael process. The reaction of **2** with cyclohexenone (**21**) was slow at room temperature in acetonitrile and was better performed under refluxing conditions to give **45** in moderate yield.[2b] Disulfones **12** and **13**[19] also reacted in the presence of **1** with acrolein (**15**) and methyl vinyl ketone (**14**) to give adducts **42** and **43**, respectively, in good yields.

The reaction of **2** with 2 equiv of **14** in the presence of only 0.1 mol % of **1** afforded a 1:1 mixture of dialkylated **23** and cyclic aldol **24a**, as a single stereoisomer, in almost quantitative yield. The stereochemistry of **24a** was assigned as shown with



24a

the hydroxyl cis to the acetyl group on the basis of the appearance in the ^{1}H NMR spectrum of a doublet for the chelated hydroxyl at δ 3.92 coupled with the axial H-5 at δ 1.26 with a ^4J = 2.3 Hz. When the same reaction was performed in the presence of 3 mol % of catalyst **1**, **24a** was cleanly obtained as the only product in excellent yield. It is interesting to note that, despite the ready availability of the starting materials, **24a** has not been previously described. Similar results were obtained in the reactions of Michael acceptor **14** with **7**, **8**, and **11** as the donors. The Michael reactions of **14** with **7** and **8** provided **34** and **37** stereoselectively, while the corresponding reaction of nitroethane (**11**) with **14** gave **41** as a mixture of four possible stereoisomers. In contrast with these reactions in which aldols were obtained as the major or exclusive products, the reaction of Meldrum acid (**6**) and anthrone (**10**) with **14** gave only 1,7-diketones **33** and **39**, respectively.

The pK_a values of the above donors in dimethyl sulfoxide (DMSO) ranged from 7 for the more acidic Meldrum acid **6**[20] to 16−20 for malonates **2**-**5** and nitroethane (**11**).[21,22] Less acidic donors reacted more sluggishly. Thus, fluorene (**46**) (pK_a = 23, DMSO)[21] reacted with **14** in the presence of 3 mol % of

(7) (a) Sawamura, M.; Hamashima, H.; Ito, Y. *J. Am. Chem. Soc.* **1992**, *114*, 8295. (b) Sawamura, M.; Hamashima, H.; Ito, Y. *Tetrahedron* **1994**, *50*, 4439. (c) Sawamura, M.; Hamashima, H.; Shinoto, H.; Ito, Y. *Tetrahedron Lett.* **1995**, *36*, 6479. (d) Sawamura, M.; Sudoh, M.; Ito, Y. *J. Am. Chem. Soc.* **1996**, *118*, 3309.

(8) Mizuho, Y.; Kasuga, N.; Komiya, S. *Chem. Lett.* **1991**, 2127.

(9) White, D. A.; Baizer, M. M. *Tetrahedron Lett.* **1973**, 3597.

(10) (a) Baraldi, P. G.; Guarneri, M.; Pollini, G. P.; Simoni, D.; Barco, A.; Benetti, S. *J. Chem. Soc., Perkin Trans. 1* **1984**, 2501. (b) Somei, M.; Karasawa, Y.; Kaneko, C. *Heterocycles* **1981**, *16*, 941.

(11) We have routinely carried out the Michael reactions one order of magnitude more diluted (0.3 M donor and acceptor and 0.01 M catalyst **1**) than those reported by Murahashi (4 M concentration of donor and acceptor and 0.1 M of **1**).[3] Catalyst 1 is almost insoluble in acetonitrile although it dissolved immediately after the addition of the acceptor alkene.

(12) α,β-Unsaturated aldehydes usually give lower yields in Michael reactions: Yamaguchi, M.; Yokota, N.; Minami, T. *J. Chem. Soc., Chem. Commun.* **1991**, 1088.

(13) Tsuji, J.; Minato, M. *Tetrahedron Lett.* **1987**. *28*, 3683.

(14) Skarzewski, J. *Synthesis* **1990**, 1125.

(15) (a) Ferappi, M.; Carotti, A.; Casini, G.; De Laurentis, N.; Giardina, D.; Cingolani, G. M.; Gavuzzo, E.; Mazza, F. *J. Heterocycl. Chem.* **1983**, *20*, 439. (b) Ogibin, Y. N.; Elison, M. N.; Kikishin, G. I.; Kadentesev, V. I.; Chizhov, O. S. *Izv. Akad. Nauk SSSR, Ser. Khim.* **1979**, *3*, 557; *Chem. Abstr.* **1979**, *91*, 38882f.

(16) Tamblyn, W. H.; Waltemire, R. E. *Tetrahedron Lett.* **1983**, *24*, 2803.

(17) (a) Certain ruthenium(II) dihydrido complexes react with alkynes to give butenynyl derivatives: Wakatsuki, Y.; Yamazaki, H.; Kumegawa, N.; Satoh, T.; Satoh, J. Y. *J. Am. Chem. Soc.* **1991**, *113*, 9604. (b) For the related reaction of ruthenium(II) dihydrido η^2-dihydrogen complexes, see: Jia, G.; Meek, D. W. Organometallics 1991, 10, 1444.

(18) Kohler, E. P.; Dewey, C. S. *J. Am. Chem. Soc.* **1924**, *46*, 1267.

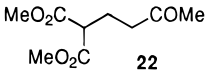
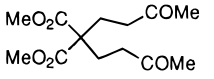
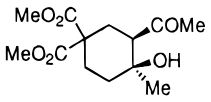
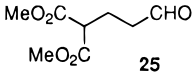
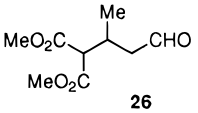
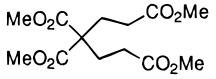
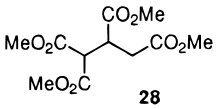
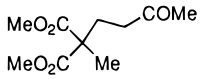
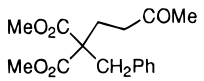
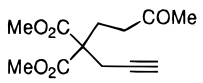
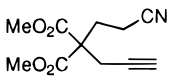
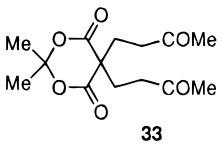
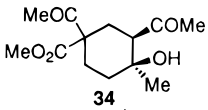
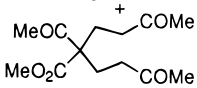
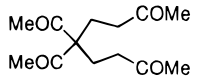
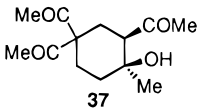
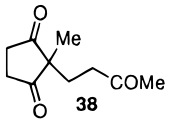
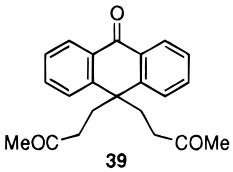
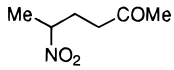
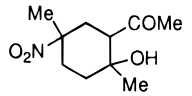
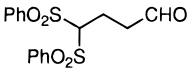
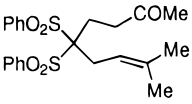
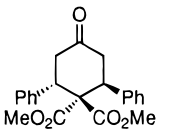
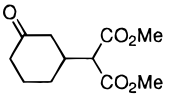
(19) Benedetti, F.; Berti, F.; Fabrissin, S.; Gianferrara, T.; Risaliti, A. *J. Org. Chem.* **1991**, *56*, 3530.

(20) For a discussion on the higher acidity of Meldrum acid, see: Evanseck, J. D.; Houk, K. N.; Briggs, J. M.; Jorgensen, W. L. *J. Am. Chem. Soc.* **1994**, *116*, 10630 and references cited therein.

(21) Equilibrium acidities in DMSO at 25 °C: Bordwell, F. G. *Acc. Chem. Res.* **1988**, *21*, 456.

(22) (a) Although relative acidities in DMSO and acetonitrile do not to differ greatly,[21] significant differences are expected in the absolute values: Kolthoff, I. M.; Chantooni, M. K.; Bhowmik, S. *J. Am. Chem. Soc.* **1968**, *90*, 23. (b) The acidity of carbon acids in DMSO and THF is comparable: Fraser, R. R.; Mansour, T. S.; Savard, S. *J. Org. Chem.* **1985**, *50*, 3232.

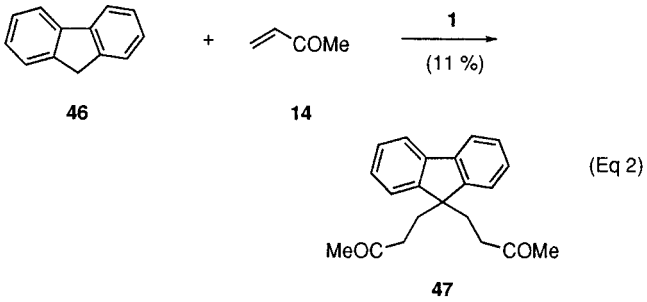
Table 1. Ruthenium-Catalyzed Michael Reaction of Activated Carbon Nucleophiles[a]

Donor	Michael acceptor	Reaction time (h)	Product	Yield (%)
2	**14**	0.5	 **22**	96
2	**14**[b]	16[c]	 **23** +  **24a**	49 + 45
2	**14**[b]	1	**24a**	93
2	**15**	1	 **25**	56
2	**16**	30	 **26**	54
2	**17**[b]	24	 **27**	99
2	**18**	30	 **28**	83
3	**14**	10	 **29**	96
4	**14**	16	 **30**	89
5	**14**	10	 **31**	86
5	**19**	24	 **32**	94
6	**14**[b]	8	 **33**	80
7	**14**[b]	12	 **34** +  **35**	57[d] + 42
8	**14**[b]	24[c]	 **36**	64
8	**14**[b]	10	 **37**	71
9	**14**	48	 **38**	71
10	**14**	30	 **39**	75
11	**14**	10	 **40**	83
11	**14**[b]	10	 **41**	94[e]
12	**15**	14	 **42**	88
13	**14**	16	 **43**	83
2	**20**	18	 **44**	57
2	**21**	24[f]	 **45**	46

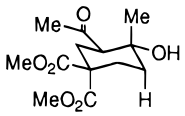
[a] Unless otherwise stated the reactions were carried out in the presence of 3 mol % ruthenium dihydride **1** in MeCN at 23 °C with 1 equiv each of donor and acceptor. [b] Reaction carried out with 2 equiv of acceptor. [c] Reaction carried out with 0.1 mol % ruthenium dihydride **2**. [d] **34** was obtained as a 3:2 mixture of C-1 epimers. [e] **41** was obtained as a 2:1:1:1 mixture of diastereomers. [f] Reaction carried out at 80 °C.

1 to give dialkylated **47** in only 11% yield even after being heated under reflux in acetonitrile for 24 h (eq 2).

Since the preparation of complex **1** according to the published procedures uses $NaBH_4$ as the reducing agent for



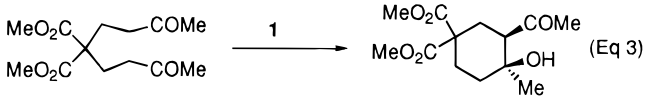
ruthenium(III)[23] or ruthenium(II),[24] it could be conceived that traces of basic $NaB(OR)_4$, the product of the reaction between $NaBH_4$ with the solvent methanol[25] or ethanol, may act as the true catalyst of the reaction. Not unexpectedly, the Michael reaction between **2** and **14** (2.5 equiv) proceeded in the presence of $NaB(OMe)_4$ as the catalyst (3 mol %, acetonitrile, 23 °C, 2 h). However, the reaction was less selective with this basic catalyst, leading to aldol **24a** (62% yield) and an inseparable mixture of its diastereomer **24b** and diketone **23** (*ca.* 3:1, 33%).[26]



24b

Elimination of any basic impurity from **1** was easily achieved by washing crude ruthenium dihydride with a large volume of water under an inert atmosphere of Ar, leading to a yellow material which showed no sign of loss of catalytic activity in the Michael addition.

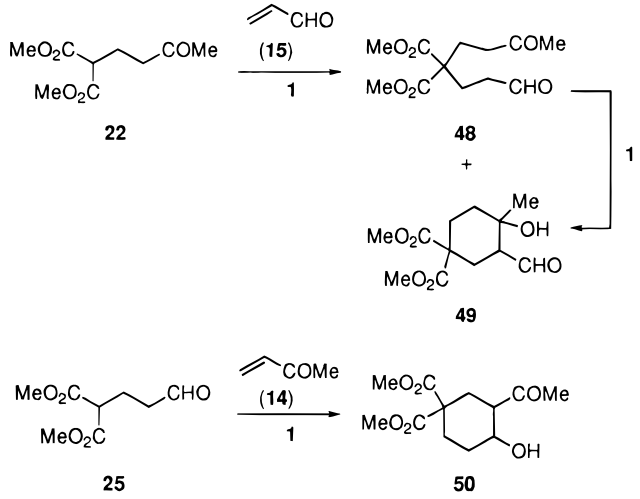
Intramolecular Aldol Reactions. Intramolecular aldol reactions occurred in the transformations leading to **24a**, **34**, **37**, and **41** (Table 1). These aldol reactions are also catalyzed by complex **1**. Thus, the intramolecular aldol reaction of diketone **23** was cleanly performed by using 5 mol % of complex **1** in acetonitrile at 23 °C for 16 h to give stereoselectively **24a** as the only product (eq 3).



