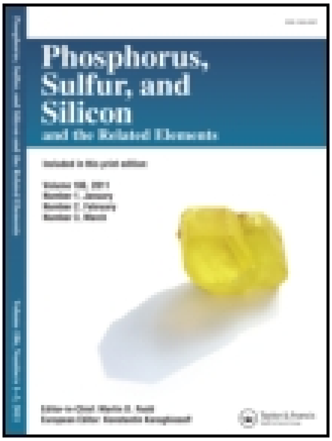
This article was downloaded by: [The Aga Khan University]
On: 18 October 2014, At: 05:26
Publisher: Taylor & Francis
Informa Ltd Registered in England and Wales Registered Number: 1072954
Registered office: Mortimer House, 37-41 Mortimer Street, London W1T 3JH, UK



Phosphorus, Sulfur, and Silicon and the Related Elements
Publication details, including instructions for authors and subscription information:
http://www.tandfonline.com/loi/gpss20

Tris(2,4,6-Trimethoxyphenyl)phosphine: Base Catalyst in the Transformation of α,β-Unsaturated Aldehydes to Saturated Carboxylic-Acid Derivatives

Masahiko Hayashi [a], Hirotoshi Kawabata [a], Kazuya Yoshimoto [a] & Takanori Tanaka [a]
[a] Department of Chemistry, Kobe University, Kobe, Japan

Published online: 18 Feb 2007.

To cite this article: Masahiko Hayashi, Hirotoshi Kawabata, Kazuya Yoshimoto & Takanori Tanaka (2007) Tris(2,4,6-Trimethoxyphenyl)phosphine: Base Catalyst in the Transformation of α,β-Unsaturated Aldehydes to Saturated Carboxylic-Acid Derivatives, Phosphorus, Sulfur, and Silicon and the Related Elements, 182:2, 433-445, DOI: 10.1080/10426500600977296

To link to this article: http://dx.doi.org/10.1080/10426500600977296

PLEASE SCROLL DOWN FOR ARTICLE

Taylor & Francis makes every effort to ensure the accuracy of all the information (the “Content”) contained in the publications on our platform. However, Taylor & Francis, our agents, and our licensors make no representations or warranties whatsoever as to the accuracy, completeness, or suitability for any purpose of the Content. Any opinions and views expressed in this publication are the opinions and views of the authors, and are not the views of or endorsed by Taylor & Francis. The accuracy of the Content should not be relied upon and should be independently verified with primary sources of information. Taylor and Francis shall not be liable for any losses, actions, claims, proceedings, demands, costs, expenses, damages, and other liabilities whatsoever or howsoever caused arising directly or indirectly in connection with, in relation to or arising out of the use of the Content.

This article may be used for research, teaching, and private study purposes. Any substantial or systematic reproduction, redistribution, reselling, loan, sub-licensing, systematic supply, or distribution in any form to anyone is expressly forbidden. Terms & Conditions of access and use can be found at http://www.tandfonline.com/page/terms-and-conditions

Downloaded by [The Aga Khan University] at 05:26 18 October 2014

Phosphorus, Sulfur, and Silicon, 182:433–445, 2007
Copyright © Taylor & Francis Group, LLC
ISSN: 1042-6507 print / 1563-5325 online
DOI: 10.1080/10426500600977296

Downloaded by [The Aga Khan University] at 05:26 18 October 2014

Tris(2,4,6-Trimethoxyphenyl)phosphine: Base Catalyst in the Transformation of α,β-Unsaturated Aldehydes to Saturated Carboxylic-Acid Derivatives

Masahiko Hayashi
Hirotoshi Kawabata
Kazuya Yoshimoto
Takanori Tanaka
Department of Chemistry, Kobe University, Kobe, Japan

We have focused on the basicity of Tris(2,4,6-trimethoxyphenyl)phosphine (TTMPP) in organic synthesis. To extend the utility of TTMPP, we examined the reaction of α,β-unsaturated aldehydes with trimethylsilyl cyanide in the presence of TTMPP. Furthermore, to clarify the basic character of TTMPP, we measured ^{31}P NMR of TTMPP and related compounds. First, the reaction of cinnamaldehydes with trimethylsilyl cyanide in the presence of a catalytic amount of TTMPP afforded the corresponding saturated carboxylic acids after hydrolysis with 1M HCl. Treatment of the reaction mixture with alcohols or amines instead of 1M HCl gave the corresponding saturated esters and amides, respectively. As a result of studies of the reaction mechanism, it was revealed that the reaction proceeded via silylcyanation of α,β-unsaturated aldehydes with trimethylsilyl cyanide to produce trimethylsilyl ethers of cyanohydrin and subsequent isomerization that formed α-trimethylsiloxy vinyl cyanides, which were hydrolyzed to give saturated carboxylic acids.

Keywords Amide; base catalyst; carboxylic acid; ester; α,β-unsaturated aldehyde

INTRODUCTION

Since the report by Wada and Higashizaki in 1984, high basicity of tris(2,4,6-trimethoxyphenyl)phosphine (TTMPP)[1] has attracted the interest of synthetic organic chemists. Matsukawa et al. reported TTMPP-catalyzed aldol reaction between ketene silyl acetals and aldehydes.[2,10] Very recently, Matsukawa and Obu reported a TTMPP-catalyzed silyl ketene acetal-imine condensation route to β-lactams.[3] We also reported

Received May 18, 2006; accepted August 1, 2006.

This work was supported by a Grant-in-Aid for Scientific Research on Priority Areas "Advanced Molecular Transformations of Carbon Resources" and No. B17340020 from the Ministry of Education, Culture, Sports, Science, and Technology.

