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Communications

The First Example of a Catalytic Wittig-Type Reaction. Tri-*n*-butylarsine-Catalyzed Olefination in the Presence of Triphenyl Phosphite†

Summary: Tri-*n*-butylarsine-catalyzed olefination was achieved by the reaction of various aldehydes with methyl bromoacetate (or ω-bromoacetophenone) in the presence of triphenyl phosphite and potassium carbonate at room temperature in good yields with high *E* stereoselectivity.

Sir: The birth of the Wittig reaction in 1953 marked the entry of ylides into the arsenal of important synthetic tools.[1] Since then, the Wittig olefination has engendered continuous synthetic and mechanistic interest.[2] Variants of the Wittig reaction have advantages over the use of phosphoranes.[3,4] The Wittig-type reaction has been extended with elements other than phosphorus such as boron,[5] aluminum,[6] silicon,[7] tin,[8a-e] lead,[8c-e] sulfur,[9] selenium,[10] and tellurium,[11] etc. Our interest was to explore the versatility of the reaction carried out with arsenic reagent.

We found that certain arsonium ylides, especially those with an electron-withdrawing substituent in the alkylidene moiety, are more reactive than the corresponding phosphonium ylides.[12] The greater nucleophilicity of arsonium ylides has been evidenced by comparison of the X-ray crystallography of (benzoylmethylene)triphenylarsorane with that of (benzoylmethylene)triphenylphosphorane.[13]

Recently, we disclosed that it is unncessary to isolate the arsonium ylides themselves. A variety of aldehydes react with arsonium salts equally well in the presence of potassium carbonate under phase-transfer conditions to accomplish the olefination.[14]

$$R(CH{=}CH)_nCHO + Ph_3As^+CH_2(CH{=}CH)_mXBr^- \xrightarrow[-Ph_3AsO,\ \text{room temperature}]{K_2CO_3,\ \text{mixed solvent}} R(CH{=}CH)_{n+m+1}X$$

where n = 0, 1; m = 0, 1; X = CHO, COOR, CN, $COCH_3$, $CONR_1R_2$

By this method, several biologically active natural products have been synthesized.[14] The simplicity of our procedure and the readiness of reconverting triphenylarsine oxide into triphenylarsine[15] stimulated us to consider the possibility of a catalytic Wittig-type reaction. To our knowledge, although the Wittig-type reaction and its alternatives have been widely used for many years, no

† This paper is the 68th report on the application of elementoorganic compounds of 15th and 16th groups in organic synthesis.

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Scheme I

$$\underset{1}{RCHO} + \underset{2}{BrCH_2X} + \underset{3}{(PhO)_3P} \xrightarrow[\text{THF–CH}_3\text{CN, room temperature}]{n\text{-Bu}_3\text{As (cat.), K}_2\text{CO}_3\text{(s)}} \underset{4}{RCH{=}CHX} + (PhO)_3PO$$

a, X = CO_2CH_3; b, X = C(O)Ph.

Table I. Reaction of Various Aldehydes with Methyl Bromoacetate (2a) and with ω-Bromoacetophenone (2b)

entry	1, R =	2	reactn time, h	isoltd yield, %	$E:Z^b$
1	p-ClC_6H_4	*a*	18	87	98:2
2	C_6H_5	*a*	30	86	99:1
3	o-ClC_6H_4	*a*	12	81	98:2
4	p-tolyl	*a*	24	80	98:2
5	n-C_5H_{11}	*a*	31	64	100
6	2-furyl	*a*	16	80	99:1
7	2-thiophenyl	*a*	17	75	97:3
8	2-pyridyl	*a*	17	68	99:1
9	PhCH=CH	*a*	18	61	E,E > 97
10	p-ClC_6H_4	*b*	24	75	>98
11	2-furyl	*b*	18	86	>98
12	n-C_4H_9	*b*	12	80	>98

[a] All the products were characterized by ^{1}H NMR. [b] The ratio of $E:Z$ isomer was determined by capillary GC.