23 **24a**

The intramolecular reactions of ketoaldehydes proceed by attack of the α-carbon of the ketone or the aldehyde depending on the strain of the formed ring and the reaction conditions.[27,28] The cyclizations outlined in Scheme 1 demonstrate that an enolate is formed under the conditions of the ruthenium-catalyzed Michael reaction, which reacts intramolecularly with the carbonyl group to afford aldols under kinetic conditions.

Scheme 1



Michael reaction of malonate **22** with 2 equiv of acrolein (**15**) (5 mol % of **1**, acetonitrile, 23 °C, 16 h) afforded **48** (43%) and cyclic aldol **49** (6%). The cyclization of ketoaldehyde **48** could be carried out with 10 mol % of **1** to give **49** as a mixture of stereoisomers (acetonitrile, 23 °C, 2 h, 35% yield). Although the yield of this cyclization was poor, the aldol reaction was selective since none of the alternative aldol **50**, resulting from the condensation of the ketone enolate with the aldehyde, was observed in the crude reaction mixture. Alternatively, aldol **50**, as a mixture of two stereoisomers, could be obtained in the reaction of malonate **25** with **14** (3 mol % **1**, acetonitrile, 23 °C, 1 h, 64%). In this example, the uncyclized ketoaldehyde was not observed in the crude reaction mixture.

Catalysis with Other Ruthenium and Rhodium Complexes. The results obtained with different ruthenium and rhodium complexes in the reactions of malonates **2** and **4** with acceptor **14** are summarized in Table 2. Ruthenium dihydride **51**[29] with triphenylarsine instead of triphenylphosphine catalyzed the slow formation of aldol **24a** from **2** in moderate yield (entry 1; compare Table 1, entry 3). The same reaction in THF was considerably slower, giving monoadduct **22** in low yield (entry 2). Slow reactions were observed with ruthenium dihydride **52**[30] and monohydrides **53**[31] and **54**.[32] These processes may be catalyzed by the phosphine released from the ruthenium complexes[33] since no reaction was observed with the related cationic hydride **55**[34] with two tightly bound trans phosphine ligands.[35] Hydrides **56** and **57**[36] were active catalysts for the Michael reaction. Noteworthy, bisacetonitrile complex **57** efficiently catalyzed the addition of **2** to **14** to give a 3:1 mixture of mono- and dialkylated derivatives **22** and **23** in quantitative

(23) Synthesis of **1** from $RuCl_3 \cdot 3H_2O$: Levison, J. J.; Robinson, S. D. *J. Chem. Soc. A* **1970**, 2947.

(24) Synthesis of **1** from $[Ru(PPh_3)3Cl_2]$ (**60**): Young, R.; Wilkinson, G. *Inorg. Synth.* **1990**, *28*, 337.

(25) Golden, J. M.; Schreier, C.; Singaram, B.; Williamson, S. M. *Inorg. Chem.* **1992**, *31*, 1533.

(26) Very similar results were obtained in the presence of $NaBH_4$ (3 mol %, 23 °C, 2 h, acetonitrile). Probably the actual catalyst in this case is the corresponding alkoxyde resulting from the reduction of the carbonyl of **14**. Under these conditions, a mixture of aldol **24a** (70%), its stereoisomer **24b** (*ca.* 20%), and diketone **23** (*ca.* 10%) was obtained.

(27) (a) Nielsen, A. T.; Houlihan, W. J. *Org. React.* **1968**, *16*, 1. (b) Reference 1e, p 940.

(28) Under kinetic conditions the rate-determining deprotonation of the more acidic aldehydes usually leads to the formation of cyclic β-hydroxy aldehydes: (a) Guthrie, J. P.; Cossar, J. *Can. J. Chem.* **1986**, *64*, 2470. (b) Guthrie, J. P. *J. Am. Chem. Soc.* **1991**, *113*, 7249.

(29) This complex was prepared by using a procedure similar to that used for the preparation of **1** with $AsPh_3$ instead of PPh_3. For an alternative preparation: Dedieu, M.; Pascal, Y.-L. *J. Mol. Catal.* **1980**, *9*, 71.

(30) (a) Knoth, W. H. *J. Am. Chem. Soc.* **1972**, *94*, 104. (b) Chaudret, B. N.; Cole-Hamilton, D. J.; Nohr, R. S.; Wilkinson, G. *J. Chem. Soc., Dalton Trans.* **1977**, 1546. (c) Cole-Hamilton, D. J.; Wilkinson, G. *Nouv. J. Chim.* **1977**, *1*, 133.

(31) Robinson, S. D.; Levison, J. J.; Ahmand, N.; Uttley, M. F. *Inorg. Synth.* **1974**, *15*, 48.

(32) Santos, A.; López, J.; Montoya, J.; Noheda, P.; Romero, A.; Echavarren, A. M. *Organometallics* **1994**, *13*, 3605.

(33) Facile substitution of the equatorial triphenylphosphine ligand has been observed in the reaction of hydride **53** with 1-alkynes: (a) Torres, M. R.; Vegas, A.; Santos, A. *J. Organomet. Chem.* **1986**, *209*, 169. (b) Torres, M. R.; Santos, A.; Ros, J.; Solans, X. *Organometallics* **1987**, *6*, 1091. (c) Torres, M. R.; Vegas, A.; Santos, A.; Ros, J. *J. Organomet. Chem.* **1987**, *326*, 413.

(34) This hydride was prepared by a procedure analogous to that used for the synthesis of the PF_6^- complex by using $NaBF_4$: López, J.; Romero, A.; Santos, A.; Vegas, A.; Echavarren, A. M.; Noheda, P. *J. Organomet. Chem.* **1989**, *373*, 249.

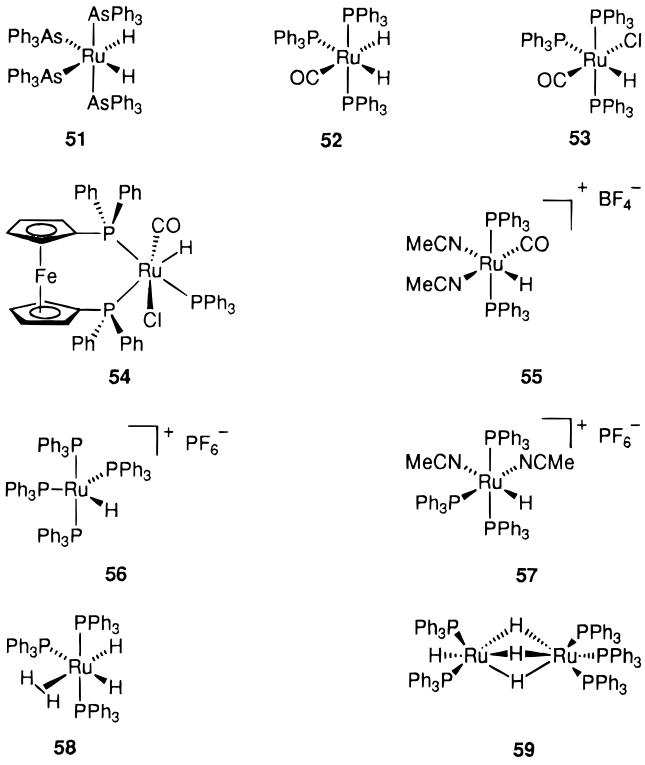
Table 2. Reactions of Malonates **2** or **4** with 3-Buten-2-one (**14**) and Complexes **51**−**62**[a]

donor	complex	solvent	reaction time (h)	product	yield (%)
2	51	MeCN	24	24a	57
2	51	THF	52	22	18
2	52	MeCN	24	b	
2	53	MeCN	23	22	27
2	53	THF	26	22	22
2	54	MeCN	22	22	13
2	54	THF	52	22	14
2	55	MeCN	26	b	
2	55	THF	26	b	
2	56	MeCN	4	22	48
2	57	THF	4	**22** + **23** (3:1)	100
2	58	MeCN	24	**22** + **23** (12:1)	79
2	58	THF	24	22	23
2	59	MeCN	24	**22** + **23** (16:1)	69
2	59	THF	24	**22** + **23** (10:1)	79
2	60	MeCN	72	22	41
2	61	MeCN	26	b	
2	61	THF	26	b	
2	62	MeCN	27	22	64
2	62	THF	52	22	40
4	51	MeCN	29	30	20
4	51	THF	29	30	30
4	52	MeCN	30	30	14
4	52	THF	26	30	13
4	54	MeCN	45	b	
4	54	THF	26	30	2
4	55	MeCN	45	b	
4	55	THF	26	b	
4	58	MeCN	24	30	56
4	58	THF	24	b	
4	59	MeCN	24	30	61
4	59	THF	24	30	33
4	61	MeCN	29	b	
4	61	THF	29	b	
4	62	MeCN	29	30	65
4	62	THF	29	30	41

[a] All reactions were performed in the presence of 3 mol % of complex at 23 °C. [b] No reaction was observed.

yield, although no intramolecular aldol reaction of **23** was observed. Dihydrogen dihydride ruthenium complex **58**[37] and binuclear hydride **59**[38] were also moderate catalysts for the addition process. $[Ru(PPh_3)_3Cl_2]$ (**60**)[39] showed some catalytic activity, whereas no reaction was observed with $[Rh(PPh_3)_3Cl]$ (**61**).[40a] The related rhodium hydride $[RhH(CO)(PPh_3)_2]$ (**62**)[40b] is only a moderate catalyst for this reaction leading to the formation of monoalkylated **22** from donor **2**. In all cases, lower conversions were obtained with more substituted malonate **4** as the Michael donor. The results of Table 2, with only two exceptions, show that acetonitrile is a superior solvent to THF for this type of Michael addition. It is important to note also

Chart 2



that none of the ruthenium and rhodium complexes examined was superior to the parent ruthenium dihydride **1**.

Nature of the Ruthenium Catalyst Species. Dihydride **1** reacts easily at room temperature with weak donor ligands by substitution of a triphenylphosphine ligand.[30,38,39,41] In fact, the ^{1}H NMR spectrum of **1** in benzene-d_6 showed, besides the multiplet at δ −10.14 corresponding to **1**,[42,43] a small quartet at δ −17.20 (J = 29.4 Hz) probably corresponding to the coordinatively unsaturated dihydride **63**[44] in equilibrium with **1**.[45] Addition of acetonitrile to **1** led to the clean formation of the ruthenium dihydride **64**[46,47,48] (Scheme 2), which showed two well differentiated signals for the hydride ligands at δ −8.90 (dtd, J = 76.3, 31.2, 7.1 Hz) and −14.96 (tdd, J = 28.5, 13.7, 7.0 Hz).

Available literature evidence suggests that dihydride **1** reacts with an alkene by ligand substitution to form coordination

(35) Cationic complexes of type **55** retain the axial triphenylphosphine ligands in the reactions with alkynes, carbon monoxide, or isocyanides: (a) See ref 34. (b) Montoya, J.; Santos, A.; Echavarren, A. M.; Ros, J. *J. Organomet. Chem.* **1990**, *390*, C57. (c) Echavarren, A. M., López, J.; Santos, A.; Romero, A.; Hermoso, J. A.; Vegas, A. *Organometallics* **1991**, *10*, 2371. (d) Montoya, J.; Santos, A.; Echavarren, A. M.; Ros, J.; Romero, A. *J. Organomet. Chem.* **1992**, *426*, 383.

(36) Sanders, J. R. *J. Chem. Soc., Dalton Trans.* **1973**, 743.

(37) (a) Harris, R. O.; Hota, N. K.; Sadavoy, L.; Yuen, J. M. C. *J. Organomet. Chem.* **1973**, *54*, 259. (b) Ashworth, T. V.; Singleton, E. *J. Chem. Soc., Chem. Commun.* **1976**, 705. (c) Crabtree, R. H.; Hamilton, D. G. *J. Am. Chem. Soc.* **1986**, *108*, 3124. (d) Hamilton, D. G.; Crabtree, R. H. *J. Am. Chem. Soc.* **1988**, *110*, 4126.

(38) Sluys, L. S.; Kubas, G. J.; Caulton, K. G. *Organometallics* **1991**, *10*, 1033.

(39) (a) Hallman, P. S.; Stephenson, T. A.; Wilkinson, G. *Inorg. Synth.* **1970**, *12*, 238. (b) Stephenson, J. A.; Wilkinson, G. *J. Inorg. Nucl. Chem.* **1966**, *28*, 945.

(40) (a) Osborn, J. A.; Jardine, F. H.; Young, J. F.; Wilkinson, G. *J. Chem. Soc. A* **1966**, 1711. (b) Evans, D.; Osborn, J. A.; Wilkinson, G. *Inorg. Synth.* **1968**, *11*, 99.

(41) (a) Ito, T.; Kitazume, S.; Yamamoto, A.; Ikeda, S. *J. Am. Chem. Soc.* **1970**, *92*, 3011. (b) Komiya, S.; Yamamoto, A. *J. Chem. Soc., Chem. Commun.* **1974**, 523.

(42) A *cis*-dihydrido stereochemistry has been demonstrated for $[RuH_2(L)_4]$ (L = phosphine or phosphite): (a) Meakin, P.; Muetterties, E. L.; Jesson, J. P. *J. Am. Chem. Soc.* **1973**, *95*, 75. (b) Dewhirst, K. C.; Keim, W.; Reilly, C. A. *Inorg. Chem.* **1968**, *7*, 546.