Address correspondence to Masahiko Hayashi, Kobe University, Department of Chemistry, Faculty of Science, Kobe, 657-8501, Japan. E-mail: mhayashi@kobe-u.ac.jp

the use of TTMPP as a selective deacetylation catalyst.[4] Since then, we have focused on the utility of TTMPP as a base in organic synthesis, and we found that TTMPP catalyzed the conversion of α,β-unsaturated aldehydes to saturated carboxylic acid via trimethylsilyl ethers of cyanohydrins. That is, treatment of α,β-unsaturated aldehydes with trimethylsilyl cyanide in the presence of a catalytic amount of TTMPP afforded the corresponding saturated carboxylic acids after hydrolysis.[5]

In 1991, Kobayashi et al. reported that Lewis bases served as efficient catalysts for the addition reaction of trimethylsilyl cyanide with some aldehydes to afford the corresponding cyanohydrin trimethylsilyl ether in an excellent yield.[6] The Lewis bases they employed were amines (Et_3N, *i*-Pr_2NEt, *i*-Pr_2NH, 1-ethylpiperidine, *N,N,N′,N′*-tetramethylethylenediamine, 2,2,6,6-tetramethylpiperidine), phosphines (*n*-Bu_3P, Ph_3P), arsine (Ph_3As), and antimony (Ph_3Sb). In all cases they examined, the reaction products were trimethylsilyl ethers of cyanohydrin.

We found, however, (*E*)-cinnamaldehyde (**1**) was converted to 3-phenylpropionic acid (**3**) in the presence of 20 mol% TTMPP under mild conditions. With respect to such direct conversion of α,β-unsaturated aldehydes to corresponding saturated carboxylic acids, several ruthenium complex-catalyzed reactions have been reported. In a report by Murahashi et al., the action of a catalytic amount of $RuH_2(PPh_3)_4$ upon crotonaldehyde in the presence of water in 1,2-dimethoxyethane at 180°C afforded butyric acid in a 68% yield (91% conversion).[7] By using a similar type of reaction, (*E*)-cinnamaldehyde (**1**) was converted to a mixture of 3-phenylpropionic acid (**3**) (46% yield) and (*E*)-cinnamic acid (15% yield) at 180°C by a catalytic system that consisted of $RuCl_3 \cdot nH_2O$ and tricyclohexylphosphine (PCy_3).[8] In this system, a high temperature was necessary, and the yields of saturated acids were only moderate. For the related reactions, Hünig et al. reported stepwise conversion of α,β-unsaturated aldehydes or saturated acyl chlorides to 1-alkylated α,β-unsaturated carbonyl compounds or 3-alkylated saturated carboxylic acid derivatives through common ambident anions, which were 1-cyano-3-aryl-1-(trimethylsiloxy)allylic anions.[9] By their methods, cyanohydrin trimethylsilyl ethers were isolated, and then the isolated intermediates were treated with a strong Lewis base such as lithium diisopropylamide, lithium bis(trimethylsilyl)amide, and sodium bis(trimethylsilyl)amide to generate allylic anion. Here we report the mild and direct transformation of cinnamaldehydes into saturated carboxylic acids, esters, and amides catalyzed by TTMPP; we also include a discussion on details of the reaction mechanism.

Downloaded by [The Aga Khan University] at 05:26 18 October 2014

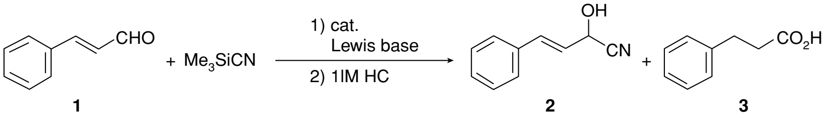
Downloaded by [The Aga Khan University] at 05:26 18 October 2014

RESULTS AND DISCUSSION

During the course of our own Lewis base–catalyzed silylcyanation of aldehydes, we examined the effect of the nature of Lewis base catalysts on the reactions. We found in some cases the reaction products were not only cyanohydrin trimethylsilyl ethers but also saturated carboxylic acid. The results of the reactions of (*E*)-cinnamaldehyde (**1**) with trimethylsilyl cyanide in the presence of a catalytic amount of several Lewis bases followed by hydrolysis by 1M HCl are shown in Table I.

Among the Lewis bases we examined, TTMPP was found to be the most effective for the conversion of (*E*)-cinnamaldehyde (**1**) to 3-phenylpropionic acid (**3**). That is, the reaction of **1** with trimethylsilyl cyanide in the presence of 20 mol% of TTMPP in acetonitrile at r.t. for 3.5 h, followed by hydrolysis with 1M HCl, afforded saturated acid **3** in 90% yield (Table I, Entry 6). When other Lewis bases such as triphenylphosphine, tris(4-methoxyphenyl)phosphine (TMPP), tris(2,6-dimethoxyphenyl)phosphine (TDMPP), and

TABLE I Reaction of (*E*)-Cinnamaldehyde With Me_3SiCN Catalyzed by a Variety of Lewis Bases[a]



Entry	Catalyst (mol%)	Temp/°C	Time/h	Products (% Yield)[b] **2**	Products (% Yield)[b] **3**
1	PPh_3 (20)	28	3.5	46	0
2	TMPP (20)	31	3.5	87	0
3	TDMPP (20)	31	3.5	23	70
4	TTMPP (5)	32	2	10	86
5	TTMPP (10)	32	2	7	87
6	TTMPP (20)	29	3.5	0	90
7	n-Bu_3P (20)	31	2.5	4	74
8	DABCO (5)	20	6	11	80
9	DABCO (10)	20	6	0	85
10	DBU (5)	25	2	0	79
11	DBU (10)	28	2	0	91
12	DBU (20)	25	2	0	94

[a] All reactions were carried out in CH_3CN with 1.2 equiv. Me_3SiCN.

