BCSJ

A Novel Abnormal Michael Reaction of 2-Acylmethyl-4,4-dimethyl-2-oxazolines with Acetylenic Ketones and Esters

Yasuo Tohda,*[1] **Takeshi Yanagidani,**[2] **and Noriko Asaka**[1]

[1]Center for Science Education, Osaka Kyoiku University, 4-698-1 Asahigaoka, Kashiwara, Osaka 582-8582

[2]Department of Material Science, Division of Arts and Science, Osaka Kyoiku University, 4-698-1 Asahigaoka, Kashiwara, Osaka 582-8582

E-mail: tohda@cc.osaka-kyoiku.ac.jp

Received: November 17, 2015; Accepted: February 5, 2016; Web Released: July 15, 2016

Yasuo Tohda
Yasuo Tohda received his Ph.D., supervised by Prof. N. Hagihara, in 1978 from Osaka University. He moved to Osaka Kyoiku University in 1976, and has been a professor of Osaka Kyoiku University since 1991 till 2014. He is an appointed professor in Center for Science Education, Osaka Kyoiku University.

Abstract
The first example of abnormal Michael reaction of an active methylene compound, 2-acylmethyl-4,4-dimethyl-2-oxazoline with acetylenic ketone in acetonitrile is reported. The reaction accompanies 1,3-migration of the acyl group of the substrate to give 2-(3-acyl-1-buten-4-on-1-yl)-2-oxazoline, which was easily cyclized to 5-acyl-2-pyridone derivatives by treatment with silica gel. Selectivity of the reaction depends on bulkiness of all the substituents of both the substrate and the reagent. The selectivity is interpreted in terms of reduced kinetic acidity of an initial anionic adduct intermediate by both steric and electronic factors.

1. Introduction

Abnormal Michael reaction of enolates with acetylenic acceptors, which accompanies a 1,3-shift of the donor acyl group, has been of interest from both synthetic and mechanistic points of view,[1] although few examples of the reaction have been reported.[2] The reaction has been applied to an [n+2] ring expansion of the cyclic ketones whose α-methine proton is activated by alkoxycarbonyl,[3,4] phosphono,[5] or sulfonio groups[6] with acetylenic esters. All the reported abnormal Michael reactions of enolates with acetylenic acceptors are thought to proceed via the same mechanism which involves 2-cylobutenolate anion as a key intermediate **C** (Scheme 1).[2–6] Although facile ring openings of 2-cyclobutenolates[7] or their benzo-analogues[8] have been well documented, abnormal Michael reaction is not so general that only Michel adducts are often yielded even under controlled conditions.[4] Difficulty of the reaction may be due to instability of highly strained 2-cyclobutenolate intermediate **C**.

Scheme 1 shows the expected mechanisms of both Michael and abnormal Michael reactions which are applied to reaction of 2-acylmethyl-4,4-dimethyl-2-oxazolines **1** (R^1), which is an active methylene compound. According to the scheme, abnormal Michael reaction of **1** seems to be quite difficult, because the first anionic adduct **A** still has one acidic proton. Thus fast proton-transfer of **A** should lead **A** to more stable anionic intermediate **B**, which is so stable that it cannot form highly strained cyclic intermediate **C**.

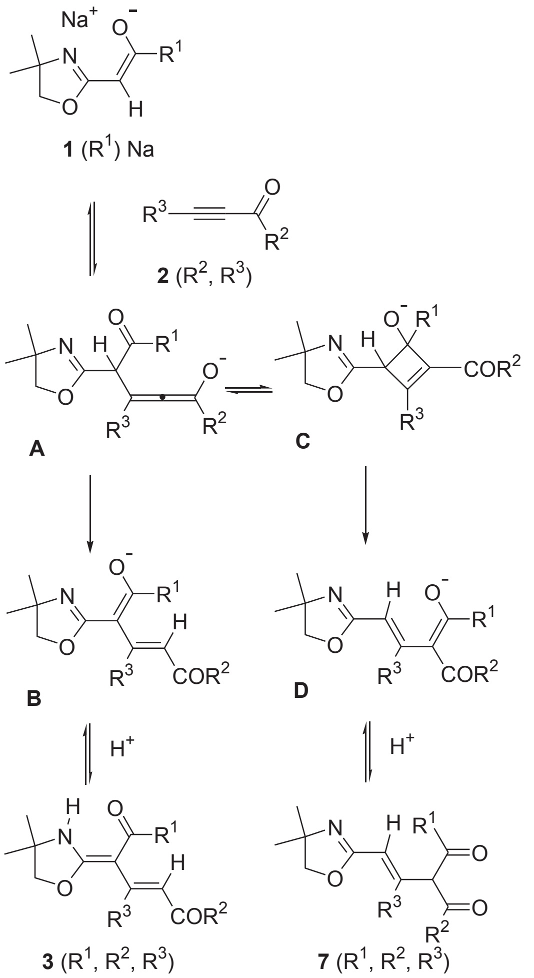
To our best knowledge, there have been reported no examples of abnormal Michael reaction of active methylene compounds as the substrate. Although this fact seems to be quite reasonable according to the accepted mechanism (Scheme 1), we have found that abnormal Michael reaction of **1** (R^1) with acetylenic ketone **2** (R^2, R^3) in acetonitrile occurs quite selectively. Here we wish to report the first example of abnormal Michael reaction of an active methylene compound **1** and scope and limitations of the reaction.

Unfortunately Michael adduct **3** is quite reactive. In a previous paper, we reported that linear Michael adduct **3** easily isomerized to 2-pyridone derivatives, **4** and **5**, or benzene derivative **6** during isolation (Scheme 2).[9] So, linear abnormal Michael adduct **7** may be isolated as some 2-pyridone derivatives by similar transformations.

2. Results and Discussion

Identification of Abnormal Michael Adducts 7–11. When sodium salt of **1** (R^1) was treated with **2** (R^2, R^3) in acetonitrile, expected Michael adducts **3**–**6** did not form at all in many cases or were yielded as minor products. The main products in this reaction were isomers **7**–**10**, of which ^{1}H NMR spectra were very similar with those of corresponding Michael adducts **3**–**5**. The results are summarized in Table 1. Because abnormal Michael reaction causes scrambling of the two acyl groups of both the donor (COR^1) and the acceptor (COR^2) as shown in Scheme 1, clear evidence for the reaction can be shown in some ways.

The first evidence was obtained from reactions in which the two acyl groups of donor **1** and accepter **2** are the same and



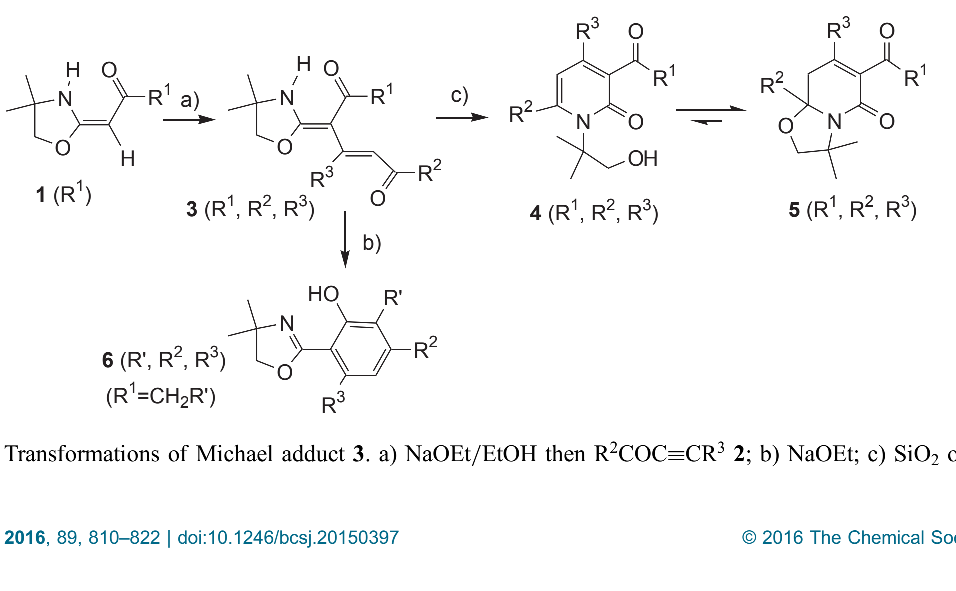
Scheme 1. Competitive mechanisms of Michael and abnormal Michael reaction of **1** with **2**.

bulky (Runs 1 and 2 in Table 1). In this case, only acyclic products **7** (*t*-Bu, *t*-Bu, Ph) and **7** (*i*-Pr, *i*-Pr, Ph) were afforded. The ^{1}H and ^{13}C NMR spectra of these adducts show that the two acyl groups are equivalent, indicating that they are abnormal Michael adducts **7** (Scheme 3). Although the conversions of **1** in Runs 1 and 2 were not good due to bulkiness of the substituents of both **1** and **2**, the selectivity of abnormal Michael reaction is so high that no Michael adducts could be found at all.

The second proof was obtained by the results of some pairs of reactions in which the two acyl groups of the donor and the acceptor were exchanged with each other (Scheme 3 and Runs 3–10 in Table 1). If abnormal Michael reaction occurred, the same scrambled product **7** (R^1, R^2, R^3) was formed from a pair of the reaction of **1** (R^1) with **2** (R^2, R^3) and that of **1** (R^2) with **2** (R^1, R^3). Actually the same 1-(2-hydroxy-1,1-dimethylethyl)-2-pyridone derivatives, **8** (R^4, R^5, R^3) or **9** (R^4, R^5, R^3), were obtained as the main product (Runs 3–8). It is evident that pyridone derivative **8** is formed by cyclization of **7**, because similar cyclization of **3** (R^1, R^2, R^3) to **4** (R^1, R^2, R^3) had been found to proceed quite smoothly (Scheme 2). In the presentation of the 2-pyridones as **8** (R^4, R^5, R^3), the left side substituent (R^4) in the parentheses is the substituent at C-6 position of 2-pyridone **8** and the middle substituent (R^5) in the parentheses is that on the 5-acyl group of **8**. A set of substituents (R^4, R^5) in **8** comes from either a set of (R^1, R^2) or (R^2, R^1) of the reaction components due to the scrambling of the acyl groups.

Another isomeric 2-pyridone derivative **9** (R^4, R^5, R^3) was also isolated (Runs 5, 6, 9, and 10). Its NMR and IR spectra are very similar to those of the 3-acyl-2-pyridone analogue **5**.[9]

Since the same scrambling of the acyl groups was also observed in a pair of the reactions (Runs 9 and 10), **9** (Me, Ph, Ph) was shown to be another type of the product derived from abnormal adduct **7** (Me, Ph, Ph). Another type of product, **10** (R^4, R^5, R^3) was also isolated from the reaction mixtures (Runs 3 and 4). Since **9** was easily converted into **10** by treatment with sodium ethoxide (Scheme 4 and Table 4), it is evident that **9** (R^4, R^5, R^3) and **10** (R^4, R^5, R^3) are tautomeric isomers of 8-acylpyrido[2,1-*b*]oxazolidines. It is quite easy to distinguish the two isomers: Among the 2-pyridone moieties of **9** and **10**, the former has a pair of methylene protons, on the other hand, the latter has two methine protons.