(43) Minor amounts of tetrahydride **58** were also observed in some of the samples of crude hydride **1** prepared according to the described procedures.[23,24]

(44) (a) For the related dihydride $[RuH_2(p\text{-}C_6H_5CH_3PPh_2)_3]$, see: Arliguie, T.; Chaudret, B.; Morris, R. H. *Polyhedron* **1988**, *7*, 2031. (b) See also: Linn, D. E.; Halpern, J. *J. Am. Chem. Soc.* **1987**, *109*, 2969.

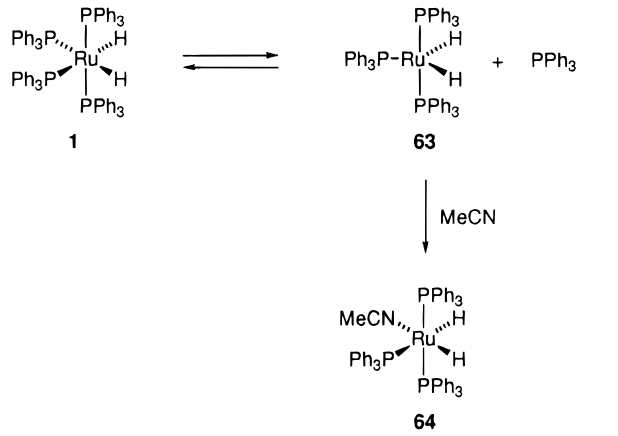
(45) We have found that the elusive coordinatively unsaturated ruthenium dihydride[39] can be readily obtained from **1** in polar solvents: Mateo, C.; Cuerva, J. M.; Echavarren, A. M. Unpublished results.

(46) $[RuH_2(RCN)(PPh_3)_3]$: (a) R = Ph: ref 30a. (b) R = Me (**64**), Ph: ref 37a.

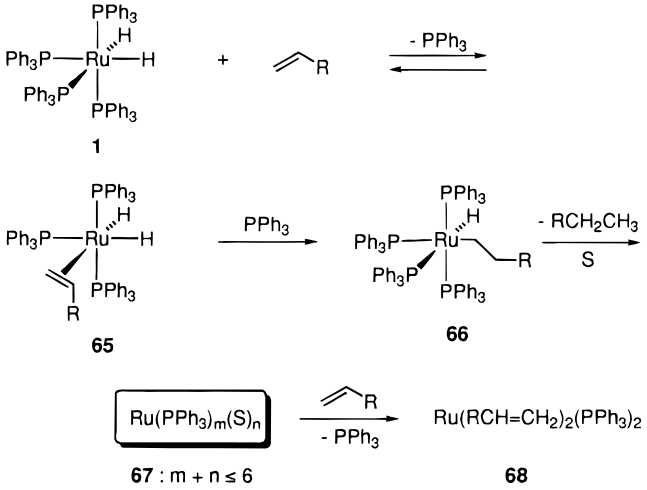
(47) For related acetonitrile ruthenium complexes, see: (a) Cole-Hamilton, D. J.; Wilkinson, G. *J. Chem. Soc., Dalton Trans.* **1979**, 1283. (b) The electrochemical reduction of $[Ru(PPh_3)_4Cl_2]$ in MeCN was reported to give $[Ru(PPh_3)_4(\pi\text{-MeCN})]\cdot$MeCN: Sherman, E. O.; Schreiner, P. R. *J. Chem. Soc., Chem. Commun.* **1976**, 3. This complex was later reformulated as $RuH(C_6H_4PPh_2)(MeCN)(PPh_3)_2$.[47a]

(48) The high affinity of Ru(II) complexes for acetonitrile has been applied for the in situ generation of active catalysts: Pertici, P.; Ballantini, V.; Salvadori, P.; Bennett, M. A. *Organometallics* **1995**, *14*, 2565 and references cited therein.

Scheme 2



Scheme 3



complex **65**, followed by a facile insertion[49] to give the hydridoalkyl ruthenium(II) complex **66**, which could suffer reductive elimination to give intermediate Ru(0) species **67** (Scheme 3).[50] Coordination of two molecules of alkene $RCH{=}CH_2$ to the ruthenium(0) intermediate then leads to stable complex $[Ru(RCH{=}CH_2)_2(PPh_3)_2]$ (**68**).[51] This type of behavior has been described for styrene[52,53,54] and, more recently, for methyl acrylate.[55] With other alkenes the highly reactive intermediate ruthenium(0) complexes of type **68** may react further with the phosphine ligand by *ortho* metalation or undergo a variety of intramolecular oxidative addition reactions.[41b,56] Dihydride **1** and related complexes have also been reported to promote the polymerization of acrylonitrile, acrolein, methyl vinyl ketone, and methyl acrylate.[56c,57,58,59] The alternative formation of a coordinatively unsaturated $[Ru(PPh_3)_4]$ as an intermediate by reductive elimination of H_2 is unlikely under the moderate conditions required for the formation of the alkene complexes.[60]

In accordance with the hypothetical involvement of ruthenium(0) complexes in the catalytic cycle, complex **68** ($R = CO_2Me$)[55] is a moderately active catalyst for the Michael reaction. Thus, the reaction between **2** and **14** (2 equiv) proceeded readily in acetonitrile in the presence of 3 mol % of **68** to give a 1:1.9 mixture of diketone **23** and aldol **24a** in 84% yield after 6 h at 23 °C. Addition of 6 mol % of triphenylphosphine increased slightly the reactivity of the catalyst leading to a 1:3.4 mixture of **23** and **24a** (91% yield) under otherwise identical conditions.

Ruthenium Hydride or Phosphine Catalyzed Reaction? As stated before, complex **1** is known to release easily one of the phosphine ligands to form a coordinatively unsaturated pentacoordinated ruthenium complex **63** which can react with a molecule of acetonitrile to form hexacoordinated complex **64**. Since phosphines are known to catalyze the Michael addition of certain active methylene compounds,[1a,9,10,61] the possibility exists that the Michael reactions may be simply catalyzed by the free triphenylphosphine released upon coordination of acetonitrile or the acceptor substrate with complex **1**. In fact, literature precedent prescribes the use of caution in proposing mechanistic hypothesis for reactions presumably catalyzed by transition metals[62] which could also be performed in the presence phosphines as the catalysts.[63,64]

(49) (a) Hill, A. F. In *Comprehensive Organometallic Chemistry II*; Abel, E. W., Stone, H. G. A., Wilkinson, G., Eds.; Pergamon: Oxford, 1995; Vol. 7, Chapter 6. (b) For a recent study on the insertion of styrenes into Ru−H bonds, see: Faller, J. W.; Chase, K. J. *Organometallics* **1995**, *14*, 1592.

(50) For a recent discussion on Ru(0) complexes, see: Ogasawara, M.; Macgregor, S. A.; Streib, W. E.; Folting, K.; Eisenstein, O.; Caulton, K. G. *J. Am. Chem. Soc.* **1995**, *117*, 8869.

(51) For lead references on (η^2-alkene)ruthenium(0) complexes, see: Bennett, M. A. In Comprehensive Organometallic Chemistry II; Abel, E. W., Stone, F. G. A., Wilkinson, G., Eds.; Pergamon: Oxford, 1995; Vol. 7, Chapter 7.

(52) (a) Komiya, S.; Yamamoto, A.; Ikeda, S. *J. Organomet. Chem.* **1972**, *42*, C65. (b) Komiya, S.; Yamamoto, A. *Bull. Chem. Soc. Jpn.* **1976**, *49*, 2553. (c) Carrondo, M.; Chaudret, B. N.; Cole-Hamilton, D. J.; Skapski, A. C.; Wilkinson, G. *J. Chem. Soc., Chem. Commun.* **1978**, 463. (d) Chaudret, B. N.; Cole-Hamilton, D. J.; Wilkinson, G. *J. Chem. Soc., Dalton Trans.* **1978**, 1739. (e) Rosete, R. O.; Cole-Hamilton, D. J.; Wilkinson, G. *J. Chem. Soc., Dalton Trans.* **1984**, 2067.

(53) For the reaction of $[Ru(CH_2{=}CHPh)2(PPh3)2]$ with other alkenes, see: (a) Chaudret, B. N.; Cole-Hamilton, D. J.; Wilkinson, G. *Acta Chem. Scand., Ser. A* **1979**, *32*, 763. (b) Reference 52d.

(54) However, it has been point out that the X-ray structure of the coordinatively unsaturated styrene complex $[Ru(Ph\text{-}CH{=}CH_2)_2(PPh_3)_2]$[52c] reveals that one of the styrene ligands may be η^3-coordinated.[50]

(55) The complex with methyl acrylate was isolated as a pentacoordinated aquo derivative $[Ru(CH_2{=}CHCO_2Me)_2(H_2O)(PPh_3)_2]$: (a) Sustmann, R.; Patzke, B.; Boese, R. *J. Organomet. Chem.* **1994**, *470*, 191. (b) See also: Patzke, B.; Sustmann, R. *J. Organomet. Chem.* **1994**, *480*, 65.

(56) (a) Cole-Hamilton, D. J.; Wilkinson, G. *Nouv. J. Chim.* **1977**, *1*, 141. (b) Smith, A. E. *Inorg. Chem.* **1972**, *11*, 2306. (c) Komiya, S.; Yamamoto, A. *J. Organomet. Chem.* **1975**, 87, 333. (d) Komiya, S.; Ito, T.; Cowie, M.; Yamamoto, A.; Ibers, J. A. *J. Am. Chem. Soc.* **1976**, *98*, 3875. (e) Komiya, S.; Aoki, Y.; Mizuno, Y.; Oyasato, N. *J. Organomet. Chem.* **1993**, *463*, 179.

(57) (a) Ito, T.; Kitazume, S.; Yamamoto, A.; Ikeda, S. *J. Am. Chem. Soc.* **1970**, *92*, 3011. (b) Yamamoto, A.; Ikeda, S. *J. Macromol. Sci.-Chem.* **1975**, *A9*, 931.

(58) However, these polymerizations may be just the result of a process catalyzed by the nucleophilic phosphine released from the ruthenium complex. Indeed, PMe_3 released from $[RuH_2(PMe_3)_4]$ initiates the rapid polymerization of acrylonitrile, methacrylonitrile, and methyl vinyl ketone: Rappert, T.; Yamamoto, A. *Organometallics* **1994**, *13*, 4984.

(59) The polymerization of methyl acrylate (**17**) by **1** has not been confirmed.[55a]

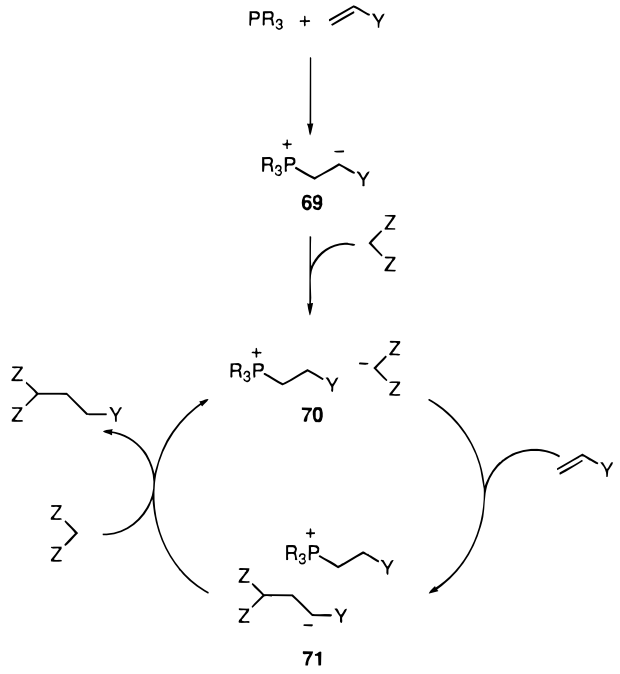
(60) (a) Elimination of H_2 from **1** and related ruthenium dihydrides proceeds very slowly and requires heating at a rather high temperature (140−200 °C).[41a] (b) $[RuH_2(PMe_3)_4]$ undergoes elimination at >180 °C: Hartwig, J. F.; Andersen, R. A.; Bergman, R. G. *J. Am. Chem. Soc.* **1991**, *113*, 6492. (c) $[RuH_2(dmpe)_2]$ (dmpe = 1,2-bis(dimethylphosphino)ethane) requires ca. 140 °C: Hsu, G. C.; Kosar, W. P.; Jones, W. D. *Organometallics* **1994**, *13*, 385. (d) No elimination was observed when $[RuH_2(CO)(PPh_3)_3]$ (**52**) was heated at 120 °C for 1.5 h: Kakiuchi, F.; Sekine, S.; Tanaka, Y.; Kamatani, A.; Sonoda, M.; Chatani, N.; Murai, S. *Bull. Chem. Soc. Jpn.* **1995**, *68*, 62.

(61) Some nucleophilic phosphines catalyze the Michael additions of nitroalkanes: (a) Polystyryltributylphosphine: Kim, B.; Kodomari, M.; Regen, S. L. *J. Org. Chem.* **1984**, *49*, 3233. (b) Tris(2,4,6-trimethoxyphenyl)phosphine: Masanori, W.; Aki, T.; Kumiko, N.; Tatsuo, E. *Nippon Kagaku Kaishi* **1987**, 1284; *Chem. Abstr.* **1988**, *108*, 149866t. (c) PBu_3: Miyakoshi, T. *Yakugaku Zasshi* **1988**, *37*, 19; *Chem. Abstr.* **1988**, *109*, 92232x.