[b] Yields of products were isolated ones after hydrolysis with 1M HCl.

Downloaded by [The Aga Khan University] at 05:26 18 October 2014

tri-*n*-butylphosphine were employed, the products were only unsaturated cyanohydrin **2** or a mixture of **2** and **3** (Table I, Entries 1–3 and 7). It should be mentioned that even in the reaction of TTMPP, the use of less amount of TTMPP led to the formation of a small amount of cyanohydrin (Table I, Entries 4 and 5). The tendency for the preference of the formation of saturated acid **3** approximately correlates with the basicity of phosphines. That is, the values of pKa of conjugated acids of each base are as follows: $Ph_3PH^+ = 2.73$, $TMPPH^+ = 4.59$, $n\text{-}Bu_3PH^+ = 8.43$, $TDMPPH^+ = 9.33$, and $TTMPPH^+ = 11.2$.[10] This basicity also correlates with the chemical shifts of ^{31}P NMR shown in Figure 1.

It was considered that basicity would play an important role to promote isomerization of the intermediate as discussed below. It is worth noting that this order of basicity also was consistent with the deacetylating ability of acetate that was previously reported by us.[4]

The nature of the solvent also affected distribution of cyanohydrin **2** and acid **3** in the reactions catalyzed by TTMPP (Table II). Among the TTMPP–catalyzed reactions, the reaction in acetonitrile produced

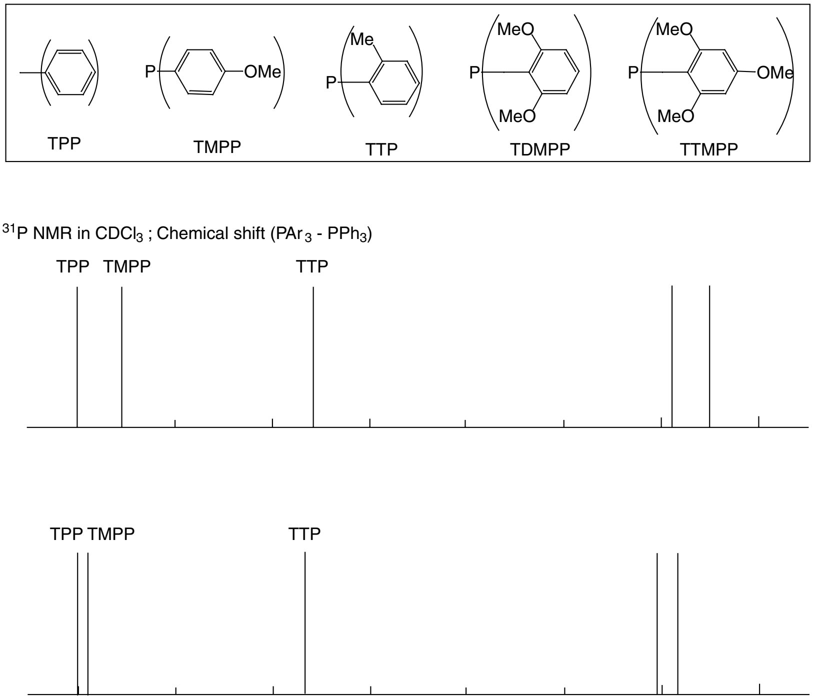


FIGURE 1

Downloaded by [The Aga Khan University] at 05:26 18 October 2014

TABLE II Solvent Effect on the Distribution of 2 and 3 in the Reaction of (*E*)-Cinnamaldehyde With Me_3SiCN in the Presence of 20 mol% TTMPP[a]

		Products (% Yield)[b]	
Entry	Solvent	**2**	**3**
1	CH_3CN	0	90
2	THF	15	76
3	toluene	14	74
4	CH_2Cl_2	42	51
5	DMF	74	14
6	Et_2O	96	1
7	EtOH	56	0

[a] All reactions were carried out in the presence of TTMPP (20 mol%) with 1.2 equiv. Me_3SiCN at r.t. for 2–3.5 h.

[b] Yields of products were the isolated ones after hydrolysis.

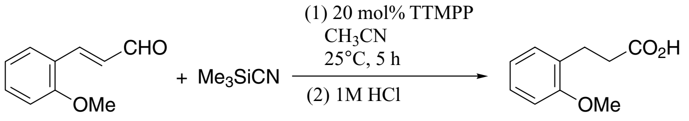
only propionic acid (**3**) in a high yield (Table II, Entry 1). Reactions in other solvents except for acetonitrile afforded a mixture of unsaturated cyanohydrin **2** and saturated acid **3**. In contrast with the reaction in acetonitrile, the reaction in diethyl ether afforded cyanohydrin **2** exclusively (Table II, Entry 6).

When the reaction was carried out in CH_2Cl_2 or DMF in the presence of a catalytic amount of TTMPP, the yield of **3** was significantly reduced and that of **2** was raised (Table II, Entries 4 and 5). In a reaction in ethanol catalyzed by TTMPP, cyanohydrin **2** was produced in a 56% yield after 1M HCl work-up and **3** was not obtained. This result would attributable to the lack of a trimethylsilyl group, which would necessary for the critical rearrangement of cyanohydrin to α-siloxyvinyl cyanide, due to the action of ethanol with trimethylsilyl cyanide to yield HCN and trimethylsilyl ether of ethanol. Actually, treatment of cyanohydrin with 20 mol% of TTMPP did not afford **3** after hydrolysis. The result that stoichiometric amount of trimethylsilyl cyanide is needed to obtain saturated acid **3** from cyanohydrin indicates that trimethylsilyl either protection of cyanohydrin is necessary for TTMPP-catalyzed isomerization.