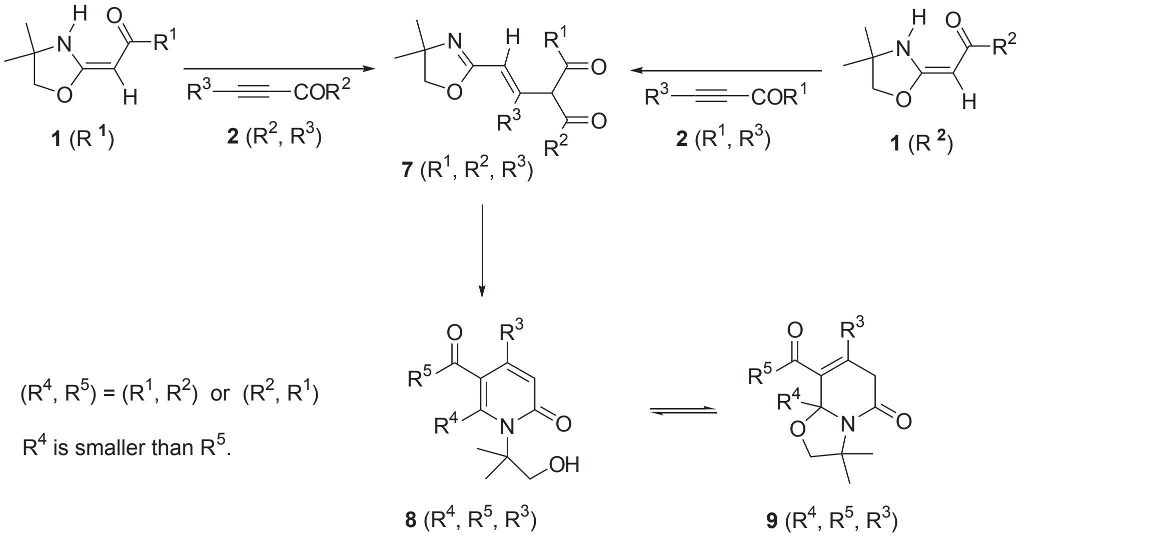


Scheme 2. Transformations of Michael adduct **3**. a) NaOEt/EtOH then $R^2COC{\equiv}CR^3$ **2**; b) NaOEt; c) SiO_2 or NaOEt.

Table 1. Selectivities of abnormal Michael addition of **1** (R^1) with acetylenic ketones **2** (R^2, R^3)

Run	Substrate **1**	Reagent **2**		Conditions		Conversion of **1**/%	Selectivity of the reaction[a)]/%	Abnormal Michael adducts/%								Michael adduct/%			
	R^1	R^2	R^3	Temp/°C	Time/h			(R^4, R^5)[c)]	**7**	**8**	**9**	**10**	**11**	**12**[b)]	**14**	**3**	**4**	**5**	**6**
1	*t*-Bu	*t*-Bu	Ph	rt	4	70	100	—	62	0	0	0	0	0	—	0	0	0	—
2	*i*-Pr	*i*-Pr	Ph	rt	28	40	100	—	87	0	0	0	0	0	—	0	0	0	—
3	*t*-Bu	Ph	Ph	rt	28	100	100	(Ph, *t*-Bu)	0	66	0	17	4	12	—	0	0	0	—
4	Ph	*t*-Bu	Ph	rt	6	84	92	(Ph, *t*-Bu)	0	68	1	7	4	3	—	7	0	0	—
5	*i*-Pr	Ph	Ph	rt	4	100	100	(Ph, *i*-Pr)	0	49	11	0	0	0	—	0	0	0	—
6	Ph	*i*-Pr	Ph	rt	6	71	100	(Ph, *i*-Pr)	0	58	29	0	0	0	—	0	0	0	—
7	*t*-Bu	2-furyl	Ph	rt	5	100	100	(2-furyl, *t*-Bu)	0	73	0	0	0	0	—	0	0	0	—
8	2-furyl	*t*-Bu	Ph	rt	6	87	100	(2-furyl, *t*-Bu)	0	81	0	0	0	0	—	0	0	0	—
9	Me	Ph	Ph	rt	5	100	65	(Me, Ph)	0	0	57	0	0	0	—	0	21	0	0
10	Ph	Me	Ph	rt	5	77	100	(Me, Ph)	0	0	84	0	0	0	—	0	0	0	0
11	Et	Ph	Ph	rt	5	100	70	(Et, Ph)	0	4	54	0	0	0	—	0	7	0	18
12	Bu	Ph	Ph	rt	5	100	71	(Bu, Ph)	0	0	46	0	0	0	—	0	14	0	5
13	Ph	Ph	Ph	rt	5	96	77	(Ph, Ph)	0	34	25	0	6	0	—	0	19	0	—
14	*p*-tolyl	Ph	Ph	rt	2	99	71	mixture[d)]	0	36	17	0	0	0	—	0	22	0	—
15	Ph	*p*-$C_6H_4NO_2$	Ph	rt	2	96	61	(*p*-$C_6H_4NO_2$, Ph)	0	0	38	0	0	0	—	0	0	24	—
16	Ph	Ph	Bu	rt	5	100	47	(Ph, Ph)	0	34	0	0	0	0	—	0	39	0	—
17	Ph	Ph	H	rt	1	100	0	—	0	0	0	0	0	0	—	97	0	0	—
18	Ph	Me	H	rt	5	100	0	—	0	0	0	0	0	0	—	94	0	0	—
19	CF_3	Ph	Ph	reflux	20	71	100	—	0	0	0	0	0	0	95	0	0	0	—
20	CCl_3	Ph	Ph	reflux	20	57	100	—	0	0	0	0	0	0	72	0	0	0	—

a) The selectivity of the reaction is given by a ratio of a total yield of abnormal Michael adducts **7**–**12** vs. a total yield of all the adducts **3**–**12**. b) Product **12** was postulated as one of the abnormal adducts. c) R^4 is the substituent at C-6 and R^5 is that of 5-acyl group of 2-pyridone derivatives **8**–**10**. d) An about 1:1 mixture of (Ph, *p*-tolyl) and (*p*-tolyl, Ph) of **8** and **9** was yielded.



Scheme 3. A proof of abnormal Michael reaction: The same products **7**–**9** were obtained from a pair of the reactions due to the scrambling of the two acyl groups.

It is worth to mention that only one of the two possible pyridone isomers **8** (R^1, R^2, R^3) or **8** (R^2, R^1, R^3) from **7** (R^1, R^2, R^3) is afforded usually, when R^1 is not the same as R^2. Although the two substituents, R^4 and R^5, on the pyridone **8**, **9**, or **10** originate from either R^1 or R^2 of the substrate and the reagent, R^4 is always smaller than R^5 (Scheme 3). Previously we had found that the conversion of linear adduct **3** (R^1, R^2, R^3) to 2-pyridone derivative **4** (R^1, R^2, R^3) was very sensitive to bulkiness of the terminal acyl group (COR^2) of **3**.[9] This fact strongly indicates that there is fatal steric hindrance between the bulky 4,4-dimethyl-2-oxasolinyl group and the large terminal acyl group in cyclization of **7** to **8**. When R^1 and R^2 were *p*-nitrophenyl and phenyl groups (Run 15), the more electron-withdrawing *p*-nitrophenyl group came to be R^4. If the two groups were similar such as phenyl and *p*-tolyl groups (Run 14), both of the two possible 2-pyridone isomers were yielded. Thus, the following sequence of reactivity of the acyl group (COR^4) of linear adduct **7** (R^4, R^5, R^3) in the cyclization to **8** (R^4, R^5, R^3) was found:

$$R^4\text{: Me} \approx \text{Et} > p\text{-C}_6\text{H}_4\text{NO}_2 > \text{Ph} \approx p\text{-tolyl} \gg i\text{-Pr}, t\text{-Bu} \quad (1)$$

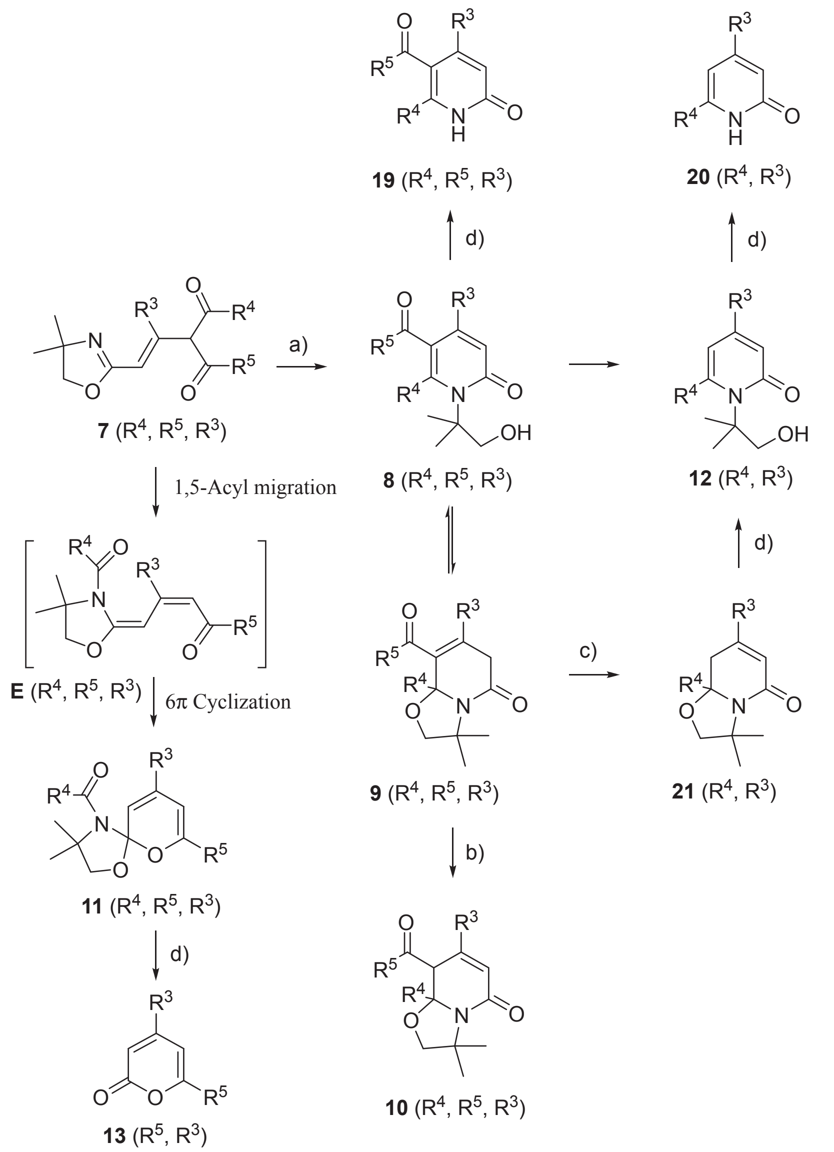
In some cases (Runs 3, 4, and 13) another type of isomer **11** (R^4, R^5, R^3) was isolated as a minor product. Hydrolysis of **11** (R^4, R^5, R^3) gave 4,6-disubstituted 2-pyrones **13** (R^5, R^3) quantitatively (Scheme 4 and Table 4). The transformation indicates that **11** has an acid-sensitive *N*,*O*-acetal function. Since the same product **11** (*t*-Bu, Ph, Ph) was obtained from the scrambling pair of the reactions (Runs 3 and 4 in Table 1), the results strongly indicated that **11** was also another type of the products via the abnormal Michael reaction. From these facts, the structure of **11** (*t*-Bu, Ph, Ph) was estimated as shown in Scheme 4. The formation of **11** can be interpreted as the following: 1,5-Acyl shift of **7** gives an *N*-acyl 2-oxazoline intermediate **E**, which undergoes 6π cyclization to give **11** (Scheme 4). The higher migrability of benzoyl group than that of pivaloyl group in **7** (*t*-Bu, Ph, Ph) is reasonable because of the bulkiness of pivaloyl group.

