P(RNCH2CH2)3N: Catalysts for the Head-to-Tail Dimerization of Methyl Acrylate

Weiping Su, Dale McLeod, and John G. Verkade*

Department of Chemistry, Iowa State University, Ames, Iowa 50011

jverkade@iastate.edu

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Abstract: The dimerization of methyl acrylate to the head-to-tail 2-methylene-pentanedioic acid dimethyl ester product was realized in 82 and 85% yield in only 4 h at room temperature in THF in the presence of catalytic amounts of $P(RNCH_2CH_2)_3N$ (R = *i*-Bu and Bn, respectively). These phosphines are to our knowledge the best nonmetallic catalysts so far reported for this reaction. In contrast, less sterically hindered $P(MeNCH_2CH_2)_3N$ failed to catalyze this dimerization, giving oligomer or polymer instead.

2-Methylene-pentanedioic acid dimethyl ester (**1** in eq 1) has been found to be a useful monomer for the synthesis of polymers[1] and as a building block for construction of larger molecules.[2]
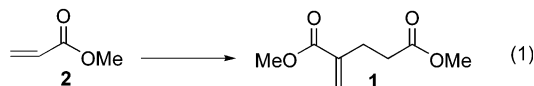
Compound **1** is generally made by head-to-tail dimerization of methyl acrylate (**2**) at elevated temperatures (50–110 °C) using phosphines[3] [e.g., $P(C_6H_5)_3$ and $P(C_4H_9)_3$] or transition metal trialkylphosphine complexes[4] as catalysts. With the exception of the Cp*Ru(PCy3)H3-catalyzed dimerization of **2** at 80 °C in 91%,[4a] the aforementioned syntheses suffer from relatively low selectivity and yields (ranging from 10 to 79%), with the highest yield of 79% arising from the use of $(c\text{-}C_6H_{11})_3P \cdot CS_2$ in refluxing pyridine for 16 h.[2b]

We have demonstrated in recent years that proazaphosphatranes **3** function as potent nonionic bases,[5]

nonmetallic catalysts,[5] or as nonmetallic cocatalysts[6] in a variety of useful organic transformations. The unexpectedly potent catalytic properties of **3** are associated with its flexible $N_{ax} \rightarrow P$ transannular interaction that can adjust the electron density at phosphorus in response to substrates that polarize the phosphorus lone pair of electrons.[5,6] Here, we disclose that **3c** and **3e** are superior phosphine catalysts for the dimerization of **2**, which function at room temperature.
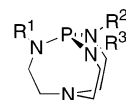
	R^1	R^2	R^3
3a	Me	Me	Me
3b	*i*-Pr	*i*-Pr	*i*-Pr
3c	*i*-Bu	*i*-Bu	*i*-Bu
3d	*i*-Bu	*i*-Bu	Bz
3e	Bz	Bz	Bz

Initially, we monitored room-temperature dimerization reactions of **2** in the presence of 10 mol % **3c** in C_6D_6, THF-d_8, and dioxane-d_8 by ^{1}H NMR spectroscopy. It was observed that **3c** catalyzed the reaction, affording the head-to-tail dimer **1** as well as about 10% trimer. In polar solvents, such as THF-d_8 or dioxane-d_8, dimerization proceeded much faster than in a nonpolar solvent such as C_6D_6. In the former two solvents, the reactions were complete after 4 h, while in the latter solvent, it took 12 h for complete conversion.

We then screened catalysts **3a**–**e** with 10 and 1 mol % catalyst loadings in three solvents as shown in Table 1. With 10 mol % **3c**, the reaction in THF and dioxane produced dimer **1** in 82 and 83% yield (entries 1 and 2), respectively. Under the same conditions, pentane as the solvent gave a significantly lower yield (77.3% entry 3). Considering that the substituents on each PN3 nitrogen in **3** can affect the electronic and steric nature of the phosphorus, several other proazaphosphatranes were also examined as dimerization catalysts. It was found that **3b** was capable of catalyzing the dimerization of **2**, although less efficiently than **3c** (entries 4–6). Use of bulkier **3d** and **3e** led to an increased yield of dimer **1** in THF and dioxane (entries 7–10) compared with those facilitated by **3b** in these solvents (entries 4 and 5). The highest yield (85%) was realized with **3e** (10 mol %) in THF. However, in the cases of **3c** and **3e**, increasing the catalyst loading from 10 to 15% did not give rise to a higher yield (entries 11 and 12, respectively).