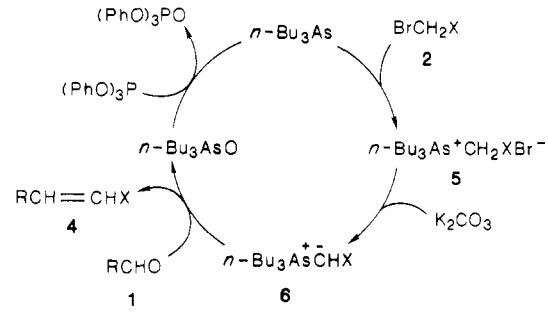
catalytic process has ever appeared in the literature. Herein we report the first example in this respect as summarized in Scheme I and Table I. A mixture of aldehyde (1 mmol), potassium carbonate (1.2 mmol), methyl bromoacetate (1.2 mmol), 0.5 mL of THF, 4 mL of acetonitrile, tributylarsine (0.2 mmol), and triphenyl phosphite (1.2 mmol) were stirred in a reaction tube under nitrogen at room temperature. After the reaction was completed (monitored by TLC), ethyl acetate was added. The resulting mixture was passed through a short column of silica gel to remove the inorganic salt. The desired product was obtained by flash chromatography.

The reaction path is proposed as shown in Scheme II.

Reaction of tri-n-butylarsine with bromo compound **2** forms arsonium salt **5**, which, in the presence of potassium carbonate, generates **6** in situ. Ylide **6** reacts with the aldehyde rapidly to afford the desired olefin **4**, and the tri-n-butylarsine is regenerated by reduction of tri-n-butylarsine oxide with triphenyl phosphite.

(16) Care should be taken for handling tri-n-butylarsine and the experiment should be carried out in an efficient hood.

Scheme II



The simplicity of our procedure, the mildness of the reaction conditions, the good yields, the high stereoselectivity, and especially the use of a catalytic amount of tri-n-butylarsine, demonstrates our method to be practical for the synthesis of α,β-unsaturated esters and ketones. Thus, our method provides the first example of a catalytic Wittig-type reaction. The extension of our method to the application of other elementoorganic compounds of nontransition elements in organic synthesis is being actively pursued.

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Registry No. **1** (R = p-ClC_6H_4), 104-88-1; **1** (R = C_6H_5), 100-52-7; **1** (R = o-ClC_6H_4), 89-98-5; **1** (R = tolyl), 104-87-0; **1** (R = C_5H_{11}), 66-25-1; **1** (R = 2-furyl), 98-01-1; **1** (R = 2-thiophenyl), 98-03-3; **1** (R = 2-pyridyl), 1121-60-4; **1** (R = PhCH=CH), 104-55-2; **1** (R = C_4H_9), 110-62-3; **2a**, 96-32-2; **2b**, 70-11-1; **3**, 101-02-0; (*E*)-**4** (R = p-ClC_6H_4, X = CO_2CH_3), 20754-21-6; (*E*)-**4** (R = C_6H_5, X = CO_2CH_3), 1754-62-7; (*E*)-**4** (R = o-ClC_6H_4, X = CO_2CH_3), 98288-14-3; (*E*)-**4** (R = tolyl, X = CO_2CH_3), 20754-20-5; (*E*)-**4** (R = C_5H_{11}, X = CO_2CH_3), 7367-81-9; (*E*)-**4** (R = 2-furyl, X = CO_2CH_3), 58293-85-9; (*E*)-**4** (R = 2-thiophenyl, X = CO_2CH_3), 119680-91-0; (*E*)-**4** (R = 2-pyridyl, X = CO_2CH_3), 81124-45-0; (*E*)-**4** (R = PhCH = CH, X = CO_2CH_3), 24196-39-2; (*E*)-**4** (R = p-ClC_6H_4, X = C(O)Ph), 22252-16-0; (*E*)-**4** (R = furyl, X = C(O)Ph), 39511-12-1; (*E*)-**4** (R = C_4H_9, X = C(O)Ph), 64235-53-6; Bu_3A_5, 5852-58-4.

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Pyrimidinone Ring Opening and Reclosure on a 1,3,4,6-Tetraazapentalene System: Syn to Anti Isomerization

Summary: Under nucleophilic attack, pyrimidinone ring opening and reclosure on syn-disubstituted 1,3,4,6-tetraazapentalenes effects syn to anti isomerization of the ring systems.

Sir: The discovery of an oxidative cyclization route to *syn*-dipyrido-substituted 1,3,4,6-tetraazapentalenes (e.g., **1**)[1,2] has led to the synthesis of covalently linked DNA/RNA cross sections representative of purine–pyrimidine, purine–purine, and pyrimidine–pyrimidine duplexes.[3,4] The synthetic methodology has now been applied to hybrid examples that are monopyrido-substituted 1,3,4,6-tetraazapentalenes. Those that have additional *syn*-pyrimidinone substitution are susceptible to pyrimidinone ring opening and reclosure on the 1,3,4,6-tetraazapentalene system, which results in overall syn to anti isomerization. While the rearrangement and isomerization are of intrinsic

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