Reactions of α,β-unsaturated aldehydes other than cinnamaldehyde **1** were also examined. 2- and 4-methoxy-(*E*)-cinnamaldehyde were converted to the corresponding saturated acid **4** and **5** in a high yield by the aid of TTMPP (92% and 77% yield, respectively) (Eqs. 1 and 2).

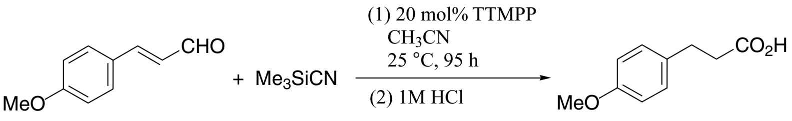
Our present method is superior to the previous ruthenium-catalyzed method in terms of yield of product and mildness of reaction conditions. On the other hand, reactions of α-methyl-(*E*)-cinnamaldehyde, (*E*)-2-

Downloaded by [The Aga Khan University] at 05:26 18 October 2014



4; 92%

(1)



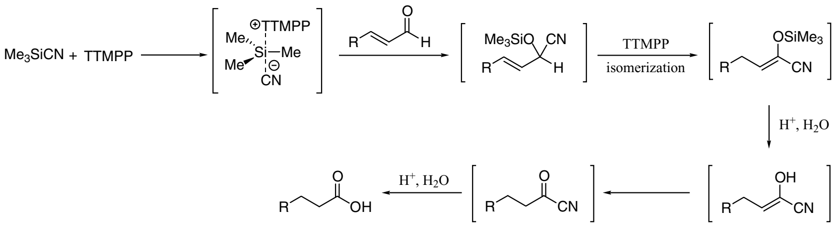
5; 77%

(2)

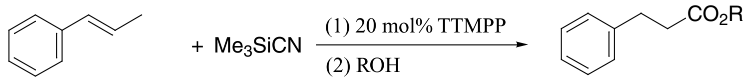
hexenal, and (*E*)-2-nonenal with trimethylsilyl cyanide in the presence of 20 mol% of TTMPP afforded trimethylsilyl ethers of cyanohydrin, exclusively under the same reaction conditions.

As for the mechanism, the reaction was initiated by the coordination of a Lewis base to trimethylsilyl cyanide to form hypervalent silicate, which led to the silylcyanation of aldehydes affording trimethylsilyl ether of cyanohydrin (Scheme 1).

The resultant cyanohydrin trimethylsilyl ether **A** was followed by base-catalyzed isomerization to produce saturated acids after hydrolysis. Trimethylsilyl ether of cyanohydrin could also be used as a substrate. Furthermore, before hydrolysis, the generation of 2-(trimethylsiloxy)acrylonitrile **B**, which was the isomerization product of cyanohydrin trimethylsilyl ether, was confirmed by ^{1}H NMR and mass spectral analyses of the reaction mixture. At this stage, acyl cyanide and cyanohydrin trimethylsilyl ether were not observed. When (*E*)-cinnamaldehyde was treated with trimethylsilyl cyanide in the presence of 5 mol% TTMPP, the ratio of *E*/*Z* isomers of α-trimethylsiloxy vinyl cyanide **B** was 87/13 as was determined by ^{1}H NMR analysis. Aqueous work-up with 1M HCl was necessary to obtain saturated carboxylic acid.



SCHEME 1



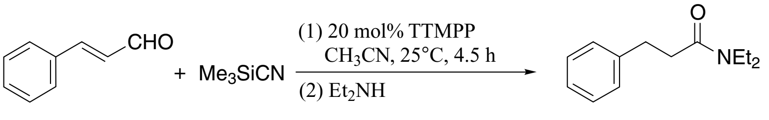
1

R = Me (**6**); 63% (28°C, 6 h)
R = Et (**7**); 69% (21°C, 4.5 h)
R = *i*-Pr (**8**); 46% (20°C, 22 h)

SCHEME 2

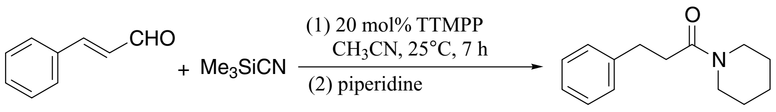
Downloaded by [The Aga Khan University] at 05:26 18 October 2014

As an application of the presented transformation, methanolysis instead of hydrolysis afforded saturated esters in good to high yield. That is, the reaction of (*E*)-cinnamaldehyde (**1**) with trimethylsilyl cyanide by the aid of 20 mol% TTMPP followed by the addition of methanol gave methyl 3-phenylpropionate (**6**) in a 63% yield (28°C, 3.5 h). Ethyl 3-phenylpropionate (**7**) and isopropylpropyl 3-phenylpropionate (**8**) were also obtained by treatment with ethanol or isopropyl alcohol (Scheme 2). Furthermore, quenching by diethylamine or piperidine afforded corresponding amides (**9** and **10**) in 77% and 95% yields, respectively (Eqs. 3 and 4).



(3)

9; 77%



(4)

10; 95%

In conclusion, TTMPP was found to be an effective catalyst for the transformation of cinnamaldehydes into saturated carboxylic acids. Treatment of the reaction mixture with alcohols or amines produced the corresponding saturated esters or amides in a high yield, respectively. We confirmed that the reaction proceeded through base-catalyzed silylcyanation and isomerization of cyanohydrin trimethylsilyl ether, and 2-(trimethylsiloxy)acrylonitrile was found to be a critical intermediate.[11] Furthermore, ^{31}P NMR spectra of TTMPP and related compounds also have been disclosed for the first time.