(62) (a) Trost, B. M.; Schmidt, T. *J. Am. Chem. Soc.* **1988**, *110*, 2301. (b) Ma, D.; Lin, Y.; Lu, X.; Yu, Y. *Tetrahedron Lett.* **1988**, *29*, 1045. (c) Ma, D.; Yu, Y.; Lu, X. *J. Org. Chem.* **1989**, *54*, 1105. (d) Guo, C.; Lu, X. *Tetrahedron Lett.* **1991**, *32*, 7549.

(63) (a) Trost, B. M.; Kazmaier, U. *J. Am. Chem. Soc.* **1992**, *114*, 7933. (b) Guo, C.; Lu, X. *J. Chem. Soc., Perkin Trans. 1* **1993**, 1921. See also: (c) Trost, B. M.; Li, C.-J. *J. Am. Chem. Soc.* **1994**, *116*, 3167. (d) Trost, B. M.; Li, C.-J. *J. Am. Chem. Soc.* **1994**, *116*, 10819. (e) Zhang, C.; Lu, X. *Synlett* **1995**, 645.

Scheme 4



The phosphine released from complex **1** could promote the Michael reaction by means of a conjugate addition to the acceptor to form a zwitterionic intermediate **69**,[65] which could then deprotonate the active methylene compound to afford a phosphonium enolate **70** as the key intermediate (Scheme 4).[9,10,66] Michael addition of **70** to the acceptor alkene would give a new phosphonium enolate **71**, which would finally lead to the Michael adduct and intermediate **70** by reaction with the starting donor.[67]

Triphenylphosphine indeed catalyzes the addition of some Michael donors to **14** (Table 3). However, the reactions of donor **2** with triphenylphosphine as the catalyst were slower than those carried out with **1** leading to lower yields of monoalkylated derivative **22** (entries 1 and 2). Furthermore, aldol **24a** was obtained in only 6% yield after 48 h at 25 °C (entry 3). As expected, no reaction was observed in the presence of acetic acid (entries 4 and 5). Similarly, more acidic donor **6** led to the dialkylated derivative in lower yield (47%, 24 h) than that obtained by using **1** as the catalyst (80%, 8 h). Other phosphines were also shown to catalyze the reaction, while triphenylarsine was ineffective. For the reaction between **2** and **14**, tributylphosphine[9] or tricyclohexylphosphine in acetonitrile were shown to be efficient catalysts leading to the formation of **24a** in very good yields (Table 3, entries 6 and 7). A substantially slower reaction was observed in THF (compare entries 7 and 8). Although the additions of **5** and **6** to **14** could be catalyzed by triphenylphosphine, the phosphine-catalyzed Michael addition is less general than the process catalyzed by ruthenium complex **1**. Thus, the reaction with diketone **9** as the donor was very slow even in the presence of the more nucleophilic tributylphosphine. Acceptors **16**, **17**, **20**, and **21** failed to react with alkylated malonates **3** or **5** in the presence of phosphine as the catalyst under the usual reaction conditions[68] and acrolein (**15**) was polymerized under the reaction conditions. The phosphine-catalyzed reaction is not a simple base-catalyzed process,[9,69] since neither NEt_3 nor *i*-Pr_2NEt led to significant (>5%) transformations under the usual reaction conditions. These results are in agreement with previous observations.[9,70]

Table 3. Phosphine-Catalyzed Michael Reactions with 3-Buten-2-one (**14**)[a]

donor	equiv of **14**	catalyst	solvent	reaction time (h)	product	yield (%)
2	2	PPh_3	MeCN	2[c]	22	21
2	2	PPh_3	MeCN	4[c]	22	39
2	2	PPh_3	MeCN	48	22	20
					24a	6
2	1	PPh_3 + HOAc[d]	MeCN	26	e	
2	1	HOAc[f]	MeCN	26	e	
2	2	PBu_3	MeCN	0.1	24a	95
2	2	PCy_3	MeCN	0.1	24a	82
2	2	PCy_3	THF	1	22	26
2	2	dppf	MeCN	8	22	84
2	2	$AsPh_3$[g]	MeCN	24	e	
4	1	PPh_3[f]	MeCN	24	30	4
4	1	HOAc[f]	MeCN	26	e	
5	1	PPh_3	MeCN	12	31	95
6	2	PPh_3	MeCN	24	33	47
9	1	PBu_3[h]	MeCN	48	38	6
9	1	PCy_3[i]	MeCN	48	38	24
9	1	PCy_3[i]	THF	48	38	55

[a] Unless otherwise stated reactions were performed in the presence of 3 mol % phosphine or arsine at 25 °C. [b] dppf = 1,1′-bis(diphenylphosphino)ferrocene. [c] Reaction temperature = 40 °C. [d] 16 mol % each was added. [e] No reaction was observed. [f] 16 mol % of additive (triphenylphosphine or HOAc was used). [g] An identical result was obtained with 12 mol % triphenylarsine. [h] 10 mol % of phosphine was used. [i] 20 mol % of phosphine was used.

Figures 1 and 2 summarize the results obtained in the reactions of donors **2** and **4** with 1 equiv of acceptor **14** catalyzed by ruthenium dihydride **1** or triphenylphosphine (acetonitrile-d_3, 25 °C). Data for reactions carried out with rhodium complex **62**[40] as the catalyst are also included. The reactions catalyzed by 3 mol % of **1** were very rapid, giving rise to quantitative conversions into **22** and **30**. Considerably slower reactions were observed with **62** as the catalyst, which apparently suffered decomposition after 1−2 h. Similar experiments (not shown) with arsine complex **51** showed considerable induction periods (1−2 h), indicating that the slow formation of an active species derived from **51** was necessary in this case. On the other hand, the reactions catalyzed by triphenylphosphine (10 mol %) were slow, leading to less than 10% conversions into the Michael adducts after 3 h.

Triphenylphosphine was also a poor catalyst in the reaction of malonate **2** with methyl acrylate (**17**). Thus, reaction between **2** and **17** (3 equiv) in the presence of 3 mol % of triphenylphosphine proceeded in acetonitrile at 23 °C to give triester **72** (17%)

(64) Formation of the Michael adduct between methanol and acrylonitrile in a cobalt carbonyl-catalyzed hydrocarbonylation reaction has also been explained as a phosphine-catalyzed process: Dubois, R. A.; Garrou, P. E. *J. Organomet. Chem.* **1984**, *241*, 69.

(65) The zwitterionic intermediate has been trapped with several electrophiles: (a) Ohmori, H.; Takanami, T.; Shimada, H.; Masui, M. *Chem. Pharm. Bull.* **1987**, *35*, 2558. (b) Cristau, H. J.; Torreilles, E.; Barois-Gacherieu, C. *Synth. Commun.* **1988**, *18*, 185. (c) Viala, J.; Santelli, M. *Synthesis* **1988**, 370.

(66) Nucleophilic phosphines catalyze the addition of electrophilic alkenes to aldehydes (Baylis−Hillman reaction). For lead references, see: (a) Roth, F.; Gygax, P.; Fráter, G. *Tetrahedron Lett.* **1992**, *33*, 1045. (b) Amri, H.; Rambaud, M.; Villieras, J. *Tetrahedron Lett.* **1989**, *30*, 7381. (c) Miyakoshi, T.; Saito, S. *Nippon Kagaku Kaishi* **1983**, 1623; *Chem. Abstr.* **1984**, *100*, 156191g. (d) For a rhodium(I)- or ruthenium(II)-catalyzed process, see: Sato, S.; Matsuda, I.; Shibata, M. J. *J. Organomet. Chem.* **1989**, *377*, 347.

(67) Alternatively, **71** may react with the acceptor to furnish oligomers: (a) Horner, L.; Jugeleit, W.; Klupfel, K. *Liebigs Ann. Chem.* **1955**, *591*, 108. (b) Kukhtin, V. A.; Kamai, G.; Sinchenko, L. A. *Dokl. Akad. Nauk. S.S.S.R.* **1958**, *118*, 505; *Chem. Abstr.* **1958**, *52*, 10956.

(68) However, it has been reported that less substituted dimethyl malonate (**2**) and methyl acrylate gave a mixture of mono- (16%) and bisadduct (66%) with tributylphosphine as the catalyst.[9]

(69) For the pK_a of common phosphines, see: Rahman, M. M.; Liu, H.-Y.; Eriks, K.; Prock, A.; Giering, W. P. *Organometallics* **1989**, *8*, 1 and references cited therein.

(70) For a recent example that stresses the different catalytic abilities of phosphines and amines, see: Vedejs, E.; Diver, S. T. *J. Am. Chem. Soc.* **1993**, *115*, 3358.

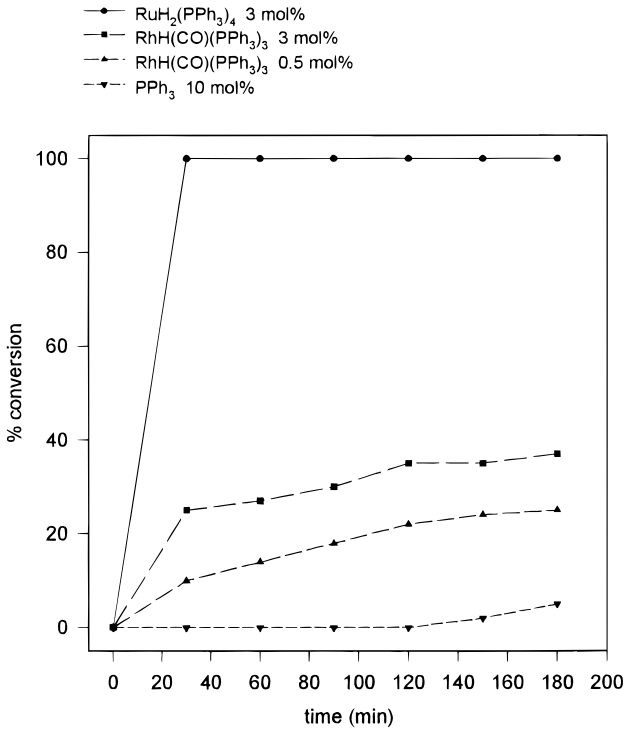


Figure 1. Reaction profile for the Michael reaction between donor **2** and acceptor **14** to give **22** (Table 1, entry 1) in acetonitrile-d_3 at 25 °C.

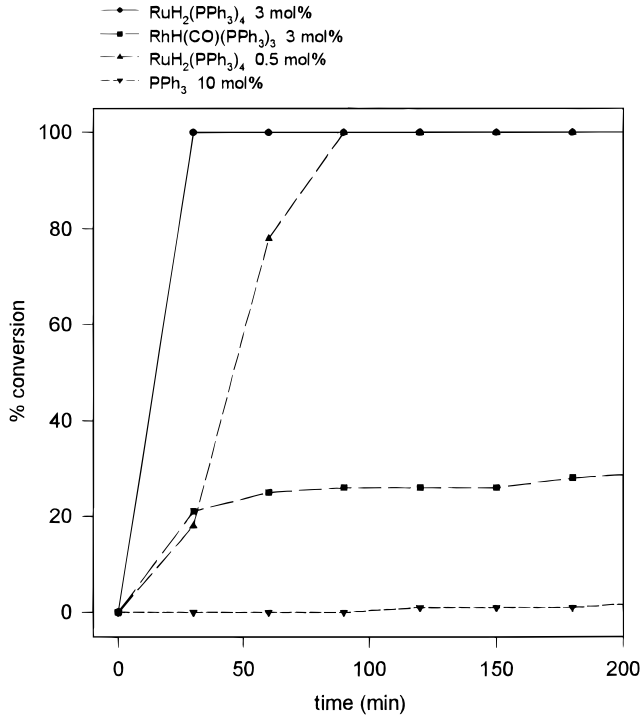
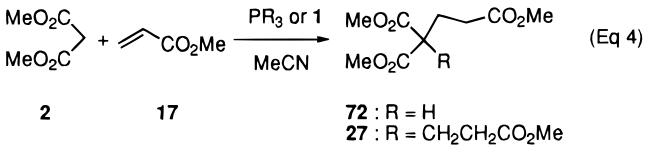


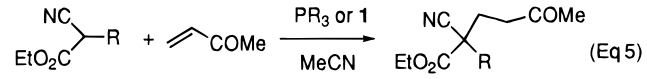
Figure 2. Reaction profile for the Michael reaction between donor **4** and acceptor **14** to give **30** (Table 1, entry 9) in acetonitrile-d_3 at 25 °C.

and tetraester **27** (13%) after 24 h (eq 4). In contrast, the reaction catalyzed by **1** led to **27** in almost quantitative yield under otherwise identical conditions (Table 1, entry 6).