In Run 3, 1-(2-hydroxy-1,1-dimethyl)-4,6-diphenyl-2-pyridone (**12**) was provided in 12% yield. This is a deacylated product from either Michael adduct **4** (*t*-Bu, Ph, Ph) or abnormal Michael adduct **8** (Ph, *t*-Bu, Ph). Because selectivities of the similar reactions in Table 1 are quite high, it is reasonable to postulate that **12** is formed via abnormal Michael adducts rather than via the corresponding Michael adducts.

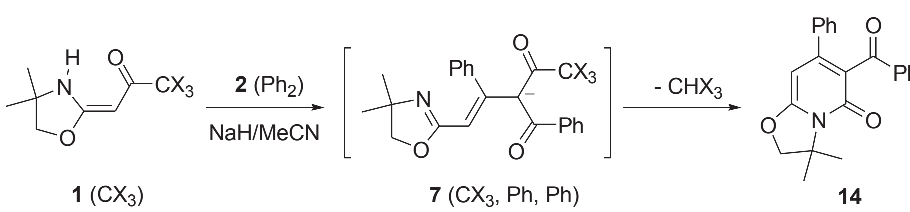
Abnormal Michael Adduct 14 of Trihalomethyl Ketones 1 (CX_3) with Acetylenic Ketone 2 (Ph_2). The reactions of trihalomethyl ketones **1** (CX_3) (X = Cl and F) with **2** (Ph_2) were very slow due to their low nucleophilicity (Runs 19 and 20 in Table 1). Only one product **14** (Ph_2) was afforded from the two substrates **1** (CCl_3) and **1** (CF_3). Product **14** (Ph_2) was the same as an abnormal Michael product of the reaction of **1** (Ph) with methyl phenylpropiolate **2** (OMe, Ph) (see next section). It is obvious that **14** is formed by elimination of trihalomethanes from **7** (CX_3, Ph, Ph) as shown in Scheme 5. In this case no products via Michael reaction were detected at all.

Abnormal Michael Adduct 14 and Michael Adduct 15 by the Reaction of 1 (Ph) with Acetylenic Esters. As the electrophile of the reaction, acetylenic esters **2** (OMe, R^3) were also reacted with **1** (Ph) in acetonitrile (Scheme 6 and Table 2). Reactive acetylenes such as DMAD and methyl propiolate gave only an 8-acylpyrido[2,1-*b*]oxazolidine **15** (Ph, R^3), which was formed via an intramolecular cyclization of Michael adduct **3** (Ph, OMe, R^3). Similar type of compounds were reported by reactions of analogous acylketene *N*,*O*-, *N*,*S*-, and *N*,*N*-acetals with acetylenic esters.[10] Methyl phenylpropiolate **2** (OMe, Ph) was less reactive than DMAD or methyl propiolate in this reaction, but gave a 6-acylpyrido[2,1-*b*]oxazolidine **14** (Ph_2), which was formed by the cyclization of abnormal Michael adduct **7** (Ph, OMe, Ph), in a selectivity of 67% as well as the isomeric pyrido[2,1-*b*]oxazolidine **15** (Ph_2). These results show that acetylenic esters are less selective than acetylenic ketones in abnormal Michael reaction of **1**.

Solvent Effect of the Reaction. Several aprotic solvents were used for the reaction of **1** (*t*-Bu) with **2** (Ph_2). The results are shown in Table 3. Acetonitrile was found to be most



Scheme 4. Transformations of abnormal Michael adduct **7**. a) SiO_2. b) NaOEt/EtOH, rt. c) NaOH/EtOH, reflux. d) H^+/EtOH, reflux.



Scheme 5. Abnormal Michael reaction of **1** (CX_3) with **2** (Ph_2).

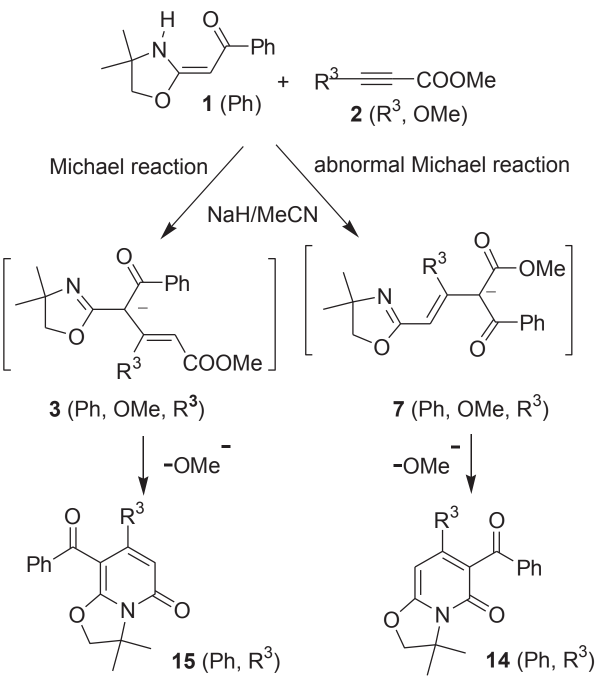
suitable for the abnormal Michael reaction. Although addition of **1** with **2** proceeds more rapidly in THF or benzene than in acetonitrile, selectivities of the abnormal Michael reaction were lower in such solvents. In ethanol, abnormal Michael reaction is perfectly quenched (Table 3, Run 4).[9] Even a small amount of methanol in acetonitrile lowered the selectivity of the reaction significantly (Table 2, Run 2).

Substituent Effects of Substrate 1 and Reagent 2. The substituent effects of R^1 on **1** and R^2 and R^3 on **2** were estimated from the distribution of the products (Table 1). By-products are Michael adducts **3–6**, but yields of them were low in many cases. The results show that the selectivity of the reaction depends on bulkiness of all the substituents (R^1, R^2, and R^3) of **1** and **2**. When the substituents are more bulky, the reaction is more selective and slower. As the substrate of abnormal Michael reaction, **1** (*t*-Bu) and **1** (*i*-Pr) are more selective but less reactive than **1** (Me) and **1** (Ph), although the latter substrates give the abnormal Michael adducts in significant selectivities. The effect of the acyl group of acetylenic ketone **2** (R^2, R^3) is similar with that of **1** (R^1). When R^2 is more bulky, **2**

is more selective and less reactive. When R^3 is hydrogen, abnormal Michael reaction does not occur even when R^1 and R^2 are bulky. The substituent effect of R^3 in the reaction decreases in the following order:

$$R^3\text{: Ph} > \text{Bu} \gg \text{H} \qquad (2)$$

Another Cyclic Imino Ester as the Substrate of Abnormal Michael Reaction. In order to understand the reason why **1** exceptionally undergoes abnormal Michael reaction, an analogous cyclic imino ester derivative **16** was treated with **2** (Ph_2)



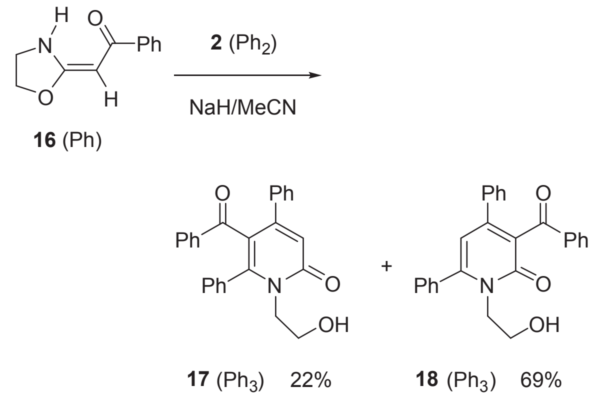
Scheme 6. Reaction of **1** (Ph) with acetylenic esters **2** (OMe, R^3).

Table 2. Reaction of **1** (Ph) with acetylenic esters **2** (OMe, R^3)

Run	Reagent **2** R^3	Conditions	Conversion of **1** /%	Yields of products/% **14**	**15**
1	Ph	reflux	72	67	33
2	Ph	reflux[a)]	90	12	88
3	CO_2Me	rt	100	0	94
4	H	rt	100	0	91

a) As a solvent, a mixture of methanol (0.1 g) and acetonitrile (20 mL) was used.

in acetonitrile. Substrate **16**, which was the 4,4-demethylated analogue of **1** (Ph), gave two isomeric 2-pyridones **17** and **18** in 22% and 69% yields, respectively (eq 3). Because **18** was the same product from the reaction of **1** with **2** (Ph_2) in ethanol,[9] **18** was a Michel adduct. Thus we assigned **17** as an abnormal Michael adduct. The selectivity of the abnormal Michael reaction is 24%. Since the selectivity of the corresponding reaction of **1** (Ph) is 77%, **1** (Ph) is a better substrate for abnormal Michael reaction than **16**.



(3)

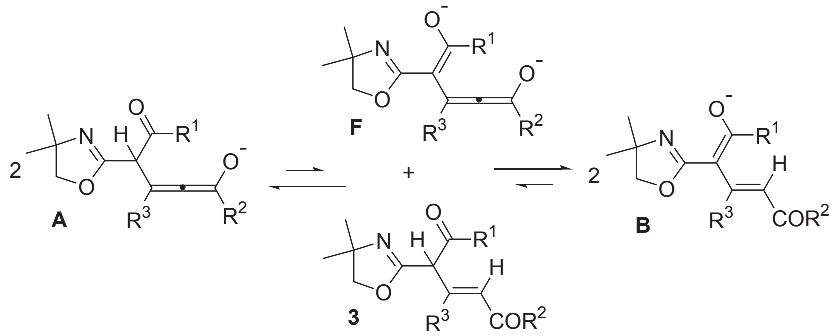
Mechanism of the Abnormal Michael Reaction. There has been no example of abnormal Michael reaction of any active methylene compounds except for 2-acylmethyl-2-oxazoline **1**. Why does **1** give abnormal Michael adducts so selectively? According to the accepted mechanism shown in Scheme 1,[2–6] the 1,3-proton-transfer process of intermediate **A** to stabilized anion **B** should be slower than the 1,3-acyl-transfer process of intermediate **A** to stabilized anion **D** in this case (Scheme 1). The difficulty of the proton-transfer in this case is interpreted by the following two factors. The first one is the kinetically reduced acidity of the active methine proton of **A** by the bulky substituents around the proton. They are R^1, R^2, R^3, and 2-(4,4-dimethyl-2-oxazolinyl) group. The second one is the thermodynamically reduced acidity of **A** by the 2-(2-oxazolinyl) group, which is less electron-withdrawing than either the acyl group of β-diketones or the alkoxycarbonyl group of β-keto esters.