EXPERIMENTAL

All melting points were measured on a Yanaco MP-500D and are uncorrected. ^{1}H and ^{13}C NMR spectra were recorded on a Varian UNITY INOVA 400 (400 and 100.6 MHz, respectively), a JEOL JNM-LA 400 (400 and 100.6 MHz, respectively), or a Bruker Avance DPX 250 (250 and 62.9 MHz, respectively) using Me_4Si as the internal standard in $CDCl_3$. IR spectra were measured on a Horiba FT-710 or Perkin-Elmer Spectrum 1000. Elemental analyses were performed on a Yanaco CHN Corder MT-5. Mass spectra were measured on a Shimadzu GCMS-QP 2000A. Preparative-column chromatography was carried out on a Fuji–Devison BW-820. TLC was carried out on foil plates, Silica Gel 60 F_{254} (layer thickness 0.2 nm, Merck KGaA, Darmstädt, Germany).

Downloaded by [The Aga Khan University] at 05:26 18 October 2014

Procedure for the Transformation of Cinnamaldehyde to Saturated Carboxylic Acids and Their Derivatives

Caution! The following reactions should be performed in a well-ventilated hood because HCN will be produced on work-up. In a flask were placed (*E*)-cinnamaldehyde (**1**) (1.06 g, 8.0 mmol) and CH_3CN (7 mL). To this mixture were added trimethylsilyl cyanide (1.3 mL, 9.75 mmol) and TTMPP (855 mg, 1.6 mmol). The mixture was stirred at 28°C for 3.5 h. After confirmation of the consumption of aldehyde by TLC analysis, the mixture was poured into the mixture of 1M HCl solution (10 mL) and diethyl ether (10 mL) and stirred vigorously for 3 h at r.t. Usual extractive work-up and then silica-gel column chromatography using hexane–ethyl acetate (3/1) as an eluent gave 3-phenylpropionic acid (**3**) (1.08 g, 90%).

(E)-2-Hydroxy-4-phenyl-3-butenenitrile (2)

In a flask were placed (*E*)-cinnamaldehyde (**1**) (206 mg, 1.56 mmol) and CH_3CN (2 mL). To this mixture were added trimethylsilyl cyanide (0.25 mL, 1.87 mmol) and TMPP (109.8 mg, 0.31 mmol). The whole was stirred at 31°C for 3.5 h. After confirmation of the consumption of aldehyde by TLC analysis, the mixture was poured into the mixture of 1M HCl solution (10 mL) and diethyl ether (10 mL) and stirred vigorously for 3 h at r.t. Usual extractive work-up and then silica-gel column chromatography using hexane–ethyl acetate (3/1) as an eluent gave (*E*)-2-hydroxy-4-phenyl-3-butenenitrile (**2**) (216 mg, 87%). R_f 0.35 (3:1 hexane–ethyl acetate); m.p. 78–79°C (lit.[12] 78°C); IR (KBr): ν_{max} (cm^{-1}) 3370, 3030, 2925, 2820, 2250, 1960, 1655, 1575, 1490, 1450, 1415, 1300, 1120, 1090, 1070, 1025, 975, 925, 820, 755; ^{1}H NMR (250 MHz, $CDCl_3$): δ 3.68 (br s, 1H), 5.13 (d, $J = 6.0$ Hz, 1H), 6.22 (dd, $J = 15.9$ Hz, $J = 6.0$Hz, 1H), 6.87 (d, $J = 15.9$ Hz, 1H), 7.3–7.4 (m, 5H); ^{13}C NMR (62.9 MHz, $CDCl_3$): δ 61.8, 118.2, 122.2, 127.0, 128.8, 129.1, 134.7, 135.3. MS m/z (relative intensity): 159 (48.1%), 130 (100%), 115 (40.0%), 103 (61.1%), 91 (78.8%), 77 (82.1%). Anal. calcd. for $C_{10}H_9NO$: C, 75.45; H, 5.70; N, 8.80. Found: C, 75.61; H, 5.66; N, 8.72.

3-Phenylpropionic Acid (3)

In a flask were placed (*E*)-cinnamaldehyde (**1**) (1.06 g, 8.0 mmol) and CH_3CN (7 mL). To this mixture were added trimethylsilyl cyanide (1.3 mL, 9.75 mmol) and TTMPP (855 mg, 1.6 mmol). The mixture was stirred at 28°C for 3.5 h. After confirmation of the consumption of aldehyde by TLC analysis, the mixture was poured into the mixture of 1M HCl solution (10 mL) and diethyl ether (10 mL) and stirred vigorously for 3 h at r.t. Usual extractive work-up and then silica-gel column chromatography using hexane–ethyl acetate (3/1) as an eluent gave 3-phenylpropionic acid (**3**) (1.08 g, 90%). R_f 0.28 (3:1 hexane–ethyl acetate); m.p. 47–49°C (lit.[13] 46°C); IR (KBr): ν_{max} (cm^{-1}) 3030, 2935, 2700, 2640, 2290, 1950, 1715, 1700, 1680, 1605, 1495, 1455, 1430, 410, 1305, 1220, 930, 785, 755, 725, 700, 535; ^{1}H NMR (250 MHz, $CDCl_3$): δ 2.72 (t, $J = 7.7$ Hz, 2H), 3.00 (t, $J = 7.7$ Hz, 2H), 7.2–7.4 (m, 5H), 11.05 (br s, 1H); ^{13}C NMR (62.9 MHz, $CDCl_3$): δ 30.5, 35.6, 126.3, 128.2, 128.5, 140.1, 179.2. MS m/z (relative intensity): 150 (35.6%), 104 (50.3%), 91 (100%). Anal. calcd. for $C_9H_{10}O_2$: C, 71.98; H, 6.71. Found: C, 71.97; H, 6.74.