2 **17** **72** : R = H; **27** : R = $CH_2CH_2CO_2Me$

In contrast with the above results obtained using malonates as the donors, the reaction of ethyl cyanoacetate (**73**) with acceptor **14** proceeded very rapidly in the presence of triphenylphosphine as the catalyst (3 mol %) to yield the double Michael adduct **74**[3] in quantitative yield (acetonitrile, 23 °C, 8 min) (eq 5). The reaction catalyzed by triphenylphosphine was

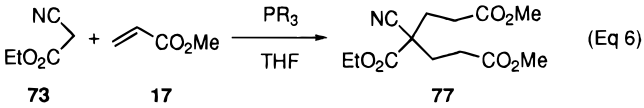


73 : R = H **14** **74** : R = CH_2CH_2COMe
75 : R = $CH_2CH{=}CMe_2$ **76** : R = $CH_2CH{=}CMe_2$

slower in THF, while ruthenium hydride **1** (3%) promotes the almost instantaneous conversion into the Michael adduct **74** (*ca.* 1 min in acetonitrile). Similarly, prenylated cyanoacetate **75**[71] gave **76** under the conditions developed by Murahashi (3 mol % **1**, THF, 25 °C, 6 h)[3] in 84% yield, while the same reaction catalyzed by 3 mol % of tricyclohexylphosphine (acetonitrile, 25 °C, 18 h) provided **76** in 91% yield. The reaction of **73** with methyl acrylate (**17**) in the presence of **1 (**THF, 25 °C, 24 h) has been reported by Murahashi to give the double adduct **77** in 95% yield.[3] We have obtained **77** in a similar yield (90%) when the reaction was catalyzed by 6 mol % of triphenylphosphine under otherwise identical conditions. By using **1** in acetonitrile, **77** was obtained in quantitative yield (24 h, 23 °C).

(71) Cuvigny, T.; Julia, M.; Rolando, C. *J. Organomet. Chem.* **1985**, *285*, 395.

Parallel experiments (acetonitrile, 23 °C) demonstrated that the reaction between **73** and **17** catalyzed by 3 mol % of **1** was much faster (>10:1) than that carried out with 6 mol % of triphenylphosphine.



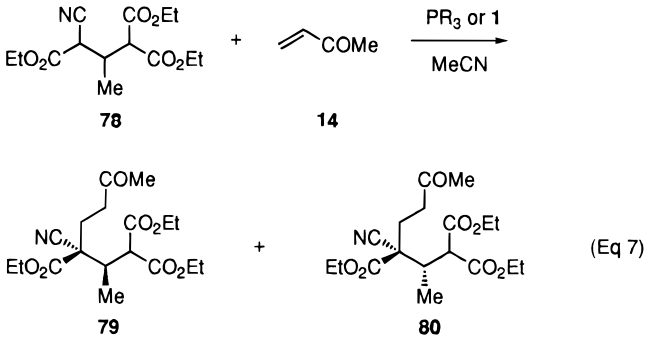
73 **17** **77**

Cyanoacetates are three orders of magnitude more acidic than malonates in DMSO solution.[72,73] Since a similar difference is also expected in nonprotic polar solvents such as THF and acetonitrile, the different reactivity observed between malonates and cyanoacetates can be simply explained by the easier deprotonation of the more acidic substrates. In fact, the selective reaction of cyanoacetates was also observed in the phosphine catalyzed reaction. A competitive experiment carried out with 1 equiv each of malonate **2**, cyanoacetate **73**, and acceptor **14** with triphenylphosphine as the catalyst (acetonitrile, 23 °C) gave exclusively adduct **77**. Cyano triester **78** has been shown by Murahashi to react regio- and stereoselectively with **14** in the presence of **1** (THF, −78 °C) to give a 97:3 mixture of **79** and **80** (73%) (eq 7).[3] A mechanistic rationale has been offered for this selectivity based on the coordination of both the nitrile and the ester carbonyl group to Ru(II).[3b] In our hands, the same regioselectivity was obtained with triphenylphosphine as the catalyst (6 mol %, THF, 2 equiv of **14**), with only slightly lower stereoselectivity (95:5; 67% yield) at the temperature required for the Michael addition (23 °C).[74] Therefore the selectivity found by Murahashi for the enolates derived from substrates

(72) (a) The pK_a of ethyl cyanoacetate (**56**) in DMSO (25 °C) is 13.1: Bordwell, F. G.; Branca, J. C.; Bares, J. E.; Filler, R. *J. Org. Chem.* **1988**, *53*, 780. (b) The pK_a of diethyl malonate in DMSO (25 °C) is 16.4.[22]

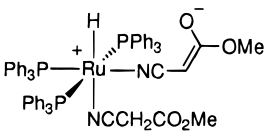
(73) (a) Reference 1d, p 210. (b) Cope, A. C.; Holmes, H. L.; House, H. O. *Org. React.* **1957**, *9*, 107.

(74) In our hands, the Michael addition of **78** to **14** was too slow at −78 °C leading to irreproducible yields of **79** and **80**. Control experiments demonstrated that these additions took place during the workup at room temperature.



like **78** is not exceptional since it is also reproduced by using triphenylphosphine as the catalyst. The regioselectivity observed with the phosphine catalyst is identical to that obtained with **1** as the catalyst,[3] and follows that expected from the relative acidities of cyanoacetates and malonates in organic solvents. A similar selectivity (95:5 mixture of **79**/**80**) was observed with **1** in acetonitrile.[75]

The reaction of methyl cyanoacetate with **1** or [Ru(C_2H_4)(PPh_3)$_4$] has been shown to give complex **81**, in which the cyanoester enolate coordinates with the ruthenium center through the nitrile group.[3b,8,4b] Complex **81** acts also as a catalyst for



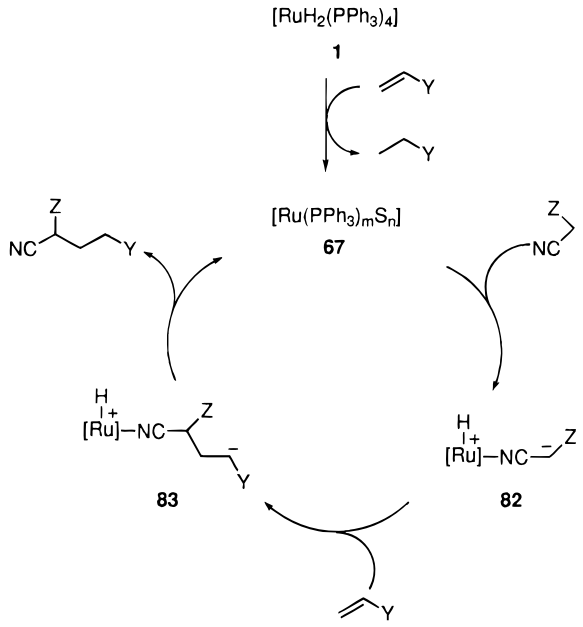
81

the Murahashi reactions and undergoes stoichiometric Knoevenagel and Michael reactions with aldehydes and acrylonitrile, respectively.[3b,8] Based on these experiments, a mechanistic rationale has been proposed by Komiya and Murahashi for the chemoselective ruthenium-catalyzed reaction of activated nitriles which involves the activation of a C−H bond of the substrate by an in situ formed ruthenium(0) complex (**67**) to give the key intermediate **82**[76] followed by a conjugate addition to give **83**, which would give rise to the observed Michael adduct by an unusual reductive elimination (Scheme 5).[3b]

In our case, a similar activation of the Michael donor should lead to the corresponding ruthenium(II) enolates.[77] However, no reaction was observed between complex **1** and malonate **2** at 23 °C ($CDCl_3$ or benzene-d_6 solutions). Addition of acceptor **14** to these solutions led to the formation of Michael adduct **22** with the simultaneous disappearance of the hydride resonance corresponding to **1**. Small amounts of aldol **24a** were also observed under these conditions. We have not been able to detect any high-field hydride resonance under these stoichiometric conditions.[78]

On the other hand, only complexes which can easily lose a phosphine ligand are satisfactory catalysts for the reaction (Table 3). In fact, the reactions catalyzed by **1** appear to require the presence of free triphenylphosphine. This was demonstrated

Scheme 5



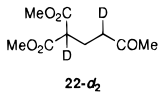
by using as an additive [Pd(COD)Cl_2] (**84**),[79] a complex which traps irreversibly triphenylphosphine leading to the formation of [Pd(PPh_3)$_2Cl_2$] (**85**).[80] Thus, the addition of a catalytic amount of **84** (1 equiv per Ru complex) almost completely inhibited the Michael additions. Reaction between **2** and **14** with **1** as the catalyst in acetonitrile in the presence of 1 equiv of **84** gave only a 21% yield of monoalkylated **22** (compare Table 1, entry 1). Addition of a second equivalent of **84** completely suppressed the Michael process. Similar results were obtained by using the Pd(0) complex [Pd_2(dba)$_3$·dba] (**86**)[81] as the trapping reagent for the released triphenylphosphine.[82] Control experiments demonstrated that neither **85** nor 1,5-cyclooctadiene[83] interfered with the Michael additions.[84] Similarly, no reaction was observed between cyanoacetate **73** and 2 equiv of **17** or **19** as the acceptors when the reactions were carried out with **1** as the catalyst (6 mol %) and **84** (12 mol %) in THF at 23 °C. The same inhibition was again observed with **86**. It is important to note that the Knoevenagel reaction of cyano nucleophiles catalyzed by **1** described also by Murahashi[3]

(75) Because of the higher reactivity of malonates with **1** in acetonitrile, the reaction was carried out with 1 equiv of **14** for 2 h at 23 °C (36% yield, 72% based on recovered starting material).

(76) For ruthenium(II) *C*-enolates derived from nitriles, see: (a) Ittel, S. D.; Tolman, C. A.; English, A. D.; Jesson, J. P. *J. Am. Chem. Soc.* **1978**, *100*, 7577. (b) Hiraki, K.; Ochi, N.; Kitamura, T.; Sasada, Y.; Shinoda, S. *Bull. Chem. Soc. Jpn.* **1982**, *55*, 2356.

(77) (a) Formation of a rhodium(I) malonate complex, in which the malonate anion was not bound to the metal center, has been recently reported: Grushin, V. V.; Kuznetsov, V. F.; Bensimon, C.; Alper, H. *Organometallics* **1995**, *14*, 3927. (b) For the formation of a cationic platinum(II) complex with disulfone anion by oxidative addition of a 1,1-disulfone to [Pt(C_2H_4)(PPh_3)$_2$], see: Siedle, A. R.; Newmark, R. A.; Gleason, W. B. *J. Am. Chem. Soc.* **1986**, *108*, 767.

(78) The addition of dideuterated malonate (**2**-d_2) to **14** in the presence of ruthenium dihydride **1** afforded adduct **22**-d_2. This deuteration pattern is consistent with either a ruthenium (Scheme 5) or phosphine (Scheme 2) catalyzed reaction.



22-d_2

(79) Chatt, J.; Vallarino, L. M.; Venanzi, L. M. *J. Chem. Soc.* **1957**, 3413.

(80) Palladium complex **84** behaves as a phosphine sponge toward phosphine-coordinated palladium(II) complexes: (a) Mateo, C.; Cárdenas, D. J.; Fernández-Rivas, C.; Echavarren, A. M. *Chem. Eur. J.* In press. (b) For a similar observation, see: Gretz, E.; Sen, A. *J. Am. Chem. Soc.* **1986**, *108*, 6038.

(81) (a) Takahashi, Y.; Ito, T.; Sakai, S.; Ishii, Y. *J. Chem. Soc., Chem. Commun.* **1970**, 1065. (b) Ukai, T.; Kawazura, H.; Ishii, Y.; Bonnet, J. J.; Ibers, J. A. *J. Organomet. Chem.* **1974**, *65*, 253.

(82) For the reaction between **86** and triphenylphosphine, see: Amatore, C.; Jutand, A.; Khalil, F.; M'Barki, M. A.; Mottier, L. *Organometallics* **1993**, *12*, 3168.

(83) 1,5-Cyclooctadiene did not interfere with the reaction between **73** and **17** in THF catalyzed by **1** (3 mol %, 23 °C) to give **77** (eq 6).[30c] Similarly, palladium complex 85 did not interfere in this Michael reaction catalyzed by 1 (6 mol %, 23 °C).

(84) Complex **1** is stable for several minutes in the presence of **84** at 23 °C in benzene-d_6. After ca. 30 min no hydride resonance was observed by ^{1}H NMR.

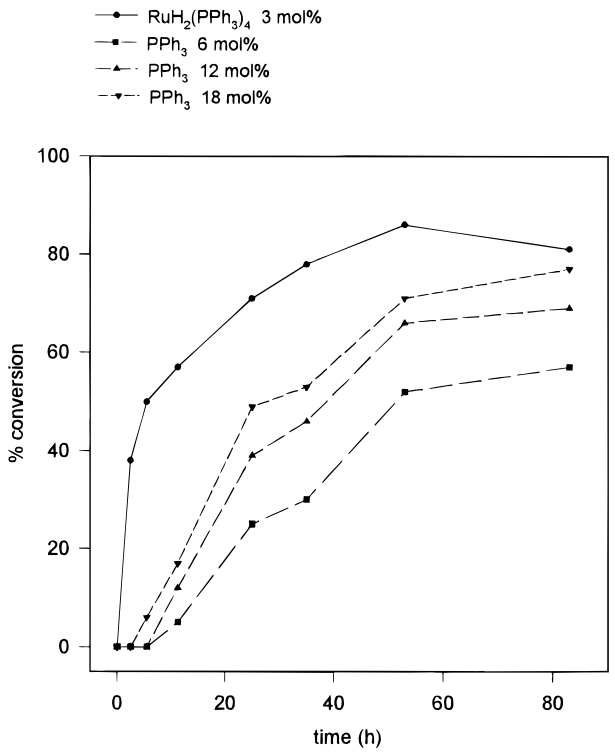


Figure 3. Reaction profile for the Michael reaction between donor **12** and acceptor **87** to give **88** (eq 8) in acetonitrile-d_3 at 25 °C.