As shown in Scheme 7, we think that the possible mechanisms of 1,3-proton shift of intermediate **A** to **B** in aprotic solvents involve two proton abstractions. The first one is intermolecular proton abstraction of **A**, which gives dianion **E** and **3**. The second one is the proton abstraction of **E** from **3** to give the final Michael adduct **B**. Because both the kinetic and thermodynamic acidities of **A** are reduced as mentioned above and the basicity of **A** is reduced by large substituent R^2, the first proton transfer is slow enough to facilitate the cyclization of **A** to cyclobutenolate intermediate **C**. These are the reasons why

Table 3. Selectivities of abnormal Michael addition of **1** (*t*-Bu) with **2** (Ph_2) and sodium hydride in some solvents

Run	Solvent	Time /h	Conversion of **1**/%	Selectivity[a)] of the reaction/%	Abnormal Michael adducts/% **7**	**8**	**9**	**10**	**11**	**12**[b)]	Michael adduct/% **3**	**4**	**5**
1	Acetonitrile	5	100	100	0	66	0	17	4	12	0	0	0
2	THF	3	100	92	0	63	0	0	7	3	0	6	0
3	Benzene	2	100	33	0	21	0	0	2	1	0	49	0.5
4	Ethanol	5	59	0	0	0	0	0	0	0	0	0	92

a) The selectivity of the reaction is given by a ratio of a total yield of abnormal Michael adducts **7**–**12** vs. a total yield of all the adducts **3**–**12**. b) Product **12** was postulated as one of the abnormal adducts.



Scheme 7. A mechanism of 1,3-proton shift of **A** to **B** in aprotic solvents.

active methylene compounds 2-acylmethyl-2-oxazoline **1** can undergo abnormal Michael reaction with acetylenic acceptors in acetonitrile. Although the effect of each factor is not so large, the total effects may make the abnormal Michael reaction of **1** with **2** possible.

In less polar solvent such as benzene or THF, relative basicity of **A** becomes stronger and cyclobutenolate intermediate **C** becomes less stable than in polar acetonitrile. Thus the transformation of **A** to **B** should be faster in less polar solvents. On the other hand, one can predict abnormal Michael reaction becomes more selective in more polar solvents such as DMF and DMSO, but we could not get better results. We think there are two reasons. One is because of more reduced nucleophilicity of **1** in more polar solvents. That makes the reaction slower. And another is because of difficulty of keeping the solvent free from water during the experiment. Water or protic solvents such as alcohols are not suitable for the reaction, because such proton sources promote the conversion of **A** to **B** quite efficiently to quench the reaction.

Transformations of the Adducts. Several transformations of the abnormal Michael adducts **8–10** were found to occur and most of them were very similar with those of the Michael adducts **3–6**.[9] Thus 5-acyl-2-pyridone derivatives **8** were formed during purification of linear adducts **7** by silica gel column chromatography unless both of the acyl substituents were bulky. Among 5-acyl-2-pyridone derivatives, **8** and **9** could be converted into *N*-dealkylated 5-acyl-2-pyridone **19** by treatment with conc. hydrochloric acid or sulfuric acid in alcohols. On the other hand, 5-acyl-2-pyridone derivatives **17** and **18**, which have a primary *N*-alkyl group, cannot dealkylate at all under similar conditions. Thus dealkylation of **8**, which has a tertiary *N*-alkyl group, to **19** should proceed via S_N1 mechanism.

When adducts **8** and **9** were treated with sodium ethoxide in hot ethanol, deacylated product **21** was obtained in good yields, which could also be converted to *N*-unsubstituted 4,6-disubstituted 2-pyridone **20** by treatment with hydrochloric acid. On the contrary, when **8** and **9** were allowed to react with sodium ethoxide at room temperature, isomeric 5-acyl-2-pyridone derivative **10** was precipitated quantitatively, which did not change at all under the reflux conditions with sodium hydroxide or hydrochloric acid (Runs 9 and 15 in Table 4). These transformations are summarized in Scheme 4 and Table 4. From these results, abnormal Michael reactions of 2-acylmethyl-4,4-dimethyl-2-oxazoline **1** with acetylenic ketone or ester **2** can afford a variety of 2-pyridone derivatives **8–10**, **12**, and **19–21**, efficiently.

3. Conclusion

Abnormal Michael reaction of 2-acylmethyl-4,4-dimethyl-2-oxazoline (**1**) with acetylenic ketones **2** in acetonitrile was found to occur selectively. This is the first example of abnormal Michael reaction of activated methylene ketones. The reason why the substrate undergoes abnormal Michael reaction so selectively is rationalized by three factors which make the 1,3-proton transfer of the initial anionic adduct **A** difficult. The first factor is reduced kinetic acidity of the active methine proton of the anionic adduct. The proton is protected by three bulky substituents on the same α-carbon atom. They are a 2-(2-oxazoinyl) group, R^1, R^2, and R^3. The second factor is reduced thermodynamic acidity of the proton by less electron-withdrawing ability of 2-(2-oxazoinyl) group compared with that of alkoxycarbonyl or acyl groups in the corresponding reagents of β-keto esters or β-diketones. The third factor is reduced basicity of **A** due to the bulky acyl substituent R^2.

4. Experimental

General. The melting points were measured on a Yanagimoto micro-melting point apparatus. IR spectra were obtained with a JEOL JIR-Diamond 20 FT-IR spectrophotometer as KBr disks. NMR spectra were recorded in chloroform-*d* using TMS as an internal standard at 400 MHz (^{1}H NMR) and 100 MHz (^{13}C NMR) on a Bruker DPX 400 spectrometer. FAB mass spectra were recorded on a JEOL JMS-AX505HA. Column chromatography was conducted on silica gel (Wakogel C-200), available from Wako Pure Chemical Industries. Solvents were dried and distilled before use. Acetonitrile was dried on calcium hidride. 2-Acylmethyl-2-oxazolines (**1**) were prepared by reported methods.[11,12] Acetylenic ketones **2** were prepared by the Sonogashira coupling[13] of terminal acetylenes with acid chlorides[14] or oxidation of acetylenic alcohols.[15]

Preparation of 4,4-Dimethyl-2-(3,3,3-trifluoro-2-oxopropyl)-2-oxazoline [1 (CF_3)]. A solution of trifluoroacetic anhydride (9.24 g, 44 mmol) in acetonitrile (30 mL) was added to a solution of 2,4,4-trimethyl-2-oxazoline[16] (2.26 g, 20 mmol) and pyridine (3.48 g, 44 mmol) in acetonitrile (10 mL) with stirring at 0 °C for 1 h. The mixture was allowed to stand at 0 °C for 5 h, then water and ice was added to the mixture. A chloroform extract was washed with brine and dried over sodium sulfate. After removal of the solvent, the residue was recrystal-

Table 4. Transformations of abnormal Michael adducts **8**–**11** and **21**

Run	Substrate	Reagent	Conditions			Product	Yield/%
			Solvent	Temp	Time/h		
1	**8** (Ph, Ph, Ph)	KOH	EtOH	rt	1	**10** (Ph, Ph, Ph)	quantitative
2	**9** (Ph, Ph, Ph)	KOH	EtOH	rt	6	**10** (Ph, Ph, Ph)	quantitative
3	**8** (Ph, *t*-Bu, Ph)	KOH	EtOH	rt	3	**10** (Ph, *t*-Bu, Ph)	97
4	**8** (Ph, *i*-Pr, Ph)	NaOEt	EtOH	rt	3	**10** (Ph, *i*-Pr, Ph)	95
5	**8** (2-furyl, *t*-Bu, Ph)	NaOEt	EtOH	rt	4	**10** (2-furyl, *t*-Bu, Ph)	88
6	**9** (Me, Ph, Ph)	NaOEt	EtOH	rt	0.5	**10** (Me, Ph, Ph)	76
7	**8** (Ph, Ph, Ph)	KOH	EtOH	reflux	6	**21** (Ph, Ph)	89
8	**9** (Ph, Ph, Ph)	KOH	EtOH	reflux	6	**21** (Ph, Ph)	92
9	**10** (Ph, Ph, Ph)	KOH	EtOH	reflux	6	no reaction	—
10	**8** (2-furyl, *t*-Bu, Ph)	KOH	EtOH	reflux	3	**10** (2-furyl, *t*-Bu, Ph)	64
11	**9** (Me, Ph, Ph)	KOH	EtOH	reflux	4	**21** (Me, Ph)	94
12	**9** (Et, Ph, Ph)	KOH	EtOH	reflux	4	**21** (Et, Ph)	96
13	**8** (Ph, Ph, Ph)	conc-HCl	MeOH	reflux	1	**19** (Ph, Ph, Ph)	97
14	**9** (Ph, Ph, Ph)	conc-HCl	MeOH	reflux	1	**19** (Ph, Ph, Ph)	96
15	**10** (Ph, Ph, Ph)	conc-HCl	MeOH	reflux	6	no reaction	—
16	**10** (Ph, Ph, Ph)	conc-HCl	MeOH	reflux	6	no reaction	—
17	**8** (Ph, *t*-Bu, Ph)	conc-HCl	MeOH	reflux	1	**19** (Ph, *t*-Bu, Ph)	97
18	**8** (Ph, *i*-Pr, Ph)	conc-HCl	MeOH	reflux	1	**19** (Ph, *i*-Pr, Ph)	96
19	**8** (2-furyl, *t*-Bu, Ph)	conc-HCl	MeOH	reflux	1	**19** (2-furyl, *t*-Bu, Ph)	91
20	**9** (Me, Ph, Ph)	conc-H_2SO_4	EtOH	reflux	2	**19** (Me, Ph, Ph)	78
21	**9** (Et, Ph, Ph)	conc-H_2SO_4	EtOH	reflux	2	**19** (Et, Ph, Ph)	96
22	**21** (Me, Ph)	conc-H_2SO_4	EtOH	reflux	30	**20** (Me, Ph)	81
23	**21** (Et, Ph)	conc-H_2SO_4	EtOH	reflux	20	**20** (Et, Ph)	83
24	**11** (Ph, *t*-Bu, Ph)	conc-H_2SO_4	EtOH	reflux	1	**13** (*t*-Bu, Ph)	96
25	**11** (Ph, Ph, Ph)	conc-H_2SO_4	EtOH	reflux	3	**13** (Ph, Ph)	82

lized from hexane to give 3.87 g (18.5 mmol, 93%) of **1** (CF_3). Mp 141–142 °C (colorless prisms). IR: 3280, 1645, 1574, 1510, 1323, 1248, 1177, 1136, 1008, 866, 768, 694 cm^{-1}. ^{1}H NMR: δ 1.47 (6H, s), 4.24 (2H, s), 5.22 (1H, q, $J = 0.6$ Hz), 9.6 (1H, broad s). ^{13}C NMR: δ 27.0 (q), 59.4 (s), 72.6 (d), 79.8 (t), 117.9 (q, $J = 288.2$ Hz), 170.6 (s), 175.970 (q, $J = 35.0$ Hz). Found: C, 46.21; H, 4.97; N, 6.85%. Calcd for $C_8H_{10}F_3NO_2$: C, 45.94; H, 4.82; N, 6.70%.

1 (CCl_3) was prepared by similar reaction of 2,4,4-trimethyl-2-oxazoline with trichloroacetyl chloride and pyridine in 90% yield. Mp 142–144 °C (colorless prisms from hexane). IR: 3290, 1637, 1570, 1494, 1302, 1200, 1172, 1135, 1016, 920, 830, 808, 772 cm^{-1}. ^{1}H NMR: δ 1.47 (6H, s), 4.24 (2H, s), 5.56 (1H, s), 9.3 (1H, broad s). ^{13}C NMR: δ 27.2 (q), 59.0 (s), 69.8 (d), 79.8 (t), 97.2 (s), 171.0 (s), 181.2 (s). Found: C, 37.39; H, 3.90; N, 5.33%. Calcd for $C_8H_{10}Cl_3NO_2$: C, 37.17; H, 3.90; N, 5.42%.