3-(2-Methoxyphenyl)propionic Acid (4)

In a flask were placed 2-methoxycinnamaldehyde (205.8 mg, 1.27 mmol) and CH_3CN (2 mL). To this mixture were added trimethylsilyl cyanide (0.2 mL, 1.52 mmol) and TTMPP (135.1 mg, 0.25 mmol). The mixture was stirred at 29°C for 3.5 h. After confirmation of the consumption of aldehyde by TLC analysis, the mixture was poured into the mixture of 1M HCl solution (10 mL) and diethyl ether (10 mL) and stirred vigorously for 3 h at r.t. Usual extractive work-up and then silica-gel column chromatography using hexane–ethyl acetate (3/1) as an eluent gave 3-(2-methoxyphenyl)propionic acid (**4**) (210.8 mg, 92%). R_f 0.30 (3:1 hexane–ethyl acetate); m.p. 90–92°C (lit.[14] 91–92°C); IR (KBr): ν_{max} (cm^{-1}) 3010, 2640, 1710, 1700, 1690, 1495, 1460, 1435, 1405, 1335, 1295, 1245, 1220, 1115, 1050, 1025, 930, 760; ^{1}H NMR (400 MHz, $CDCl_3$): δ 2.66 (t, $J = 7.7$ Hz, 2H), 2.94 (t, $J = 7.7$ Hz, 2H), 3.81 (s, 3H), 6.8–6.9 and 7.1–7.2 (each m, 2H), 10.99 (br s, 1H); ^{13}C NMR (62.9 MHz, $CDCl_3$): δ 25.8, 33.9, 55.1, 110.1, 120.4, 127.7 and 129.9, 128.4, 157.4, 180.0. MS m/z (relative intensity): 180 (35.8%), 121 (100%), 91 (20.6%),

Downloaded by [The Aga Khan University] at 05:26 18 October 2014

77 (24.6%). Anal. calcd. for $C_9H_{10}O_2$: C, 66.65; H, 6.71. Found: C, 66.86; H, 6.71.

3-(4-Methoxyphenyl)propionic Acid (5)

In a flask were placed 4-methoxycinnamaldehyde (226.8 mg, 1.40 mmol) and CH_3CN (2 mL). To this mixture were added trimethylsilyl cyanide (0.22 mL, 1.68 mmol) and TTMPP (148.9 mg, 0.28 mmol). The mixture was stirred at 25°C for 95 h. After confirmation of the consumption of aldehyde by TLC analysis, the mixture was poured into the mixture of 1M HCl solution (10 mL) and diethyl ether (10 mL) and stirred vigorously for 3 h at r.t. Usual extractive work-up and then silica-gel column chromatography using hexane–ethyl acetate (3/1) as an eluent gave 3-(4-methoxyphenyl)propionic acid (**5**) (195.2 mg, 77%). R_f 0.29 (2:1 hexane-ethyl acetate); m.p. 99–104°C (lit.[15] 95–102°C); IR (KBr): $\nu_{\max}$ (cm^{-1}) 2960, 2640, 1710, 1615, 1585, 1510, 1460, 1440, 1420, 1410, 1300, 1280, 1245, 1215, 1180, 1160, 1110, 1030, 960; ^1H NMR (250 MHz, $CDCl_3$): δ 2.65 (t, $J = 7.6$ Hz, 2H), 2.91 (t, $J = 7.6$ Hz, 2H), 3.79 (s, 3H), 6.84 (d, $J = 8.6$ Hz, 2H), 7.13 (d, $J = 8.6$ Hz, 2H), 12.32 (br s, 1H); ^{13}C NMR (62.9 MHz, $CDCl_3$): δ 29.6, 35.8, 55.2, 113.9, 129.2, 132.2, 158.0, 179.3. MS m/z (relative intensity): 180 (33.1%), 134 (20.4%), 121 (84.2%), 91 (100%), 77 (21.1%). Anal. calcd. for $C_9H_{10}O_2$: C, 66.65; H, 6.71. Found: C, 66.62; H, 6.79.

Methyl 3-Phenylpropionate (6)

In a flask were placed (*E*)-cinnamaldehyde (170.7 mg, 1.29 mmol) and CH_3CN (2 mL). To this mixture were added trimethylsilyl cyanide (0.21 mL, 1.55 mmol) and TTMPP (137.6 mg, 0.26 mmol). The mixture was stirred at 28°C for 6 h. After confirmation of the consumption of aldehyde by TLC analysis, the mixture was poured into MeOH (10 mL) and stirred vigorously for 3 h at r.t. Usual extractive work-up and then silica-gel column chromatography using hexane–ethyl acetate (3/1) as an eluent gave methyl 3-phenylpropionate (**6**) (134.2 mg, 63%). R_f 0.41 (10:1 hexane–ethyl acetate); IR (KBr): $\nu_{\max}$ (cm^{-1}) 3030, 2950, 1740, 1730, 1700, 1685, 1655, 1635, 1495, 1455, 1435, 1365, 1295, 1200, 1160, 1080, 1030, 985, 840, 752, 700; ^1H NMR (250 MHz, $CDCl_3$): δ 2.63 (t, $J = 7.8$ Hz, 2H), 2.95 (t, $J = 7.8$ Hz, 2H), 3.66 (s, 3H), 7.2–7.3 (m, 5H); ^{13}C NMR (62.9 MHz, $CDCl_3$): δ 30.8, 35.6, 51.4, 126.1, 128.1, 128.4, 140.4, 173.2. MS m/z (relative intensity): 164 (18.2%), 104 (100%), 91 (71.4%), 77 (19.6%), 65 (13.4%). Anal. calcd. for $C_{10}H_{12}O_2$: C, 73.15; H, 7.37. Found: C, 72.91; H, 7.50.