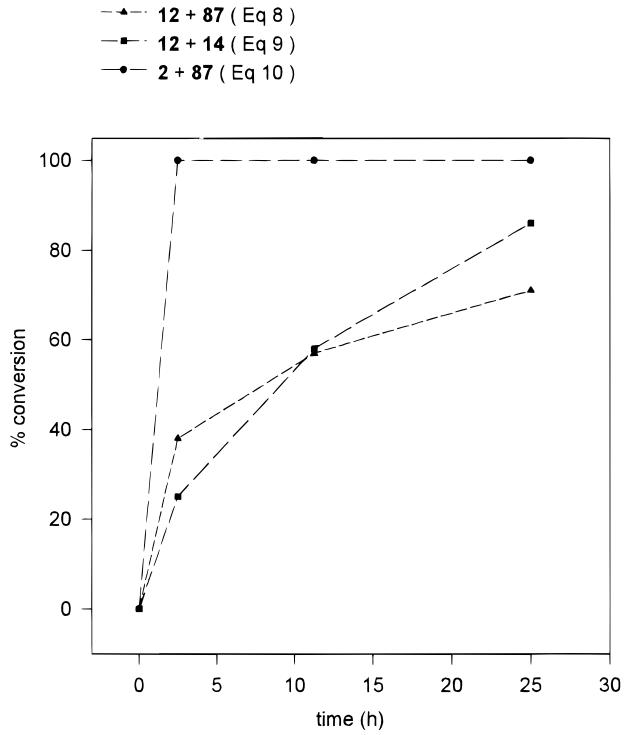
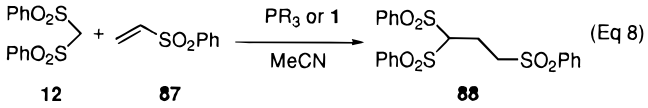


Figure 4. Reaction profile for the Michael reactions of donors **2** and **12** with acceptors **14** and **87** (eqs 8−10) catalyzed by **1** in acetonitrile-d_3 at 25 °C.

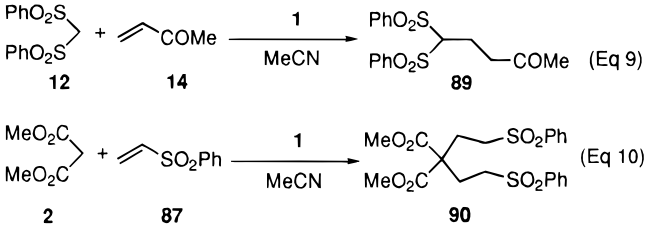
is not inhibited in the presence of **84**,[85] which demonstrates that the catalytically active ruthenium species in this reaction is stable in the presence of this palladium complex.

Therefore, the puzzling obtainment of the same products in the processes catalyzed by **1** or triphenylphosphine and the observation of considerable rate differences in both processes can be reconciled if the Michael reaction is catalyzed by both the triphenylphosphine released from **1** and a ruthenium species derived from **1**. Particularly enlightening was the observation of identical regio- and stereoselectivities in the addition of **78** to **14** catalyzed by **1** or triphenylphosphine (eq 7).

The ruthenium catalyst in the Michael addition may be acting as a highly efficient Lewis acid[86,87] complexing the carbonyl or the cyano group of the acceptor and thus favoring the conjugate addition of intermediates like **70** (Scheme 4). In order to ascertain this point, we carried out the Michael addition with a sulfone as the acceptor, since the sulfonyl functional group does not coordinate tightly to Lewis acids.[88] If the ruthenium catalytic species acts only as a Lewis acid, similar rates are expected in the Michael addition reactions catalyzed by **1** or triphenylphosphine. On the other hand, a faster reaction is expected with 1,1-disulfones because of their relatively high acidity (the pK_a of **12** is 12.25 in DMSO[22]). However, this Michael reaction was considerably slower than that of malonates **2** or **4** (see Figures 1 and 2). Thus, the Michael addition of disulfone **12** to phenyl vinyl sulfone (**87**) was performed with **1** (3 mol %) as the catalyst in acetonitrile at 23°C to furnish adduct **88** in 87% yield after 85 h (eq 8 and Figure 3). The reactions between **12** and **87** with 3−18 mol % of phosphine as the catalyst were slower than that catalyzed by **1** (Figure 3), although the differences were not as marked as with the malonates.



The relatively slow reaction of donor **12** with acceptor **87** appears to be in accord with the proposed role of ruthenium catalyst acting as a Lewis acid. However, the reaction between **12** and α,β-unsaturated acceptor **14** to give adduct **89**[89] proceeded with a similar rate (eq 9 and Figure 4). Additionally the reaction of malonate **2** with vinyl sulfone **87** proceeded very rapidly under the usual conditions affording bisadduct **90** in 97% yield after 1 h (eq 10 and Figure 4).



Although **2** reacts faster than **12** with Michael acceptor **14**, an in situ competition between **2** and **12** with acceptor **14** (1 equiv each; 3 mol % of **1**, acetonitrile, 23 °C) led to the selective formation of Michael adduct **89** (ca. 4.3:1 mixture of **89** and **22** after 43 h). This apparent contradiction could be explained if the more acidic donor **12** interferes with the catalytic ruthenium species derived from malonate **2** leading to the

(85) The reaction of ethyl cyanoacetate (**73**) with benzaldehyde (1 equiv each) with **1** (3 mol %) and **84** (6 mol %) in THF at 23 °C for 24 h afforded ethyl (*E*)-2-cyano-3-phenyl-2-propenoate[3] (75% yield).

(86) For lead references of Michael additions of 1,3-dicarbonyl catalyzed by Lewis acids, see: (a) Bonadies, F.; Lattanzi, A.; Orelli, L. R.; Scettri, A. *Tetrahedron Lett.* **1993**, *34*, 7649. (b) Keller, E.; Feringa, B. L. *Tetrahedron Lett.* **1996**, *37*, 1879.

(87) No Michael reactions were observed by using $RuCl_3$ and triphenylphosphine (≥4 equiv per Ru) as the promoting agents.

(88) (a) For example, the dienophilic reactivity of phenyl vinyl sulfone (**87**) is not enhanced by the addition of Lewis acids: Carr, R. V. C.; Paquette, L. A. *J. Am. Chem. Soc.* **1980**, *102*, 853. (b) For a review of sulfone chemistry, see: Simpkins, N. S. *Sulfones in Organic Synthesis*; Pergamon: Oxford, 1993.

(89) de Lucchi, O.; Pasquato, L.; Modena, G. *Tetrahedron Lett.* **1984**, *25*, 3647.

selective formation of the anion of **12**. Indeed, **2**-d_2 suffered deuterium scrambling with **12** (1 equiv) in acetonitrile-d_3 at 23 °C in the presence of ruthenium dihydride **1** (10 mol %) and **14**. In the absence of **1** and/or **14**, the deuterium label scramble between **2**-d_2 and **12** was slower under these conditions.

Conclusions

The above results indicate that the Michael reaction of the examined donors is catalyzed by ruthenium complex **1**. Although triphenylphosphine is also a catalyst for some of the reactions examined, very significant rate differences were found in the reactions of donors **2** or **4** with acceptor **14** catalyzed by hydride **1** or triphenylphosphine. Slight, but significant, acceleration was also observed in the reaction between α,β-unsaturated carbonyl compound **14** and vinyl sulfone **87** catalyzed by **1** as compared with the same reaction in the presence of triphenylphosphine. The reaction only proceeds satisfactorily in the presence of free phosphine. Accordingly, the Michael reaction of stabilized enolates appears to be a ruthenium and phosphine catalyzed reaction. On the other hand, the observation of identical chemo-, regio-, and/or stereoselectivities in the reactions catalyzed by phosphines or ruthenium complexes suggests that similar pathways are followed in both processes.

The similar rates found for reaction of **12** with **14** or **87** and the rapid reaction between **2** and **87** indicates that the ruthenium catalyst does not behave as a simple Lewis acid that coordinates with the Michael acceptor. Although the available data do not allow us to unequivocally determine the precise role of the ruthenium complex, scientific economy principles (Occam's razor) suggest that a similar pathway is followed for the Michael addition of cyano and non-cyano substituted donors. The ruthenium catalyst may activate the Michael donor by coordination through the basic functional groups facilitating their deprotonation by zwitterionic **69**. Additionally, the ruthenium catalytic species may facilitate the Michael addition by coordinating with the alkene acceptor and the anion derived from the donor. This is supported by the ready reaction of substrates like **2**[90] toward a wide variety of donors and the relatively slow reactions of disulfone **14**, whose anion is not expected to coordinate tightly with an intermediate ruthenium(II) species.[88] Additionally, the interference of disulfone **12** with the Michael reaction between malonate **2** and acceptor **14** also points to the required activation of donor **2** by ruthenium. Another piece of evidence supporting the activation of the donors bearing carbonyl groups by ruthenium is the formation of intramolecular aldol products in some of the reactions examined. The effect of acetonitrile on the acidity of the Michael donors appears to be, at most, secondary, since acetonitrile is actually expected to decrease the relative acidity of carbon acids in comparison with THF.[22]

In summary, we have uncovered that the ruthenium-catalyzed Michael addition is a more general process than originally described.[3] The reaction proceeds well in acetonitrile under mild and neutral conditions with malonates, β-ketoesters, 1,3-diketones, 1,1-disulfones, nitro compounds, Meldrum acid, and anthrone as the Michael donors. In a number of cases, intramolecular aldol reactions catalyzed by **1** were also observed as side reactions. Cyano acetates, more acidic than malonates in organic solvents, are excellent substrates for this reaction. Although some of the reactions that we have studied can also be catalyzed by nucleophilic tertiary phosphines, the use of readily prepared ruthenium dihydride **1** as the catalyst in acetonitrile provided the best general solution from a practical point of view for the Michael addition of activated nucleophiles.

(90) Coordination of ruthenium(II) with carbonyl groups has been frequently observed.[49a]

Experimental Section

NMR spectra were recorded on a Bruker AC-200 (200 MHz for ^{1}H and 50 MHz for ^{13}C NMR) or a Bruker AMX-300 (300 MHz for ^{1}H, 75 MHz for ^{13}C NMR, and 121.5 MHz for ^{31}P). Mass spectra (electron impact ionization, 70 eV) were obtained on a VG AutoSpec apparatus. Only the most significant molecular ions and/or base peaks in the MS are given. IR spectra were recorded on a Pye-Unicam SP 3−300-S apparatus. Microanalysis were recorded at the SIdI (UAM) with a Perkin Elmer 2400 apparatus. Chromatography was performed with flash grade silica gel. All reactions were carried out under an atmosphere of Ar. Dry THF was obtained by distillation under Ar from sodium−benzophenone ketyl. Dry acetonitrile was obtained by distillation from CaH_2 and was stored over activated 4 Å molecular sieves under Ar.

The following known compounds showed NMR identical with the reported data: **13**,[19] **22**,[13] **25**,[14] **26**,[14] **27**,[9] **28**,[15] **29**,[16] **38**,[91] **40**,[92] **44**,[17] **45**,[2c] **72**,[9] **74**,[3] **75**,[71] **77**,[3] **78**,[3] **79**,[3] **80**,[3] and **89**.[90b] Methyl vinyl ketone (**14**), acroleine (**15**), and methyl acrylate (**17**) were purified by distillation. All other commercial compounds were used without further purification. The following complexes were prepared according to known procedures: **52**,[30] **53**,[31] **54**,[32] **55**,[34] **56**,[36] **57**,[36] **58**,[37] **59**,[38] **60**,[39] **62**,[4b] **84**,[81] **85**,[93] and **86**.[81] Complex **61** was commercially available. $NaB(OMe)_4$ was prepared as a white solid by heating $NaBH_4$ with a large amount of methanol.[25]

Preparation of [$RuH_2(PPh_3)_4$] (1). This complex was prepared according to the described procedures from $RuCl_3 \cdot 3H_2O$[23] or [$Ru(PPh_3)_3Cl_2$] (**60**)[24] and PPh_3 using $NaBH_4$ as the reductant (90−97% yields). This complex could be further purified by washing with a large amount of degasified water at room temperature under Ar to furnish **1** as a yellow powder. **1**: ^{1}H NMR (300 MHz, benzene-d_6) δ 7.40−6.74 (m, 60H), −10.14 (m, 2H); ^{31}P{^{1}H} NMR (121.5 MHz, benzene-d_6) δ 49.80 (t, J = 13.9 Hz, 2P), 41.65 (t, J = 13.9 Hz, 2P). In some of the preparations a high-field signal corresponding to tetrahydride **58** was also observed at δ −7.10 (br s). In benzene-d_6 solution (23 °C) dihydride **1** slowly leads to coordinatively unsaturated complex **63**: ^{1}H NMR (200 MHz, benzene-d_6) δ −17.52 (q, J = 25.9 Hz, 2H).