Reaction of 1 (Me) with 2 (Ph, Ph) in Acetonitrile (Table 1, Run 9). In a 100 mL round bottom flask, 0.09 g (2.25 mmol) of sodium hydride (60% in mineral oil) was rinsed with hexane and 0.31 g (2 mmol) of **1** (Me) in 10 mL of acetonitrile was added to the flask. After a few minutes, evolution of gas ceased. A solution of **2** (Ph, Ph) (0.45 g, 2.2 mmol) in 10 mL of acetonitrile was added. The solution turned red-brown and the mixture was stirred at rt for 5 h. Ice-cooled water (150 mL) and toluene (90 mL) was added. The organic layer was washed with brine and dried over sodium sulfate. After removal of the solvent, the residual oil was purified by silica gel column chromatography. The first toluene eluate was 0.02 g of the recovered acetylene. The second eluate using toluene–chloroform (9:1) gave 0.41 g (1.14 mmol, 57%) of **9** (Me, Ph, Ph). The third eluate using toluene–ethyl acetate (9:1) gave 0.15 g (0.41 mmol, 21%) of **4** (Me, Ph, Ph).

9 (Me, Ph, Ph): Mp 152.5–153.5 °C (colorless prisms from chloroform–hexane). IR: 2920, 2887, 1660, 1595, 1580, 1448, 1406, 1275, 1236, 1066, 1030, 706, 694 cm^{-1}. ^{1}H NMR: δ 1.57 (3H, s), 1.63 (3H, s), 1.85 (3H, s), 3.44 (2H, s), 3.80 (1H, d, $J = 9.0$ Hz), 3.92 (1H, d, $J = 9.0$ Hz), 7.0–7.4 (8H, m), 7.5–7.7 (2H, m). ^{13}C NMR: δ 24.3 (q), 24.5 (q), 24.8 (q), 40.8 (t), 60.4 (s), 77.5 (t), 95.8 (s), 128.1 (d), 128.2 (d), 128.4 (d), 128.7 (d), 129.2 (d), 133.0 (d), 136.2 (s), 136.9 (d), 136.9 (s), 137.6 (s), 165.1 (s), 196.1 (s). Found: C, 76.58; H, 6.52; N, 3.80%. Calcd for $C_{23}H_{23}NO_3$: C, 76.43; H, 6.41; N, 3.88%.

Reaction of 1 (Ph) with 2 (Ph, Ph) in Acetonitrile (Table 1, Run 13). Sodium salt of **1** was prepared in situ by treatment of **1** (Ph) (0.65 g, 3.0 mmol) with hexane-rinsed 60% NaH (3.3 mmol) in acetonitrile (20 mL). After ceasing evolution of gas, a solution of **2** (Ph, Ph) (0.66 g, 3.2 mmol) in acetonitrile (32 mL) was added. The solution turned deep red and it was stirred for 5 h at rt. Ice-cooled water (200 mL) and chloroform (80 mL) was added to the mixture. The organic layer was washed with brine and dried over sodium sulfate. After removal of the solvent, the mixture was separated by silica gel column chromatography. The first toluene eluate was the recovered acetylene and some other components. The second toluene eluate gave 70 mg (0.17 mmol) of **11** (Ph_3). The third toluene eluate gave 0.30 g (0.79 mmol, 25%) of **9** (Ph_3). The fourth eluate (toluene–ethyl acetate 9:1) gave 28 mg (0.13

mmol) of recovered **1** (Ph). The fifth eluate (toluene–ethyl acetate 2:1) gave 0.23 g (0.55 mmol) of **4** (Ph_3). The sixth eluate (toluene–ethyl acetate 1:2) gave 0.34 g (0.98 mmol) of **8** (Ph_3).

11 (Ph_3): Colorless oil. ^{1}H NMR: δ 1.72 (3H, s), 1.83 (3H, s), 3.86 (1H, d, $J = 8.2$ Hz), 4.36 (1H, d, $J = 8.2$ Hz), 5.05 (1H, d, $J = 1.0$ Hz), 5.99 (1H, d, $J = 1.0$ Hz), 7.0–7.6 (13H, m), 7.7 (2H, m). ^{13}C NMR: δ 23.8 (q), 23.9 (q), 62.4 (s), 75.8 (t), 96.8 (d), 111.6 (d), 111.9 (d), 124.9 (d), 125.9 (d), 127.3 (d), 127.6 (d), 128.2 (d), 128.3 (d), 128.6 (d), 129.1 (d), 129.3 (d), 133.7 (s), 137.8 (s), 138.0 (s), 138.9 (s), 150.9 (s), 170.4 (s). HRMS (FAB) found: m/z 423.1857 $[M]^+$; calcd for $C_{28}H_{25}NO_3$: m/z 423.1834.

9 (Ph_3): Mp 190–193 °C (Colorless needles from chloroform–hexane). IR: 3057, 2983, 2968, 2885, 1653, 1595, 1446, 1398, 1277, 1024, 922, 775, 710, 698, 687 cm^{-1}. ^{1}H NMR: δ 1.55 (3H, s), 1.68 (3H, s), 3.48 (1H, d, $J = 20.1$ Hz), 3.52 (2H, d, $J = 8.9$ Hz), 3.57 (1H, d, $J = 20.1$ Hz), 3.79 (2H, d, $J = 8.9$ Hz), 7.04–7.11 (5H, m), 7.18 (2H, t, $J = 7.7$ Hz), 7.32 (1H, t, $J = 7.4$ Hz), 7.35–7.44 (3H, m), 7.62 (2H, d, $J = 7.4$ Hz), 7.70 (2H, d, $J = 7.2$ Hz). ^{13}C NMR: δ 23.0 (q), 24.8 (q), 41.0 (t), 60.9 (s), 77.3 (t), 97.1 (s), 126.6 (d), 128.0 (d), 128.1 (d), 128.3 (d), 128.5 (d), 128.7 (d), 128.8 (d), 129.4 (d), 132.9 (d), 135.8 (s), 136.9 (s), 137.1 (s), 137.4 (s), 140.1 (s), 166.0 (s), 195.3 (s). Found: C, 79.55; H, 6.00; N, 3.22%. Calcd for $C_{28}H_{25}NO_3$: C, 79.41; H, 5.95; N, 3.31%.

8 (Ph_3): Mp 157–159 °C (Colorless needles from chloroform–hexane). IR: 3321 (br), 1672, 1641, 1602, 1587, 1516, 1485s, 1392, 1273s, 1153, 1076, 1057, 955, 870, 775, 704 cm^{-1}. ^{1}H NMR: δ 1.36 (6H, s), 3.81 (2H, d, $J = 5.5$ Hz), 5.36 (1H, t, $J = 5.5$ Hz), 6.63 (1H, s), 7.0–7.5 (15H, m). ^{13}C NMR: δ 28.1 (broad q), 70.8 (s), 72.2 (t), 120.4 (d), 124.6 (s), 127.6 (d), 128.0 (d), 128.3 (d), 128.5 (d), 128.7 (d), 128.8 (d), 129.3 (d), 132.8 (d), 135.6 (s), 136.4 (s), 147.5 (s), 150.8 (s), 168.1 (s), 195.5 (s). Found: C, 79.25; H, 6.08; N, 3.21%. Calcd for $C_{28}H_{25}NO_3$: C, 79.41; H, 5.95; N, 3.31%.

Reaction of 1 (Ph) with 2 (*t*-Bu, Ph) in Acetonitrile (Table 1, Run 4). Similar treatment of 3 mmol of **1** (Ph) with 3.3 mmol of **2** (*t*-Bu, Ph) gave the following products. The first toluene eluate was the recovered acetylene and other unidentified materials. The second toluene eluate was 40 mg (0.10 mmol) of **11** (Ph, *t*-Bu, Ph). The second toluene eluate was 10 mg (0.03 mmol) of **9** (Ph, *t*-Bu, Ph). The third toluene eluate was 0.19 g of a mixture of **1** (Ph) (0.49 mmol) and **8** (Ph, *t*-Bu, Ph) (0.21 mmol). The ratio of the products was determined by the ^{1}H NMR spectrum of the mixture. The fourth toluene–ethyl acetate (2:1) eluate gave 0.53 g of a mixture of **8** (Ph, *t*-Bu, Ph) (1.14 mmol) and **3** (Ph, *t*-Bu, Ph) (0.17 mmol). The fifth toluene–ethyl acetate (1:2) eluate gave 0.16 g of a mixture of **8** (Ph, *t*-Bu, Ph) (0.33 mmol) and **12** (Ph_2) (0.08 mmol).

11 (Ph, *t*-Bu, Ph): Mp 107–109 °C (colorless needles from chloroform–hexane). IR: 3062, 2972, 2881, 1660, 1643, 1589, 1446, 1383, 1362, 1311, 1093, 1028, 1001, 985, 972, 870, 756, 731, 698 cm^{-1}. ^{1}H NMR: δ 1.27 (9H, s), 1.69 (3H, s), 1.77 (3H, s), 3.78 (1H, d, $J = 8.1$ Hz), 4.20 (1H, d, $J = 8.1$ Hz), 4.84 (1H, d, $J = 1.0$ Hz), 5.36 (1H, d, $J = 1.0$ Hz), 6.59–6.92 (2H, m), 7.14–7.25 (6H, m), 7.32–7.35 (2H, m). ^{13}C NMR: δ 23.8 (q), 24.0 (q), 28.0 (q), 35.3 (s), 62.3 (s), 75.7 (t), 94.3 (d), 110.9 (d), 111.4 (s), 125.9 (d), 127.2 (d), 127.5 (d), 127.9 (d), 128.1 (d), 129.1 (d), 138.2 (s), 138.3 (s), 138.6 (s), 162.0 (s), 170.0 (s). Found: C, 77.38; H, 7.25; N, 3.42%. Calcd for $C_{26}H_{29}NO_3$: C, 77.39; H, 7.24; N, 3.47%.

8 (Ph, *t*-Bu, Ph): Mp 159–161 °C (colorless needles from chloroform–hexane). IR: 3346 (br), 2972, 2868, 1693, 1637, 1485, 1444, 1392, 1365, 1265, 1078, 1055, 978, 870, 770, 716, 706 cm^{-1}. ^{1}H NMR: δ 0.17 (9H, s), 1.07 (3H, s), 1.52 (3H, s), 3.48 (1H, dd, $J = 6.5$ and 11.9 Hz), 4.02 (1H, dd, $J = 4.1$ and 11.9 Hz), 5.70 (1H, dd, $J = 4.1$ and 6.5 Hz), 6.60 (1H, s), 7.31–7.43 (8H, m), 7.47–7.51 (2H, m). ^{13}C NMR: δ 26.9 (q), 27.3 (q), 28.7 (q), 44.6 (s), 70.6 (s), 72.0 (t), 120.4 (d), 127.5 (d), 127.8 (s), 128.5 (d), 128.6 (d), 129.4 (d), 129.6 (d), 129.7 (d), 130.7 (d), 132.7 (d), 136.0 (s), 136.8 (s), 144.5 (s), 149.0 (s), 168.1 (s), 213.8 (s). Found: C, 77.35; H, 7.32; N, 3.49%. Calcd for $C_{26}H_{29}NO_3$: C, 77.39; H, 7.24; N, 3.47%.