Downloaded by [The Aga Khan University] at 05:26 18 October 2014

Downloaded by [The Aga Khan University] at 05:26 18 October 2014

Ethyl 3-Phenylpropionate (7)

In a flask were placed (*E*)-cinnamaldehyde (232.0 mg, 1.76 mmol) and CH_3CN (2 mL). To this mixture were added trimethylsilyl cyanide (0.28 mL, 2.11 mmol) and TTMPP (187.0 mg, 0.35 mmol). The mixture was stirred at 21°C for 4.5 h. After confirmation of the consumption of aldehyde by TLC analysis, EtOH (2 mL) was poured into the mixture and stirred vigorously for 3 h at r.t. Usual extractive work-up and then silica-gel column chromatography using hexane–ethyl acetate (3/1) as an eluent gave ethyl 3-phenylpropionate (**7**) (216.7 mg, 69%). R_f 0.43 (10:1 hexane–ethyl acetate); IR (KBr): ν_{max} (cm^{-1}) 3065, 3030, 2980, 2935, 1735, 1605, 1500, 1455, 1375, 1295, 1255, 1205, 1180, 1160, 1080, 1040, 750, 700; ^1H NMR (400 MHz, $CDCl_3$): δ 1.22 (t, $J = 7.3$ Hz, 3H), 2.61 (t, $J = 7.7$ Hz, 2H), 2.94 (t, $J = 7.7$ Hz, 2H), 4.11 (q, 2H, $J = 7.3$ Hz, 2H), 7.2–7.3 (m, 5H); ^{13}C NMR (100.6 MHz, $CDCl_3$): δ 14.1, 30.9, 35.9, 60.3, 126.1, 128.2, 128.4, 140.5, 172.8. MS m/z (relative intensity): 178 (16.3%), 104 (100%), 91 (65.0%), 77 (21.1%). Anal. calcd. for $C_{11}H_{14}O_2$: C, 74.13; H, 7.92. Found: C, 73.96; H, 8.01.

Isopropyl 3-Phenylpropionate (8)

In a flask were placed (*E*)-cinnamaldehyde (258.8 mg, 1.96 mmol) and CH_3CN (2 mL). To this mixture were added trimethylsilyl cyanide (0.31 mL, 2.35 mmol) and TTMPP (208.6 mg, 0.39 mmol). The mixture was stirred at 20°C for 22 h. After confirmation of the consumption of aldehyde by TLC analysis, *i*-PrOH (2 mL) was poured into the mixture and stirred vigorously for 3 h at r.t. Usual extractive work-up and then silica-gel column chromatography using hexane–ethyl acetate (3/1) as an eluent gave isopropyl 3-phenylpropionate (**8**) (172.9 mg, 46%). R_f 0.43 (15:1 hexane–ethyl acetate); IR (KBr): ν_{max} (cm^{-1}) 3090, 3065, 3030, 2980, 2935, 2875, 1725, 1500, 1470, 1455, 1375, 1290, 1260, 1210, 1180, 1145, 1110, 1080, 750, 700; ^1H NMR (400 MHz, $CDCl_3$): δ 1.20 (d, $J = 6.4$ Hz, 6H), 2.58 (t, $J = 7.9$ Hz, 2H), 2.94 (t, $J = 7.9$ Hz, 2H), 5.00 (sept, $J = 6.4$ Hz, 1H), 7.2–7.3 (m, 5H); ^{13}C NMR (100.6 MHz, $CDCl_3$): δ 21.7, 30.9, 36.2, 67.7, 126.1, 128.2, 128.3, 140.5, 172.3. MS m/z (relative intensity): 192 (5.6%), 150 (31.8%), 133 (17.7%), 104 (100%), 91 (99.9%), 77 (22.2%). Anal. calcd. for $C_{12}H_{16}O_2$: C, 74.97; H, 8.39. Found: C, 74.83; H, 8.50.

N,N-Diethyl-3-phenylpropanamide (9)

In a flask were placed (*E*)-cinnamaldehyde (261.6 mg, 1.98 mmol) and CH_3CN (2 mL). To this mixture were added trimethylsilyl cyanide (0.32 mL, 2.38 mmol) and TTMPP (210.8 mg, 0.40 mmol). The mixture was stirred at 20°C for 4.5 h. After confirmation of the consumption of

Downloaded by [The Aga Khan University] at 05:26 18 October 2014

aldehyde by TLC analysis, diethylamine (0.25 mL, 2.38 mmol) was poured into the mixture and stirred vigorously for 3 h at r.t. Usual extractive work-up and then silica-gel column chromatography using hexane–ethyl acetate (3/1) as an eluent gave *N*,*N*-diethyl-3-phenylpropanamide (**9**) (312.6 mg, 77%). R_f 0.13 (6:1 hexane–ethyl acetate); IR (KBr): $\nu_{\max}$ (cm^{-1}) 3060, 3025, 2970, 2935, 2875, 1640, 1605, 1495, 1455, 1430, 1380, 1365, 1265, 1245, 1220, 1140, 1095, 1075, 755, 700; ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.10 (t, $J = 7.3$ Hz, 3H), 1.11 (t, $J = 7.3$ Hz, 3H), 2.59 (t, $J = 7.9$ Hz, 2H), 2.98 (t, $J_{H2-H3} = 7.9$ Hz, 2H), 3.22 (q, $J = 7.3$ Hz, 2H), 3.38 (q, $J = 7.3$ Hz, 2H), 7.2–7.3 (m, 5H); ^{13}C NMR (100.6 MHz, $CDCl_3$): δ 12.9, 14.1, 31.5, 34.9, 40.0, 41.7, 125.9, 128.2, 128.3, 141.3, 171.0. MS m/z (relative intensity): 205 (23.9%), 114 (14.1%), 105 (21.7%), 91 (39.9%), 77 (10.5%), 74 (10.8%), 72 (37%), 58 (100%). Anal. calcd. for $C_{13}H_{19}NO$: C, 76.06; H, 9.33; N, 6.82. Found: C, 76.03; H, 9.36; N, 6.78.