Preparation of [$RuH_2(AsPh_3)_4$] (51). This complex was prepared by following a procedure analogous to that used in the synthesis of **1**: To a solution of $AsPh_3$ (1.868 g, 6.1 mmol) in ethanol (40 mL) under reflux was added a hot solution of $RuCl_3.3H_2O$ (271 mg, 1.2 mmol) in ethanol (7 mL). The resulting mixture was heated under refluxing conditions for 10 min and a hot suspension of $NaBH_4$ (200 mg, 5.1 mmol) in ethanol (7 mL) was added in 2−3 portions. After being heated under reflux conditions for 10 min, the mixture was cooled to room temperature. The resulting solid was filtered off and washed with ethanol to give **51** as a reddish solid (1.275 g, 80%): ^{1}H NMR (200 MHz, $CDCl_3$) δ 7.80−6.55 (m, 60H), −12.45 (s, 2H).[29]

Preparation of [$RuH_2(MeCN)(PPh_3)_3$] (64). This complex was prepared from **1** in benzene-d_6 solution in an NMR tube with excess MeCN:[37a] ^{1}H NMR (300 MHz, benzene-d_6) δ 7.78−6.83 (m, 45H), 0.59 (s, 3H), −8.90 (dtd, J = 76.3, 31.2, 7.1 Hz, 1H), −14.99 (tdd, J = 28.5, 13.7, 7.0 Hz, 1H); ^{31}P{^{1}H} NMR (121.5 MHz, benzene-d_6) δ 61.72 (d, J = 16.7 Hz, 2P), 49.38 (t, J = 16.7 Hz, 1P).

Ruthenium-Catalyzed Michael Addition: General Procedure. To a mixture of Michael donor (1.0 mmol) and ruthenium dihydride **1** (35 mg, 0.03 mmol, 3 mol %) in MeCN (3 mL) at 23 °C was added the Michael acceptor (1 or 2 equiv, see Table 1).[11] The resulting solution was stirred at 23 °C (see Table 1 for reaction times). The solvent was evaporated and the residue was chromatographed (hexane−EtOAc mixtures) to give the adducts in the stated yields.

Dimethyl 2,2-Bis(3-oxobutyl)malonate (23). White solid: mp 76−77 °C; ^{1}H NMR (200 MHz, $CDCl_3$) δ 3.71 (s, 6H), 2.46 (t, J = 7.1 Hz, 4H), 2.13 (s, 6H), 2.12 (t, J = 7.1 Hz, 4H); ^{13}C{^{1}H} NMR (50

(91) Kagechika, K.; Shibasaki, M. *J. Org. Chem.* **1991**, *56*, 4093.
(92) (a) Bergbreiter, D. E.; Lalonde, J. J. *J. Org. Chem.* **1987**, *52*, 1601. (b) Sasson, Y.; Arrd, O. *J. Org. Chem.* **1989**, *54*, 4993. (c) Ballini, R.; Petrini, M. *Tetrahedron Lett.* **1989**, *30*, 5329. (d) Turner, M. J.; Luckenbach, L. A.; Turner, E.-L. *Synth. Commun.* **1986**, *16*, 1377.
(93) Heck, R. F. *Palladium Reagents in Organic Synthesis*; Academic: Orlando, FL, 1985; p 18.

MHz, $CDCl_3$) δ 206.7, 171.2, 55.8, 52.2, 38.3, 29.7, 27.0. Anal. Calcd for $C_{13}H_{20}O_6$: C, 57.34; H, 7.40. Found: C, 57.34; H, 7.47.

Dimethyl 4-Hydroxy-4-methyl-3-(1-oxoethyl)cyclohexane-1,1-dicarboxylate (24a). (a) Colorless oil: ^{1}H NMR (300 MHz, $CDCl_3$) δ 3.80 (d, J = 2.3 Hz, OH), 3.71 (s, OMe), 3.63 (s, OMe), 2.66 (dd, J = 13.1, 3.4 Hz, H-3), 2.25 (ddd, J = 13.1, 3.4, 2.2 Hz, H-2eq), 2.17 (s, Me), 2.16 (td, J = 13.5, 4.0, H-6ax), 2.09−2.02 (m, H-6eq), 1.96 (t, J = 13.1 Hz, H-2ax), 1.60 (ddd, J = 14.3, 3.8, 3.1 Hz, H-5eq), 1.18 (td, J = 13.6, 4.2 Hz, H-5ax), 1.09 (s, Me) (the assignments were based on a COSY experiment); ^{13}C{^{1}H} NMR (50 MHz, $CDCl_3$; DEPT) δ 214.6 (C), 171.5 (C), 171.1 (C), 68.4 (C), 54.0 (C), 52.9 (CH_3), 52.7 (CH), 52.6 (CH_3), 35.2 (CH_2), 30.9 (CH_3), 29.3 (CH_2), 28.5 (CH_3), 25.8 (CH_2). Anal. Calcd for $C_{13}H_{20}O_6$: C, 57.34; H, 7.40. Found: C, 57.26; H, 7.40. **(b)** This compound could also be obtained from **23** (eq 3): A mixture of **22** (27 mg, 0.1 mmol) and **1** (5 mg, 0.005 mmol, 5 mol %) in MeCN (1 mL) was stirred at 23 °C for 16 h. The solvent was evaporated and the residue was filtered through flash grade silica gel (EtOAc) to give **24a** (22 mg, 81%). Its diastereomer **24b** was obtained as an inseparable mixture with diketone **23** in the addition reaction catalyzed by $NaB(OMe)_4$ and showed the following NMR data: ^{1}H NMR (200 MHz, $CDCl_3$) δ 3.75 (s, 3H), 3.68 (s, 3H), 2.84 (s, OH), 2.70 (dd, J = 13.1, 3.7 Hz, 1H), 2.50 (ddd, J = 11.8, 3.7, 2.6 Hz, 1H), 2.37−2.28 (m, 1H), 2.23 (s, 3H), 1.88 (t, J = 13.1 Hz, 1H), 1.51 (td, J = 13.5, 3.8 Hz, 1H), 1.18 (s, 3H); ^{13}C{^{1}H} NMR (50 MHz, $CDCl_3$) δ 211.31, 171.66, 170.76, 71.17, 55.34, 54.21, 52.64, 52.35, 41.51, 31.46, 29.78, 28.19, 21.43.

Dimethyl 2-(3-Oxobutyl)-2-(phenylmethyl)malonate (30). White solid: mp 72−73 °C; ^{1}H NMR (200 MHz, $CDCl_3$) δ 7.25−7.19 (m, 6H), 7.07−7.02 (m, 2H), 3.71 (s, 6H), 3.24 (s, 2H), 2.50 (t, J = 7.1 Hz, 2H), 2.12 (s, 3H), 2.07 (t, J = 7.1 Hz, 2H); ^{13}C{^{1}H} NMR (50 MHz, $CDCl_3$) δ 207.0, 171.3, 137.52, 129.8, 128.3, 127.1, 58.2, 52.3, 39.7, 38.8, 29.8, 26.5. Anal. Calcd for $C_{16}H_{20}O_5$: C, 65.73; H, 6.89. Found: C, 65.47; H, 7.00.

Dimethyl 2-(3-Oxobutyl)-2-(2-propynyl)malonate (31). Colorless oil: ^{1}H NMR (200 MHz, $CDCl_3$) δ 3.71 (s, 6H), 2.78 (d, J = 2.7 Hz, 2H), 2.49 (t, J = 7.4 Hz, 2H), 2.31 (t, J = 7.2 Hz, 2H), 2.13 (s, 3H), 2.07 (t, J = 2.7 Hz, 1H); ^{13}C{^{1}H} NMR (50 MHz, $CDCl_3$; DEPT) δ 206.6 (C), 170.0 (C), 78.1 (CH), 71.6 (C), 55.6 (C), 52.5 (CH_3), 38.1 (CH_2), 29.5 (CH_3), 26.0 (CH_2), 23.4 (CH_2). Anal. Calcd for $C_{12}H_{16}O_5$: C, 59.99; H, 6.71. Found: C, 59.55; H, 6.75.

Dimethyl 2-(2-Cyanoethyl)-2-(2-propynyl)malonate (32). Pale yellow oil: ^{1}H NMR (200 MHz, $CDCl_3$) δ 3.79 (s, 6H), 2.86 (d, J = 2.7 Hz, 2H), 2.47 (t, J = 5.2 Hz, 2H), 2.46 (t, J = 5.3 Hz, 2H), 2.09 (t, J = 2.7 Hz, 1H); ^{13}C{^{1}H} NMR (50 MHz, $CDCl_3$; DEPT) δ 169.3 (C), 118.7 (C), 77.48 (CH), 72.5 (C), 55.5 (C), 53.1 (CH_3), 28.4 (CH_2), 23.4 (CH_2), 12.8 (CH_2). Anal. Calcd for $C_{11}H_{13}NO_4$: C, 59.18; H, 5.87; N, 6.27. Found: C, 59.06; H, 5.90; N, 6.23.

5,5-Bis(3-oxobutyl)-2,2-dimethyl-1,3-dioxan-4,6-dione (33). White solid: mp 100−101 °C; ^{1}H NMR (200 MHz, $CDCl_3$) δ 2.55 (t, J = 7.7 Hz, 4H), 2.27 (t, J = 7.4 Hz, 4H), 2.14 (s, 6H), 1.84 (s, 6H); ^{13}C-{^{1}H} NMR (50 MHz, $CDCl_3$; DEPT) δ 205.9 (C), 168.9 (C), 105.5 (C), 50.7 (C), 37.8 (CH_2), 30.7 (CH_2), 29.6 (CH_3), 28.9 (CH_3). Anal. Calcd for $C_{14}H_{20}O_6$: C, 59.14; H, 7.09. Found: C, 59.10; H, 6.92.

Methyl 1,3-Bis(1-oxoethyl)-4-hydroxy-4-methylcyclohexanecarboxylate (34). Colorless oil. Major diastereomer: ^{1}H NMR (200 MHz, $CDCl_3$) δ 3.91 (d, J = 2.4 Hz, 1H, OH), 3.80 (s, 3H), 2.69 (dd, J = 12.7, 3.3 Hz, 1H), 2.27 (s, 3H), 2.40−2.10 (m, 3H), 2.19 (s, 3H), 1.90 (m, 1H), 1.71 (m, 1H), 1.40−1.20 (m, 1H), 1.18 (s, 3H); ^{13}C{^{1}H} NMR (50 MHz, $CDCl_3$; DEPT) δ 206.2 (C), 204.9 (C), 172.8 (C), 68.4 (C), 60.8 (C), 53.0 (CH_3), 52.3 (CH), 35.5 (CH_2), 31.0 (CH_3), 28.4 (CH_3), 28.2 (CH_2), 26.0 (CH_3), 25.4 (CH_2). Minor diastereomer: ^{1}H NMR (200 MHz, $CDCl_3$) δ 3.96 (d, J = 2.3 Hz, 1H, OH), 3.72 (s, 3H), 2.75 (dd, J = 12.8, 3.5 Hz, 1H), 2.28 (s, 3H), 2.40−2.10 (m, 3H), 2.22 (s, 3H), 1.90 (m, 1H), 1.71 (m, 1H), 1.40−1.20 (m, 1H), 1.15 (s, 3H); ^{13}C{^{1}H} NMR (50 MHz, $CDCl_3$; DEPT) δ 206.1 (C), 204.4 (C), 172.1 (C), 68.41 (C), 59.1 (C), 52.6 (CH_3), 52.5 (CH), 34.9 (CH_2), 31.0 (CH_3), 28.4 (CH_3), 28.2 (CH_2), 25.5 (CH_3), 25.4 (CH_2). Anal. Calcd for $C_{13}H_{20}O_5$: C, 60.92; H, 7.86. Found: C, 60.86; H, 7.94.

Methyl 5-Oxo-2-(3-oxobutyl)-2-(1-oxoethyl)hexanoate (35). White solid: mp 77−78 °C; ^{1}H NMR (200 MHz, $CDCl_3$) δ 3.74 (s, 3H), 2.45−2.30 (m, 4H), 2.17 (s, 3H), 2.14 (s, 6H), 2.20−2.00 (m, 4H); ^{13}C{^{1}H} NMR (50 MHz, $CDCl_3$; DEPT) δ 206.9 (C), 204.72 (C), 172.1 (C), 61.3 (C), 52.3 (CH_3), 37.8 (CH_2), 29.7 (CH_3), 26.6 (CH_3), 25.2 (CH_2). Anal. Calcd for $C_{13}H_{20}O_6$: C, 60.92; H, 7.86. Found: C, 60.92; H, 7.85.

5,5-Bis(1-oxoethyl)-2,8-nonadione (36). White solid: mp 57−58 °C; ^{1}H NMR (200 MHz, $CDCl_3$) δ 2.27 (t, J = 7.0 Hz, 4 H), 2.12 (s, 12 H), 2.09 (t, J = 7.0 Hz, 4 H); ^{13}C{^{1}H} NMR (50 MHz, $CDCl_3$) δ 207.0, 206.8, 68.2, 37.8, 30.0, 27.0, 24.7. Anal. Calcd for $C_{13}H_{20}O_4$: C, 64.98; H, 8.39. Found: C, 64.81; H, 8.43.