1-(1-Methyl-2-hydroxyethyl)-4,6-diphenyl-2-pyridone (**12**): Mp 139.5–140 °C (Colorless needles from chloroform–hexane). IR: 3294, 3056, 3010, 1639, 1583, 1560, 1537, 1491, 1479, 1448, 1390, 1360, 1263, 1153, 1080, 1065, 1036, 1026, 984, 874, 858, 775, 762, 748, 698, 669, 635 cm^{-1}. ^{1}H NMR: δ 1.35 (6H, s), 3.85 (2H, d, $J = 5.5$ Hz), 5.94 (1H, t, $J = 5.5$ Hz), 6.38 (1H, d, $J = 2.2$ Hz), 6.78 (1H, d, $J = 2.2$ Hz), 7.41–7.47 (3H, m), 7.43 (5H, s), 7.60–7.62 (2H, m). ^{13}C NMR: δ 28.1 (q), 69.8 (s), 72.3 (t), 113.1 (d), 116.7 (d), 126.7 (d), 128.0 (d), 128.5 (d), 128.8 (d), 128.9 (d), 129.7 (d), 136.4 (s), 140.2 (s), 149.7 (s), 150.8 (s), 169.3 (s). Found: C, 78.80; H, 6.61; N, 4.23%. Calcd for $C_{21}H_{21}NO_2$: C, 78.97; H, 6.63; N, 4.39%.

Similarly the following products were isolated from reaction of **1** with **2** in acetonitrile.

7 (*i*-Pr, *i*-Pr, Ph): An enol tautomer. Mp 137.5–138.5 °C (Colorless needles from hexane). IR: 2970, 2931, 2872, 1643, 1587, 1470, 1363, 1354, 1302, 1205, 1101, 991, 970, 926, 771 cm^{-1}. ^{1}H NMR: δ 0.90 (6H, d, $J = 6.9$ Hz), 1.03 (6H, d, $J = 6.9$ Hz), 1.20 (6H, s), 2.54 (2H, septet, $J = 6.9$ Hz), 3.92 (2H, s), 6.82 (1H, s), 7.36–7.42 (3H, m), 7.53–7.57 (2H, m), 17.36 (1H, s). ^{13}C NMR: δ 19.34 (q), 28.3 (q), 33.7 (d), 66.3 (s), 79.1 (t), 108.1 (d), 117.6 (d), 126.8 (d), 128.8 (s), 129.3 (s), 139.5 (s), 144.8 (s), 161.2 (s), 197.3 (s). Found: C, 74.11; H, 8.47; N, 3.75%. Calcd for $C_{22}H_{29}NO_3$: C, 74.33; H, 8.22; N, 3.94%.

7 (*t*-Bu, *t*-Bu, Ph): A keto tautomer. Mp 131–131.5 °C (colorless needles from hexane). IR: 3055, 2964, 1705, 1684, 1614, 1481, 1360, 1267, 1192, 1153, 1074, 897, 762, 690 cm^{-1}. ^{1}H NMR: δ 1.08 (18H, s), 1.34 (6H, s), 3.93 (2H, s), 6.24 (1H, s), 7.27–7.30 (3H, m), 7.33 (1H, s), 7.43–7.45 (2H, m). ^{13}C NMR: δ 27.4 (q), 28.6 (q), 45.1 (s), 63.6 (d), 68.0 (s), 77.6 (t), 117.0 (d), 128.0 (d), 128.6 (d), 129.5 (d), 139.6 (s), 149.0 (s), 160.2 (s), 213.8 (s). Found: C, 75.44; H, 8.81; N, 3.64%. Calcd for $C_{24}H_{33}NO_3$: C, 75.16; H, 8.67; N, 3.65%.

8 (Ph, *i*-Pr, Ph): Mp 137.5–138 °C (colorless needles from hexane). IR: 3348 (br), 2970, 1699, 1645, 1485, 1446, 1385, 1057, 993, 868, 771, 706 cm^{-1}. ^{1}H NMR: δ 0.25 (6H, d, $J = 6.9$ Hz), 1.31 (6H, s), 1.65 (1H, septet, $J = 6.9$ Hz), 3.76 (2H, broad d, $J = 5.2$ Hz), 5.65 (1H, broad t, $J = 5.2$ Hz), 6.01 (1H, s), 7.34–7.43 (10H, m). ^{13}C NMR: δ 17.4 (q), 28.1 (q), 42.3 (d), 70.7 (s), 72.0 (t), 120.6 (d), 127.1 (s), 127.8 (d), 128.5 (d), 129.0 (d), 129.2 (d), 129.6 (d), 131.2 (d), 135.8 (s), 136.7 (s), 146.2 (s), 149.5 (s), 168.1 (s), 208.8 (s). Found: C, 77.09; H, 7.05; N, 3.47%. Calcd for $C_{25}H_{27}NO_3$: C, 77.09; H, 6.99; N, 3.60%.

9 (Ph, *i*-Pr, Ph): Mp 150–151 °C (colorless needles from hexane). IR: 3058, 2976, 1693, 1666, 1446, 1398, 1200, 1034, 914, 770, 706 cm^{-1}. ^{1}H NMR: δ 0.72 (3H, d, $J = 7.0$ Hz), 1.01 (3H, d, $J = 7.0$ Hz), 1.52 (3H, s), 1.62 (3H, s), 2.03 (1H, septet, $J = 7.0$ Hz), 3.35 (2H, s), 3.47 (1H, d, $J = 8.8$ Hz), 3.75 (1H, d, $J = 8.8$ Hz), 7.1–7.4 (8H, m), 7.6–7.8 (2H, m). ^{13}C NMR: δ 19.3 (q), 22.9 (q), 24.8 (q), 41.3 (t), 41.9 (d), 60.8 (s), 77.2 (t), 96.9 (s), 126.9 (d), 128.3 (d), 128.4 (d), 128.7 (d), 128.8 (d), 129.4 (d), 137.4 (s), 137.9 (s), 139.0 (s), 140.2 (s), 165.8 (s), 208.5 (s). Found: C, 77.06; H, 6.97; N, 3.64%. Calcd for $C_{25}H_{27}NO_3$: C, 77.09; H, 6.99; N, 3.60%.

8 (2-furyl, *t*-Bu, Ph): Mp 151–152.5 °C (colorless needles from hexane). IR: 3496, 3143, 2978, 1684, 1641, 1581, 1506, 1479, 1392, 1068, 1059, 972, 770, 700 cm^{-1}. ^{1}H NMR: δ 0.37 (9H, s), 1.13 (3H, s), 1.45 (3H, s), 3.46 (1H, dd, $J = 7.4$ and 11.4 Hz), 4.32 (1H, dd, $J = 4.0$ and 11.4 Hz), 5.13 (1H, dd, $J = 4.0$ and 7.4 Hz), 6.4 (2H, m), 6.60 (1H, s), 7.33 (5H, s), 7.50 (1H, m). ^{13}C NMR: δ 25.5 (q), 26.0 (q), 27.2 (q), 45.1 (s), 70.5 (s), 71.0 (t), 112.5 (d), 116.3 (d), 122.2 (d), 127.2 (s), 128.6 (d), 129.4 (d), 129.5 (d), 133.6 (s), 136.8 (s), 142.7 (d), 147.1 (s), 148.7 (s), 167.2 (s), 212.3 (s). Found: C, 73.21; H, 6.88; N, 3.36%. Calcd for $C_{24}H_{27}NO_4$: C, 73.26; H, 6.91; N, 3.55%.

8 (Et, Ph, Ph): Colorless oil. ^{1}H NMR: δ 0.33 (3H, t, $J = 8.0$ Hz), 1.30 (6H, s), 2.2–2.7 (2H, m), 3.80 (2H, s), 5.33 (1H, s), 6.53 (1H, s), 7.1–7.4 (10H, m).

9 (Et, Ph, Ph): Mp 158–159 °C (colorless needles from hexane). IR: 3064, 2970, 1653, 1416, 1396, 1311, 1271, 1063, 768, 743, 708 cm^{-1}. ^{1}H NMR: δ 1.12 (3H, t, $J = 7.2$ Hz), 1.65 (6H, s), 2.1–2.4 (2H, m), 3.43 (2H, s), 3.82 (1H, d, $J = 9.0$ Hz), 3.88 (1H, d, $J = 9.0$ Hz), 6.9–7.3 (3H, m), 7.1 (5H, s), 7.5–7.7 (2H, m). ^{13}C NMR: δ 8.7 (q), 25.1 (q), 25.2 (q), 32.4 (t), 41.1 (t), 60.8 (s), 77.7 (t), 98.7 (s), 128.1 (d), 128.2 (d), 128.5 (d), 128.8 (d), 129.3 (d), 132.0 (d), 135.1 (s), 137.1 (s), 137.3 (s), 137.7 (s), 165.9 (s), 196.3 (s). Found: C, 76.51; H, 6.70; N, 3.78%. Calcd for $C_{24}H_{25}NO_3$: C, 76.77; H, 6.71; N, 3.70%.

9 (Bu, Ph, Ph): Mp 105–106 °C (colorless needles from hexane). IR: 3047, 1653, 1597, 1581, 1495, 1450, 1398, 1367, 766, 704 cm^{-1}. ^{1}H NMR: δ 0.97 (3H, t, $J = 7.0$ Hz), 1.37–1.59 (4H, m), 1.64 (3H, s), 1.67 (3H, s), 2.14–2.22 (1H, m), 2.34–2.41 (1H, m), 3.46 (1H, d, $J = 21.2$ Hz), 3.50 (1H, d, $J = 21.2$ Hz), 3.82 (1H, d, $J = 9.0$ Hz), 3.98 (1H, d, $J = 9.0$ Hz), 7.08–7.13 (3H, m), 7.16–7.20 (4H, m), 7.32 (1H, t, $J = 7.4$ Hz), 7.64 (2H, t, $J = 7.4$ Hz). ^{13}C NMR: δ 14.1 (q), 22.9 (t), 25.0 (q), 25.1 (q), 26.1 (t), 39.2 (t), 41.0 (t), 60.7 (s), 77.6 (t), 98.2 (s), 128.0 (d), 128.2 (d), 128.4 (d), 128.7 (d), 129.3 (d), 132.9 (d), 135.5 (s), 137.0 (s), 137.3 (s), 137.4 (s), 165.8 (s), 196.2 (s). Found: C, 77.44; H, 7.22; N, 3.47%. Calcd for $C_{22}H_{29}NO_3$: C, 77.39; H, 7.24; N, 3.47%.

8 (Ph, Ph, Bu): Mp 123–124 °C (pale yellow needles from hexane). IR: 3334, 1662, 1653, 1635, 1597, 1576, 1516, 781, 690 cm^{-1}. ^{1}H NMR: δ 0.83 (3H, t, $J = 6.0$ Hz), 1.3–1.7 (4H, m), 1.33 (6H, s), 2.33 (2H, t, $J = 6.0$ Hz), 3.78 (2H, d, $J = 5.6$ Hz), 5.55 (1H, t, $J = 5.6$ Hz), 6.53 (1H, s), 7.10–7.30 (10H, m). ^{13}C NMR: δ 13.7 (q), 22.3 (t), 27.7 (q), 28.7 (q), 30.5 (t), 32.1 (t), 70.5 (s), 72.3 (t), 119.2 (d), 125.2 (s), 128.1 (d), 128.7 (d), 129.2 (d), 133.1 (s), 136.0 (s), 137.3 (s), 146.2 (s), 152.0 (s), 168.5 (s), 196.5 (s). Found: C, 77.41; H, 7.35; N, 3.46%. Calcd for $C_{22}H_{29}NO_3$: C, 77.39; H, 7.24; N, 3.47%.