1-(3-Phenylpropanoyl)piperidine (10)

In a flask were placed (*E*)-cinnamaldehyde (310.6 mg, 2.35 mmol) and CH_3CN (2 mL). To this mixture were added trimethylsilyl cyanide (0.38 mL, 2.82 mmol) and TTMPP (250.3 mg, 0.47 mmol). The whole was stirred at 25°C for 7 h. After confirmation of the consumption of aldehyde by TLC analysis, cyclohexylamine (0.28 mL, 2.82 mmol) was poured into the mixture and stirred vigorously for 3 h at r.t. Usual extractive work-up and then silica-gel column chromatography using hexane–ethyl acetate (3/1) as an eluent gave 1-(3-phenylpropanoyl)piperidine(**10**) (483.7 mg, 95%). R_f 0.24 (2:1 hexane–ethyl acetate); IR (KBr): $\nu_{\max}$ (cm^{-1}) 3025, 2935, 2855, 1645, 1605, 1495, 1470, 1435, 1280, 1250, 1220, 1140, 1025, 1010, 855, 750, 700; ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.4–1.6 (m, 6H), 2.62 (t, $J = 7.9$ Hz, 2H), 2.97 (t, $J = 7.9$ Hz, 2H), 3.33 (t, $J = 5.6$ Hz, 2H), 3.56 (t, $J = 5.6$ Hz, 2H), 7.2–7.3 (m, 5H); ^{13}C NMR (62.6 MHz, $CDCl_3$): δ 24.3, 25.3, 26.1, 31.4, 34.9, 42.5, 46.4, 125.9, 128.2, 128.3, 141.2, 170.2. MS m/z (relative intensity): 217 (32.2%), 126 (100%), 105 (15.6%), 91 (37.1%), 84 (55.9%), 77 (11.2%). Anal. calcd. for $C_{14}H_{19}NO$: C, 77.38; H, 8.81; N, 6.45. Found: C, 77.20; H, 8.98; N, 6.50.

REFERENCES

[1] M. Wada and S. Higashizaki, *J. Chem. Soc., Chem. Commun.*, 482 (1984).

[2] S. Matsukawa, N. Okano, and T. Imamoto, *Tetrahedron Lett.*, **41,** 103 (2000).

[3] S. Matsukawa and K. Obu, *Chem. Lett.,* **33,** 1626 (2004).

[4] K. Yoshimoto, H. Kawabata, N. Nakamichi, and M. Hayashi, *Chem. Lett.,* **30,** 934 (2001).

[5] H. Kawabata and M. Hayashi, *Tetrahedron Lett.,* **43,** 5645 (2002) (For preliminary results).

[6] S. Kobayashi, Y. Tsuchiya, and T. Mukaiyama, *Chem. Lett.,* **20,** 537 (1991).

[7] S.-I. Murahashi, T. Naota, K. Ito, Y. Maeda, and H. Taki, *J. Org. Chem.*, **52,** 4319 (1987).

[8] J. G. de Vries, G. Roelfes, and R. Green,*Tetrahedron Lett.*, **39,** 8329 (1998).

[9] (a) U. Hertenstein, S. Hünig, H. Reichelt, and R. Schaller, *Chem. Ber.*, **119,** 722 (1986); (b) S. Hünig and H. Reichelt, *Chem. Ber.*, **119,** 1772 (1986); (c) U. Hertenstein, S. Hünig, H. Reichelt, and R. Schaller, *Chem. Ber.*, **115,** 261 (1982).

[10] Y. Yamashoji, T. Matsushita, M. Tanaka, T. Shono, and M. Wada, *Polyhedron*, **8,** 1053 (1989).

[11] The conversion of (*E*)-cinnamaldehydes to saturated carboxylic acids by treatment of trimethylsilyl cyanide is also catalyzed by amine bases such as 1,4-diazabicyclo[2,2,2]octane (DABCO) (DABCOH$^+ = 8.82$) (R. L. Benoit, M. Lefechette, *Can. J. Chem.*, **65,** 996 (1987) and 1,8-diazabicyclo[5,4,0]undec-7-ene (DBU) (DBUH$^+ = 11.5$) (Ref. 1). For examples, treatment of **1** with 10 mol% DABCO or 5 mol% of DBU also gave **3** in an 85% and 79% yield, respectively. In each case, cyanohydrin **2** was not obtained. However, piperidine (piperidineH$^+ = 11.2$) was inert for the previously discussed conversion. The details will be reported in the near future.

[12] P. J. Gerrits, F. Zumbrägel, and J. Marcus, *Tetrahedron*, **57,** 8691 (2001).

[13] L. D. Luca, G. Giacomelli, S. Masala, and A. Porcheddu, *J. Org. Chem.*, **68,** 4999 (2003).

[14] J. H. P. Tyman, J. Grundy, and G. R. Brown, *J. Chem. Soc., Perkin Trans.* 1, **2,** 336 (1981).

[15] H. O. House and W. C. McDaniel, *J. Org. Chem.,* **42,** 2155 (1977).

Downloaded by [The Aga Khan University] at 05:26 18 October 2014