1-[1,3-Bis(1-oxoethyl)-4-hydroxy-4-methylcyclohexyl]ethanone (37). White solid: mp 80−81 °C; ^{1}H NMR (200 MHz, $CDCl_3$) δ 3.91 (d, J = 2.3 Hz, 1H, OH), 2.64 (dd, J = 13.0, 3.4 Hz, 1H), 2.38 (dd, J = 13.2, 3.6 Hz, 1H), 2.30 (s, 3H), 2.30−2.15 (m, 2H), 2.16 (s, 3H), 2.14 (s, 3H), 1.82 (t, J = 12.4 Hz, 1H), 1.72 (dt, J = 14.4, 3.4 Hz, 1H), 1.15 (s, 3H), 1.20−1.10 (m, 1H); ^{13}C{^{1}H} NMR (50 MHz, $CDCl_3$; DEPT) δ 206.5 (C), 68.4 (C), 67.2 (C), 52.5 (CH), 35.0 (CH_2), 31.0 (CH_3), 28.4 (CH_3), 27.8 (CH_2), 26.3 (CH_3), 25.7 (CH_3), 24.7 (CH_2). Anal. Calcd for $C_{13}H_{20}O_4$: C, 64.98; H, 8.39. Found: C, 65.81; H, 8.48.

10,10-Bis(3-oxobutyl)-9-anthracenone (39). White solid: mp 159−160 °C; ^{1}H NMR (200 MHz, $CDCl_3$) δ 8.40 (d, J = 7.8 Hz, 2H), 7.68 (dd, J = 6.8, 1.5 Hz, 2H), 7.62 (dt, J = 8.2, 1.5 Hz, 2H), 7.49 (dt, J = 7.9, 1.4 Hz, 2H), 2.53 (m, 4H), 1.79 (s, 6H), 1.65 (m, 4H); ^{13}C-{^{1}H} NMR (50 MHz, $CDCl_3$; DEPT) δ 208.1 (C), 207.6 (C), 145.5 (C), 134.3 (CH), 132.4 (C), 127.6 (CH), 127.4 (CH), 125.9 (CH), 44.3 (C), 38.5 (CH_2), 38.3 (CH_2), 29.8 (CH_3). MS *m/z* 334 (M^+, 3), 263 (100), 245 (34), 220 (40).

1-(2,5-Dimethyl-2-hydroxy-5-nitrocyclohexyl)ethanone (41). White solid: mp 52−54 °C. Major diastereomer: ^{1}H NMR (200 MHz, $CDCl_3$) δ 3.90 (d, J = 2.6 Hz, 1H, OH), 2.65 (m, 1H), 2.55 (m, 1H), 2.45 (m, 1H), 2.29 (s, 3H), 2.08 (m, 1H), 1.96 (t, J = 13.0 Hz, 1H), 1.64 (dt, J = 14.5, 3.8 Hz, 1H), 1.59 (s, 3H), 1.26 (m, 1H), 1.19 (s, 3H); ^{13}C{^{1}H} NMR (50 MHz, $CDCl_3$; DEPT) δ 206.5 (C), 87.76 (C), 68.3 (C), 52.5 (CH), 34.6 (CH_2), 33.3 (CH_2), 31.2 (CH_3), 30.4 (CH_2), 28.6 (CH_3), 28.2 (CH_3). Anal. Calcd for $C_{10}H_{17}NO_4$: C, 55.80; H, 7.96; N, 6.51. Found: C, 55.66; H, 7.63; N, 6.41.

4,4-Bis(phenylsulfonyl)butanal (42). Colorless solid: mp 82−83 °C; ^{1}H NMR (200 MHz, $CDCl_3$) δ 9.71 (s, 1H), 8.00−7.90 (m, 4H), 7.70−7.50 (m, 6H), 4.77 (t, J = 6.1 Hz, 1H), 3.01 (t, J = 7.0 Hz, 2H), 2.46 (q, J = 6.5 Hz, 2H); ^{13}C{^{1}H} NMR (50 MHz, $CDCl_3$; DEPT) δ 199.9 (CH), 137.5 (C), 134.6 (CH), 129.3 (CH, 2C), 129.1 (CH, 2C), 81.3 (CH), 40.4 (CH_2), 18.4 (CH_2). Anal. Calcd for $C_{14}H_{16}O_5S_2$: C, 54.53; H, 4.58. Found: C, 54.30; H, 4.78.

5,5-Bis(phenylsulfonyl)-8-methyl-7-nonen-2-one (43). White solid: mp 96−97 °C; ^{1}H NMR (200 MHz, $CDCl_3$) δ 8.06−7.97 (m, 4H), 7.67−7.59 (m, 6H), 5.08 (tqq, J = 6.4, 1.5, 1.4 Hz, 1H), 2.98 (t, J = 7.5 Hz, 2H), 2.81 (d, J = 6.4 Hz, 2H), 2.49 (t, J = 7.6 Hz, 2H), 2.14 (s, 3H), 1.64 (d, J = 1.3 Hz, 3H), 1.48 (t, J = 1.2 Hz, 3H); ^{13}C-{^{1}H} NMR (50 MHz, $CDCl_3$) δ 206.3, 137.1, 136.9, 134.6, 131.3 (2C), 128.6 (2C), 115.1, 90.1, 34.0, 30.0, 29.3, 25.9, 23.5, 18.0. Anal. Calcd for $C_{22}H_{26}O_5S_2$: C, 60.81; H, 6.03. Found: C, 60.58; H, 6.30.

9,9-Bis(3-oxobutyl)fluorene (47) (Eq 2). White solid: mp 90−91 °C; ^{1}H NMR (200 MHz, $CDCl_3$) δ 7.74−7.72 (m, 2H), 7.41−7.29 (m, 6H), 2.34 (t, J = 7.7 Hz, 4H), 1.75 (s, 6H), 1.62 (t, J = 7.7 Hz, 4H); ^{13}C{^{1}H} NMR (50 MHz, $CDCl_3$) δ 208.5, 148.1, 141.1, 127.6, 127.5, 123.1, 119.9, 53.3, 38.1, 33.4, 29.8; MS *m/z* 306 (M^+, 71), 235 (100), 217 (54), 178 (73).

Dimethyl 2-(3-Oxobutyl)-2-(3-oxopropyl)malonate (48) and Dimethyl 4-Hydroxy-4-methyl-3-formylcyclohexane-1,1-dicarboxylate (49) (Scheme 1). (a) A mixture of **22** (400 mg, 1.98 mmol), **15** (221 mg, 3.96 mmol), and **1** (24 mg, 0.023 mmol, 1 mol %) was stirred in MeCN (3 mL) at 23 °C for 24 h. The solvent was evaporated and the residue was chromatographed (7:3 hexane−EtOAc) to give **48** (220 mg, 43%) and **49** (30 mg, 6%) as colorless oils. **48**: ^{1}H NMR (200 MHz, $CDCl_3$) δ 9.74 (t, J = 0.2 Hz, 1H), 3.73 (s, 6H), 2.51 (td, J = 6.8, 0.2 Hz, 2H), 2.47 (t, J = 6.8 Hz, 2H), 2.18 (t, J = 6.8 Hz, 2H), 2.14 (s, 3H), 2.14 (t, J = 7.9 Hz, 2H); ^{13}C{^{1}H} NMR (50 MHz, $CDCl_3$) δ 207.1, 200.5, 171.1, 55.9, 52.5, 38.4, 29.78, 27.2, 25.6. **(b)** A mixture of **48** (20 mg, 0.078 mmol) and **1** (14 mg, 0.012 mmol, 16 mol %) in MeCN (3 mL) was stirred at 23 °C for 24 h. The solvent was evaporated and the residue was chromatographed (7:3 hexane−EtOAc) to give **49** (7 mg, 35%) as a colorless oil: ^{1}H NMR (200 MHz, $CDCl_3$) δ 9.80 (d, J = 1.7 Hz, 1H), 3.73 (s, 3H), 3.71 (s, 3H), 2.89−2.54 (m, 1H), 2.35−2.50 (m, 1H), 2.20−2.00 (m, 3H), 1.77−1.60 (m, 1H), 1.55−

1.44 (m, 1H), 1.35 (s, 3H); $^{13}C\{^1H\}$ NMR (50 MHz, $CDCl_3$) δ 204.5, 171.8, 171.0, 68.9, 53.8, 53.5, 52.84 (2C), 36.2, 28.7, 26.7, 26.1.

Dimethyl 4-Hydroxy-3-(1-oxoethyl)cyclohexane-1,1-dicarboxylate (50) (Scheme 1). A mixture of **25** (181 mg, 0.96 mmol), **14** (135 mg, 1.9 mmol), and **1** (7 mg, 0.006 mmol, 0.5 mol %) in MeCN (5 mL) was stirred at 23 °C for 24 h. the solvent was evaporated and the residue was chromatographed (7:3 EtOAc−hexane) to give **50** (160 mg, 64%) as a colorless oil. NMR showed a 2:1 mixture of isomers. Major diastereomer: ^1H NMR (300 MHz, $CDCl_3$) δ 4.20 (m, 1H), 3.72 (s, 3H), 3.67 (s, 3H), 3.06 (br, 1H), 2.65 (ddd, J = 13.0, 3.6, 2.2 Hz, 1H), 2.35 (m, 2H), 2.17 (s, 3H), 2.10 (m, 2H), 1.84 (dq, J = 14.5, 6.9 Hz, 1H), 1.43 (m, 1H); $^{13}C\{^1H\}$ NMR (75 MHz, $CDCl_3$) δ 211.9, 171.8, 171.1, 64.3, 54.3, 52.9, 52.7, 50.3, 38.5, 28.8, 26.7, 24.2. Minor diastereomer (only distinctive $^{13}C\{^1H\}$ NMR signals): δ 207.1, 69.7, 28.50, 27.11. Anal. Calcd for $C_{12}H_{18}O_6$: C, 55.81; H, 7.02. Found: C, 55.65; H, 7.05.

Ethyl 2-Cyano-2-(3-methyl-2-butenyl)-5-oxohexanoate (76) (Eq 5). Colorless oil: ^1H NMR (200 MHz, $CDCl_3$) δ 5.18 (tsept, J = 6.9, 1.2 Hz, 1H), 4.25 (q, J = 7.1 Hz, 2H), 2.75−2.55 (m, 4H), 2.18 (s, 3H), 2.20−2.00 (m, 2H), 1.74 (d, J = 0.9 Hz, 3H), 1.65 (d, J = 0.8 Hz, 3H), 1.32 (t, J = 7.1 Hz, 3H); $^{13}C\{^1H\}$ NMR (50 MHz, $CDCl_3$) δ 205.7, 168.2, 137.8, 118.7, 116.0, 62.5, 61.2, 48.8, 39.0, 35.8, 29.7, 25.7, 17.9, 13.8; IR (neat) 2980, 2920, 2240, 1710, 1430 cm^{-1}; MS m/z 251 (M^+, 2), 206 (4), 183 (17), 136 (33), 69 (100).

Reactions of Donors 2, 4, or 12 with Acceptors 14 or 87 (Tables 2 and 3 and Figures 1−4). The general procedure outlined above was followed for the reactions summarized in Tables 2 and 3. Yields correspond to isolated products purified by chromatography. The reactions over time outlined in Figures 1−4 were carried out at 25 °C in acetonitrile-d_3 with accurately determined amounts of donors and acceptors (0.9−1.4 M) and the corresponding catalyst. Progress of the reactions was monitored by integration against the rest of undeuterated acetonitrile (0.2%) or *t*-BuOMe as internal standard.

Reaction of Donor 78 with Acceptor 14 (Eq 7). The reaction between **78** and **14** in the presence of triphenylphosphine (6 mol %) was carried out in THF at 23 °C.[3,11] The similar transformation with **1** (3 mol %) in acetonitrile was performed under the conditions described before for the general procedure. Diastereoselectivities were determined by integration at 300 MHz of the well-separated doublet signals for the C-2 hydrogen of **79** and **80**.

1,1,3-Triphenylsulfonylpropane (88) (Eq 8). White solid: mp 122−124 °C; ^1H NMR (200 MHz, $CDCl_3$) δ 7.91−7.86 (m, 4H), 7.75−7.52 (m, 6H), 3.65 (s, 6H), 3.11−3−03 (m, 4H); $^{13}C\{^1H\}$ NMR (50 MHz, $CDCl_3$) δ 169.6, 138.5, 134.0, 129.5 (3C), 128.0 (3C), 55.1, 53.1, 51.5, 26.5. Anal. Calcd for $C_{21}H_{20}O_6S$: C, 54.29; H, 4.34. Found: C, 54.26; H, 4.41.

Dimethyl 2,2-Bis(2-phenylsulfonyl)malonate (90) (Eq 10). White solid: mp 54−56 °C; ^1H NMR (200 MHz, $CDCl_3$) δ 7.95−7.82 (m, 6H), 7.75−7.64 (m, 3H), 7.61−7.44 (m, 6H), 5.09 (t, J = 6.0 Hz, 1H), 3.58 (t, J = 6.9 Hz, 2H), 2.58 (q, J = 6.6 Hz, 2H); $^{13}C\{^1H\}$ NMR (50 MHz, $CDCl_3$) δ 137.5, 134.8, 134.1, 129.5 (2C), 129.2 (2C), 128.2, 79.7, 52.2, 19.6. Anal. Calcd for $C_{21}H_{24}O_8S_2$: C, 53.83; H, 5.16; S, 13.68. Found: C, 53.64; H, 4.99; S, 13.84.

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Supporting Information Available: Selected NMR spectra for **24a**, **24b**, **39**, **47**-**49**, and **76** (11 pages). See any current masthead page for ordering and Internet access instructions.

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