9 (tolyl, Ph, Ph) and **9** (Ph, tolyl, Ph) (a 1:1 scrambled mixture). Mp 159–161 °C (colorless needles from hexane). IR: 3346, 1668, 1637, 1603, 1483, 1271, 1055, 868, 768, 702 cm^{-1}. ^{1}H NMR: δ 1.37 (6H, br), 2.19 (3H, s), 3.8 (2H, br), 5.55 (1H, t, $J = 5.5$ Hz), [6.61 and 6.63] (1H, s), 6.8–6.9 (2H, m), 7.0–7.3 (12H, m). Found: C, 79.53; H, 6.38; N, 3.32%. Calcd for $C_{29}H_{27}NO_3$: C, 79.68; H, 6.22; N, 3.20%.

9 (*p*-nitrophenyl, Ph, Ph): Decomp 210–215 °C (pale yellow needles from hexane). IR: 1660, 1595, 1518, 1390, 1344, 1275, 854, 771, 698 cm^{-1}. ^{1}H NMR: δ 1.53 (3H, s), 1.70 (3H, s), 3.48 (1H, d, $J = 9.1$ Hz), 3.54 (1H, d, $J = 20.5$ Hz), 3.58 (1H, d, $J = 20.5$ Hz), 3.85 (1H, d, $J = 9.1$ Hz), 7.08 (5H, s), 7.20–7.27 (3H, m), 7.34–7.36 (2H, m), 7.93 (2H, d, $J = 8.9$ Hz), 8.29 (2H, d, $J = 8.9$ Hz). ^{13}C NMR: δ 23.3 (q), 24.7 (q), 40.9 (t), 61.3 (s), 77.5 (t), 96.5 (s), 123.8 (d), 127.8 (d), 128.12 (d), 128.16 (d), 128.5 (d), 129.1 (d), 129.3 (d), 133.3 (d), 134.5 (s), 136.3 (s), 137.1 (s), 138.4 (s), 147.5 (s), 148.2 (s), 165.7 (s), 195.2 (s). Found: C, 72.08; H, 5.24; N, 5.82%. Calcd for $C_{28}H_{24}N_2O_5$: C, 71.78; H, 5.16; N, 5.98%.

Reaction of 1 (CCl_3) with 2 (Ph_2) (Table 1, Run 20). A solution of sodium salt of **1** (CCl_3) (1 mmol) and **2** (Ph_2) (1.5 mmol) in acetonitrile (10 mL) was refluxed for 20 h. After the usual work-up, crude brown oil (0.51 g) was column-chromatographed on silica gel. The first eluate (benzene eluent) gave 0.11 g of the recovered acetylene. The second eluate (benzene) gave 0.11 g (0.43 mmol) of the recovered oxazoline (conversion 57%). The third eluate with benzene–ethyl acetate (20:1–10:1) gave 0.14 g (0.41 mmol, 72%) of 6-benzoyl-3,3-dimethyl-5-oxo-7-phenyl-5*H*-pyrido[2,1-*b*]oxazolidine, **14** (Ph_2): Mp 196.5–197 °C (pale yellow prisms from chloroform–isooctane). IR: 3055, 1660, 1645, 1591, 1579, 1522, 1267, 1113, 958, 764, 700 cm^{-1}. ^{1}H NMR: δ 1.80 (6H, s), 4.39 (2H, s), 5.73 (1H, s), 7.20–7.37 (7H, m), 7.45 (1H, tt, $J = 7.4$ and 1.6 Hz), 7.78–7.84 (2H, m). ^{13}C NMR: δ 24.3 (q), 63.7 (s), 80.8 (t), 85.9 (d), 120.7 (s), 127.8 (d), 128.2 (d), 128.3 (d), 128.7 (d), 129.2 (d), 132.7 (d), 138.0 (s), 138.2 (s), 155.7 (s), 157.0 (s), 158.7 (s), 195.5 (s). Found: C, 76.40; H, 5.62; N, 3.94%. Calcd for $C_{22}H_{19}NO_3$: C, 76.50; H, 5.44; N, 4.06%.

Reaction of 1 (Ph) with an Acetylenic Ester 2 (OMe, R^3) (Table 2, Run 1). A solution of sodium salt of **1** (Ph) (0.43 g, 2 mmol) and **2** (OMe, Ph) (0.36 g, 2.25 mmol) in acetonitrile (20 mL) was refluxed for 4.5 h. After usual work-up, a product was chromatographed. The first toluene eluate gave recovered **1** (Ph) (0.12 g, 0.55 mmol), the second eluate (toluene–ethyl acetate 20:1) gave 0.35 g (1.01 mmol) of a 2:1 mixture of **14** (Ph_2) and **15** (Ph_2).

Similarly reaction of **1** (Ph) with DMAD or methyl propiolate gave the following 5*H*-pyrido[2,1-*b*]oxazolidine, **15** (Ph, R^3).

8-Benzoyl-3,3-dimethyl-5-oxo-7-methyxycarbonyl-5*H*-pyrido[2,1-*b*]oxazolidine, **15** (Ph, CO_2Me): Mp 133–136 °C (red needles from chloroform–hexane). IR: 1738, 1674, 1641, 1603, 1531, 1450, 1323, 1240, 1072, 1024, 951, 764, 700 cm^{-1}. ^{1}H NMR: δ 1.78 (6H, s), 3.59 (3H, s), 4.31 (2H, s), 6.46 (1H, s), 7.45 (2H, t, $J = 7.5$ Hz), 7.56 (1H, t, $J = 7.5$ Hz), 7.77 (2H, d, $J = 7.5$ Hz). ^{13}C NMR: δ 24.3 (q), 52.7 (q), 63.7 (s), 81.2 (t), 96.9 (s), 114.3 (d), 128.4 (d), 128.9 (d), 132.9 (d), 138.4 (s), 145.2 (s), 157.2 (s), 160.0 (s), 166.1 (s), 190.3 (s). Found: C, 66.00; H, 5.20; N, 4.25%. Calcd for $C_{18}H_{17}NO_5$: C, 66.05; H, 5.23; N, 4.28%.

8-Benzoyl-3,3-dimethyl-5-oxo-5*H*-pyrido[2,1-*b*]oxazolidine, **15** (Ph, H): Mp 180–182 °C (colorless needles from chloroform–hexane). IR: 1676, 1630, 1606, 1539, 1423, 1317, 1298, 1120, 960 cm^{-1}. ^{1}H NMR: δ 1.79 (6H, s), 4.39 (2H, s), 6.06 (1H, d, $J = 9.5$ Hz), 7.45 (2H, t, $J = 7.6$ Hz), 7.54 (1H, t, $J = 7.3$ Hz), 7.64–7.66 (2H, m), 7.67 (1H, d, $J = 9.5$ Hz). ^{13}C NMR: δ 24.4 (q), 63.2 (s), 81.2 (t), 98.8 (s), 111.8 (d), 128.1 (d), 128.7 (d), 128.8 (d), 131.8 (d), 138.9 (s), 142.7 (d), 159.4 (s), 161.1 (s), 190.8 (s). Found: C, 71.14; H, 5.63; N, 5.10%. Calcd for $C_{16}H_{15}NO_3$: C, 71.36; H, 5.61; N, 5.20%.

Reaction of 1 (Ph) with 2 (OMe, Ph) in the Presence of Methanol (Table 2, Run 2). Methanol (0.10 g, 3.12 mmol) was added to a solution of sodium salt of **1** (Ph) (0.43 g, 2 mmol) and **2** (OMe, Ph) (0.36 g, 2.25 mmol) in acetonitrile (20 mL). After similar treatment to above, 0.02 g (0.1 mmol) of **1** (Ph) was recovered and 0.28 g (0.81 mmol) of a 1:7 mixture of **14** and **15**. Crystallization of the mixture from chloroform–hexane gave 8-benzoyl-3,3-dimethyl-5-oxo-7-phenyl-5*H*-pyrido[2,1-*b*]oxazolidine, **15** (Ph_2): Mp 196.5–197 °C (colorless needles from chloroform–hexane). IR: 1668, 1647, 1595, 1518, 1446, 1435, 1290, 970, 779, 756, 700 cm^{-1}. ^{1}H NMR: δ 1.83 (6H, s), 4.33 (2H, s), 6.13 (1H, s), 7.18 (5H, s), 7.29 (2H, br t, $J = 7.4$ Hz), 7.41 (1H, t, $J = 7.4$ Hz), 7.69 (2H, br d, $J = 7.4$ Hz). ^{13}C NMR: δ 24.5 (q), 63.4 (s), 81.2 (t), 98.7 (s), 113.1 (d), 127.8 (d), 128.1 (d), 128.3 (d), 128.6 (d), 129.4 (d), 132.7 (d), 138.1 (s), 138.6 (s), 155.5 (s), 157.1 (s), 160.2 (s), 192.0 (s). Found: C, 76.37; H, 5.44; N, 4.08%. Calcd for $C_{22}H_{19}NO_3$: C, 76.50; H, 5.44; N, 4.06%.

Addition of 16 to 2 (Ph_2) in Acetonitrile (eq 1). Diphenylpropynone, **2** (Ph_2), (0.66 g, 3.20 mmol) in acetonitrile (10 mL) was added slowly to a solution of sodium salt of 2-benzoylmethyl-2-oxazoline (**16**)[11] (0.58 g, 3.07 mmol) in acetonitrile (20 mL) at rt (20 °C) with stirring. The orange solution turned deep purple. After 4 h, the reaction was quenched with cold water (200 mL). The color of the solution turned yellow and products were extracted with toluene. The organic layer was washed with brine and dried over sodium sulfate. The products were treated with a silica gel column. The first toluene eluate was the recovered acetylene. The second toluene–chloroform (2:1 to 1:1) eluate gave 0.83 g (2.1 mmol, 69%) of 3-benzoyl-1-(2-hydroxyethyl)-4,6-diphenyl-2-pyridone (**18**).[9] The third chloroform to toluene–ethyl acetate (1:1) gave 0.26 g (0.67 mmol, 22%) of 5-benzoyl-1-(2-hydroxyethyl)-4,6-diphenyl-2-pyridone (**17**): Mp 173–175 °C (colorless needles from toluene–hexane). IR: 3398, 3057, 1645, 1601, 1520, 1489, 1288, 1066, 768, 702 cm^{-1}. ^{1}H NMR: δ 3.79 (2H, br q, $J = 4.6$ Hz), 3.92 (1H, br s), 4.10 (2H, t, $J = 5.1$ Hz), 6.64 (1H, s), 7.14–7.35 (13H, m), 7.43–7.46 (2H, m). ^{13}C NMR: δ 49.2 (t), 62.7 (t), 118.9 (d), 121.4 (s), 127.98 (d), 128.07 (d), 128.44 (d), 128.50 (d), 128.8 (d), 129.1 (d), 129.6 (br d), 129.7 (d), 132.0 (s), 132.9 (d), 136.8 (s), 137.2 (s), 138.0 (s), 148.2 (s), 152.2 (s), 164.2 (s), 194.8 (s). Found: C, 78.85; H, 5.34; N, 3.48%. Calcd for $C_{26}H_{21}NO_3$: C, 78.97; H, 5.35; N, 3.54%.