In contrast to **3b**–**e**, the less sterically hindered **3a** failed to catalyze the dimerization of **2**, instead giving polymers or oligomers as dominant products (entries 13 and 14). Thus, upon addition of a pentane solution of **3a** to a solution of **2** in pentane, a sticky oil precipitated from

(1) (a) Trumbo, D. C.; Zander, R. A. *J. Polym. Sci. Polym. Chem.* **1991**, *29*, 1053. (b) Nguyen, H. A.; Marechal, E. *J. Macromol. Sci.-Rev. Macromol. Chem. Phys.* **1998**, *187*, C27. (c) Gegnas, L. D.; Waddell, S. T.; Chabin, R. M.; Reddy, S.; Wong, K. K. *Bioorg. Med. Chem. Lett.* **1998**, *8*, 1643.

(2) (a) Tanne, M. E.; Vaganay, S.; Heijenoort, J. V.; Blanot, D. *J. Org. Chem.* **1996**, *61*, 1756. (b) Cookson, R. C.; Smith, S. A. *J. Chem. Soc., Perkin. Trans. 1* **1979**, 2447.

(3) (a) McClure, J. D. *J. Org. Chem.* **1970**, *35*, 3045. (b) Baizer, M. M.; Anderson, J. D. *J. Org. Chem.* **1965**, *30*, 1357. (c) Tembe, G. L.; Bandyopadhyay, A. R.; Ganeshpure, P. A.; Satish, S. *Catal. Rev. Sci. Eng.* **1996**, *38*, 299. (d) White, D. A. *Synth. React. Inorg. Met. Org. Chem.* **1977**, *7*, 433. (e) Rauhut, M. M.; Currier, H. U.S. Patent 3,-074,999, 1963. (f) Jenner, G. *Tetrahedron Lett.* **2000**, *41*, 3091.

(4) (a) Yi, C. S.; Liu, N. *J. Organomet. Chem.* **1998**, *553*, 157. (b) Grenouillet, P.; Nelbecker, D.; Tkatchenko, I. *Organometallic* **1984**, *3*, 1130. (c) McKinney, R. J.; Cotton, M. C. *Organometallics* **1986**, *5*, 1080. (d) Aresta, M.; Dibenedetto, A.; Quaranta, E. *Organometallics* **2000**, *19*, 4199.

(5) For a recent review, see: Verkade, J. G. *Top. Curr. Chem.* **2003**, *233*, 1.

(6) (a) Urgaonkar, S.; Nagarajan, M.; Verkade, J. G. *Org. Lett.* **2003**, *5*, 815. (b) Urgaonkar, S.; Nagarajan, M.; Verkade, J. G. *Tetrahedron Lett.* **2002**, *43*, 8921. (c) Urgaonkar, S.; Verkade, J. G. *J. Org. Chem.* **2003**, *68*, 452.

(7) (a) Schmidt, H.; Lensink, C.; Xi, S. K.; Verkade, J. G. *Z. Anorg. Allg. Chem.* **1989**, *578*, 75. (b) Kisanga, P. B.; Verkade, J. G. *Tetrahedron* **2001**, *57*, 467.

TABLE 1. Dimerization of 2 Catalyzed by 3 at Room Temperature

entry	catalyst (mol %)	solvent	time (h)	yield (%)[a]
1	**3c** (10%)	dioxane	3	82.8
2	**3c** (10%)	THF	4	82.0
3	**3c** (10%)	pentane	12	77.6
4	**3b** (10%)	dioxane	3	66.0
5	**3b** (10%)	THF	4	73.0
6	**3b** (10%)	pentane	12	62.6
7	**3d** (10%)	THF	4	73.0
8	**3d** (10%)	dioxane	3	81.0
9	**3e** (10%)	THF	4	85.0
10	**3e** (10%)	dioxane	3	84.0
11	**3c** (15%)	THF	4	83.0
12	**3e** (15%)	THF	4	85.0
13	**3a** (10%)	pentane	1	b
14	**3a** (10%)	THF	4	b
15	**3c** (1%)	dioxane	24	77.9
16	**3c** (1%)	THF	24	77.4
17	**3c** (1%)	pentane	30	62.0
18	**3d** (1%)	THF	24	76.0
19	**3e** (1%)	THF	24	82.4

[a] Isolated yield (average of two runs). [b] Product was identified as a polymer or a oligomer on the basis of the ^{1}H NMR spectral evidence in which the peaks corresponding to the methylene group virtually disappear and broad peaks between 0.6 and 2.6 ppm appear. Due to the intractable nature of the product, yields were not possible to calculate.

SCHEME 1
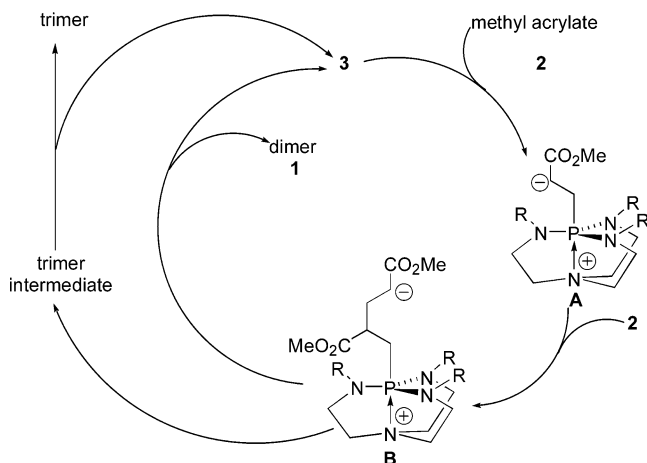
solution in approximately 1 min. Our observation that the ratio of methylene to ester group protons calculated from integrations of the corresponding peaks in the ^{1}H NMR spectrum of the isolated oil is considerably lower than 2:3 (the ratio of the same types of protons in **1**), as well as the presence of broad peaks ranging from 0.6 to 2.6 ppm, indicates that an oligomer or polymer had formed. Removing the THF solvent used for the reaction of **2** in the presence of **3a** as catalyst also left an oily oligomer or polymer that was very similar (on the basis ^{1}H NMR spectroscopic examination) to that produced in the same reaction carried out in pentane. When the amount of **3c−e** was reduced from 10 to 1%, the dimerization of **2** became slower, but good yields of **1** were still achieved (entries 15−19).

It is likely that dimerization of **2** catalyzed by **3** follows a pathway (Scheme 1) discussed by McClure,[2a] Anderson,[2b] and Yi[3a] and co-workers for such dimerizations catalyzed by trialkylphosphines. The formation of transannulated **A** is believed to be the rate-determining step, which

agrees with our observation that the reaction rate depends on the concentration of **3**. The flexibility of a transannular interaction in **3** could stabilize intermediate **A**, thus reducing the activation energy for its formation, compared with other acyclic phosphines that catalyze the dimerization of **1**. Supporting evidence for this idea is our observation that **3** catalyzes the dimerization of **1** at room temperature, whereas acyclic phosphines reported previously to catalyze this reaction[2,3] required elevated temperatures. Thus, for example, the $P(C_4H_9)_3$-catalyzed dimerization of **2** was carried out without solvent at 50 °C.[2f] Formation of zwitterionic intermediate **A** is also favored by more polar solvents such as THF or dioxane, which promoted faster reactions, in our experience, than those carried out in pentane or benzene.

1,4-Addition of a second methyl acrylate molecule to **A** would form **B**, which can eliminate **3**. **B** could then undergo subsequent 1,3-hydrogen migration or an intermolecular proton transfer, perhaps mediated by **3** to give dimer **1**. The latter option was substantiated by carrying out the dimerization in an NMR tube in the presence of **3c** plus added [D**3c**]O_2CCF_3 (isolated from the reaction of HO_2CCF_3 with **3c** in THF). Monitoring the reaction by ^{31}P proton-coupled NMR spectroscopy revealed that the three-line ^{31}P spectrum due to D−P coupling in [D**3c**]$^+$ was completely replaced by a doublet for [H**3c**]$^+$, thus indicating that proton-transfer had occurred. 1,4-Addition of **B** to a third methyl acrylate molecule would lead to trimer formation.

Because both dimer and trimer formation is expected to go through intermediate **B**, production of trimers is difficult to avoid. The sterically bulky nature of **3c−e** would tend to disfavor addition of **B** to an additional methyl acrylate molecule, thus allowing the yield of dimer to increase with the size of the substituents on the catalysts. In contrast, intermediate **B** formed from sterically less bulky **3a** would permit the zwitterionic intermediate to successively add methyl acrylate molecules to give oligomer and polymer.

In summary, we have shown that **3b−e** catalyze head-to-tail dimerization of methyl acrylate at room temperature. Moreover, **3c** and **3e** appear to be superior phosphine catalysts for this reaction in that they provide the best yields so far reported, they operate at room temperature and they circumvent the use of toxic heavy metals. The results of efforts underway to broaden the scope of this methodology to other acrylates and to utilize solid-supported versions of **3** in order to realize the advantages of a heterogeneous catalyst for the dimerization of acrylates and related compounds will be reported in due course.

Experimental Section

Typical Procedure for Reactions in Table 1. A stock solution of **3** (in the amount and solvent indicated in Table 1) was added by syringe to 2 mL of a solution of 431 mg (5 mmol) of methyl acrylate in the same solvent. The reaction mixture was stirred for the indicated time at room temperature, and the resulting solution was concentrated under vacuum. The crude product was purified by chromatography on silica gel with an eluent of 20% ethyl acetate in hexanes. The ^{1}H and ^{13}C NMR spectra of the dimer[4a] and trimer[2b] compared favorably to those in the literature. The products in entries 7 and 8 were not separated by chromatography but instead were collected directly

after removing the solvent under vacuum and washing the residue with 3×2 mL of cold pentane.