Conversion of 8 or 9 to 10 (Table 4, Run 4). Sodium ethoxide (1 mol L^{-1} solution, 0.5 mmol) was added to a solution of 0.39 g (1 mmol) of **9** (Ph, *i*-Pr, Ph) in ethanol (10 mL). Color of the solution turned orange. The mixture was allowed to stand at rt for 3 h and then it was poured to ice water. The solution turned colorless. It was extracted with toluene. The organic layer was washed with brine, dried over sodium sulfate. After removal of the solvent, 0.37 g (95%) of pure 5-isobutyryl-9,9-dimethyl-4,6-diphenyl-7-oxa-1-azabicyclo[4.3.0]non-3-en-2-one, **10** (Ph, *i*-Pr, Ph): Mp 177–179 °C (colorless needles from hexane). IR: 3061, 1720, 1659, 1612, 1419, 1381, 1022, 908, 768, 702, 692 cm^{-1}. ^{1}H NMR: δ 0.90 (3H, d, $J = 7.1$ Hz), 1.11 (3H, d, $J = 7.1$ Hz), 1.48 (3H, s), 1.50 (3H, s), 3.01 (1H, septet, $J = 7.1$ Hz), 3.31 (1H, d, $J = 8.8$ Hz), 3.69 (1H, d, $J = 8.8$ Hz), 4.53 (1H, s), 6.34 (1H, s), 7.07–7.10 (2H, m), 7.22–7.34 (3H, m), 7.34–7.40 (3H, m), 7.51–7.53 (2H, m). ^{13}C NMR: δ 17.4 (q), 18.1 (q), 23.6 (q), 23.7 (q), 43.0 (d), 59.3 (d), 60.3 (s), 77.2 (t), 97.9 (s), 124.8 (d), 126.2 (d), 126.4 (d), 128.4 (d), 128.7 (d), 129.3 (d), 137.0 (s), 141.5 (s), 144.0 (s), 163.2 (s), 206.3 (s). Found: C, 77.21; H, 7.04; N, 3.63%. Calcd for $C_{25}H_{27}NO_3$: C, 77.09; H, 6.99; N, 3.60%.

Similarly other variants of **10** were isolated by treatment of **8** or **9** with sodium ethoxide.

10 (Ph_3): Mp 248 °C (colorless powder). IR: 3061, 1689, 1659, 1610, 1423, 1018, 770, 702 cm^{-1}. ^{1}H NMR: δ 1.47 (3H, s), 1.50 (3H, s), 3.25 (1H, d, $J = 8.7$ Hz), 3.56 (1H, d, $J = 8.7$ Hz), 5.24 (1H, s), 6.57 (1H, s), 7.10–7.13 (2H, m), 7.17–7.21 (3H, m), 7.32–7.42 (3H, m), 7.56–7.67 (5H, m), 8.15–8.17 (2H, m). ^{13}C NMR: δ 23.5 (q), 23.7 (q), 55.0 (d), 60.2 (s), 77.1 (t), 97.9 (s), 125.1 (d), 125.8 (d), 126.3 (d), 128.5 (d), 128.6 (d), 128.7 (d), 128.9 (d), 129.3 (d), 133.3 (d), 136.7 (s), 138.3 (s), 141.7 (s), 143.8 (s), 163.2 (s), 192.8 (s). Found: C, 79.47; H, 5.94; N, 3.24%. Calcd for $C_{28}H_{25}NO_3$: C, 79.41; H, 5.95; N, 3.31%.

10 (Ph, *t*-Bu, Ph): Mp 184–185 °C (colorless needles from hexane). IR: 2974, 2868, 1714, 1659, 1616, 1608, 1408, 1381, 1363, 1026, 768, 700 cm^{-1}. ^{1}H NMR: δ 1.07 (9H, s), 1.50 (6H, s), 3.30 (1H, d, $J = 8.4$ Hz), 3.68 (1H, d, $J = 8.4$ Hz), 4.80 (1H, s), 6.30 (1H, s), 7.0–7.6 (10H, m). ^{13}C NMR: δ 23.4 (q), 23.7 (q), 26.5 (q), 45.1 (s), 54.9 (d), 60.1 (s), 77.2 (t), 98.2 (s), 125.4 (d), 126.3 (d), 126.5 (d), 128.5 (d), 128.6 (d), 128.7 (d), 129.2 (d), 137.4 (s), 141.7 (s), 145.2 (s), 163.4 (s), 207.6 (s). Found: C, 77.63; H, 7.34; N, 3.46%. Calcd for $C_{22}H_{29}NO_3$: C, 77.39; H, 7.24; N, 3.47%.

10 (Me, Ph, Ph): Mp 173–174 °C (colorless needles from hexane). IR: 3059, 2991, 2875, 1682, 1651, 1614, 1416, 1219, 1034, 764, 725 cm^{-1}. ^{1}H NMR: δ 1.38 (3H, s), 1.61 (3H, s), 1.71 (3H, s), 3.63 (1H, d, $J = 8.5$ Hz), 3.79 (1H, d, $J = 8.5$ Hz), 5.03 (1H, s), 6.51 (1H, s), 7.3 (5H, m), 7.51 (2H, m), 7.61 (1H, t, $J = 7.0$ Hz), 8.02 (2H, m). ^{13}C NMR: δ 23.7 (q), 25.5 (q), 25.6 (q), 53.7 (d), 59.4 (s), 77.6 (t), 96.3 (s), 124.1 (d), 125.9 (d), 128.7 (d), 128.9 (d), 129.5 (d), 133.2 (d), 136.7 (s), 138.0 (s), 145.3 (s), 161.9 (s), 193.5 (s). Found: C, 76.32; H, 6.39; N, 3.84%. Calcd for $C_{23}H_{23}NO_3$: C, 76.43; H, 6.41; N, 3.88%.

10 (2-furyl, *t*-Bu, Ph): Mp 109–110 °C (colorless needles from hexane). IR: 3462, 2974, 1705, 1653, 1605, 1419, 1032, 876, 800, 750, 689 cm^{-1}. ^{1}H NMR: δ 1.07 (9H, s), 1.44 (3H, s), 1.61 (1H, br s), 1.66 (3H, s), 3.55 (1H, d, $J = 8.7$ Hz), 3.71 (1H, d, $J = 8.7$ Hz), 5.28 (1H, s), 6.16 (1H, s), 6.33 (1H, dd, $J = 1.8$ and 3.3 Hz), 6.41 (1H, m), 7.19–7.21 (2H, m), 7.31–7.32 (3H, m), 7.49 (1H, m). ^{13}C NMR: δ 23.4 (q), 24.0 (q), 26.4 (q), 45.1 (s), 50.3 (d), 60.1 (s), 77.1 (t), 94.0 (s), 110.3 (d), 110.7 (d), 124.9 (d), 126.8 (d), 128.7 (d), 129.3 (d), 137.3 (s), 143.4 (d), 146.1 (s), 152.0 (s), 163.0 (s), 207.8 (s). Found: C, 71.45; H, 7.06; N, 3.48%. Calcd for $C_{24}H_{27}NO_4/0.5H_2O$: C, 71.62; H, 7.01; N, 3.48%.

Hydrolysis of 11 (R^4, R^5, R^3) to 4,6-Disubstituted 2-Pyrone 13 (R^5, R^3) (Table 4, Run 24). A solution of **11** (Ph, *t*-Bu, Ph) (70 mg, 0.17 mmol) and 1.0 mL of sulfuric acid in 10 mL of ethanol was refluxed for 3 h. It was poured into ice water, extracted with chloroform, washed with brine, and dried over sodium sulfate. After removal of the solvent, 37 mg (96%) of pure 6-(*t*-butyl)-4-phenyl-2-pyrone, **13** (*t*-Bu, Ph) was obtained: Colorless oil. IR: 3062, 2970, 1736, 1632, 1547, 1107, 850, 768, 700, 681 cm^{-1}. ^{1}H NMR: δ 1.34 (9H, s), 6.35 (2H, s), 7.45 (3H, m), 7.57 (2H, m). ^{13}C NMR: δ 28.0 (q), 36.3 (s), 99.6 (d), 108.4 (d), 126.7 (d), 129.1 (d), 130.5 (d), 136.3 (s), 155.6 (s), 163.5 (s), 172.6 (s). HRMS (FAB) found: m/z 228.1162 $[M]^+$; calcd for $C_{15}H_{16}O_2$: m/z 228.1150.

Similarly, 4,6-diphenyl-2-pyrone **13** (Ph_2) was yielded from **11** (Ph_3): Mp 160 °C (color less needles). IR: 3059, 1649, 1448, 1273, 700 cm^{-1}. ^{1}H NMR: δ 6.44 (1H, d, $J = 1.0$ Hz), 6.93 (1H, d, $J = 1.0$ Hz), 7.20–7.63 (8H, m), 7.80 (2H, m). Mass (FAB) m/z 248 $[M]^+$, 220, 115. Found: C, 82.03; H, 4.84%. Calcd for $C_{17}H_{12}O_2$: C, 82.24; H, 4.87%.

Dealkylation of 8 or 9 to 19 (Table 4, Run 20). Concentrated sulfuric acid (3 mL) was added to a solution of 0.18 g (0.50 mmol) of **9** (Me, Ph, Ph) in ethanol (30 mL). The mixture was refluxed for 2 h, then poured into ice water (100 g), and extracted with chloroform. The organic layer was washed with brine and dried over sodium sulfate. Removal of the solvent afforded 0.16 g of crude 5-benzoyl-6-methyl-4-phenyl-2-pyridone, **19** (Me, Ph, Ph): Mp 204–207 °C (colorless needles from chloroform–hexane). IR: 2976–2700 (br), 1652, 1580, 1470, 1267, 924, 698, 634 cm^{-1}. ^{1}H NMR: δ 2.43 (3H, s), 6.56 (1H, s), 7.16–7.42 (8H, m), 7.59–7.61 (2H, m), 13.7 (1H, broad s). ^{13}C NMR: δ 17.9 (q), 116.2 (d), 119.7 (s), 127.9 (d), 128.4 (s), 128.5 (d), 128.9 (d), 129.3 (d), 133.3 (d), 137.7 (s), 137.8 (s), 146.0 (s), 155.1 (s), 164.6 (s), 195.7 (s). Found: C, 76.57; H, 5.25; N, 4.68%. Calcd for $C_{19}H_{15}NO_2/0.5H_2O$: C, 76.42; H, 5.41; N, 4.69%.

Similarly the following compounds were obtained.

19 (Et, Ph, Ph): Mp 180–181.5 °C (colorless needles from chloroform–hexane). IR: 3502, 3200–2400 (br), 1660, 1653, 1635, 1527, 1448, 1313, 1267, 702, 611 cm^{-1}. ^{1}H NMR: δ 1.33 (3H, t, $J = 7.6$ Hz), 1.7 (1H, br), 2.69 (2H, q, $J = 7.6$ Hz), 6.51 (1H, s), 7.1–7.3 (7H, m), 7.38 (1H, t, $J = 7.4$ Hz), 7.53–7.63 (2H, m), 13.25 (1H, broad s). ^{13}C NMR: δ 14.4 (q), 25.2 (t), 116.8 (d), 118.3 (s), 127.9 (d), 128.4 (s), 128.6 (d), 128.7 (d), 129.7 (d), 133.1 (d), 138.0 (s), 138.2 (s), 151.2 (s), 154.7 (s), 165.0 (s), 196.0 (s). Found: C, 77.02; H, 5.63; N, 4.52%. Calcd for $C_{20}H_{17}NO_2/0.5H_2O$: C, 76.90; H, 5.81; N, 4.48%.

19 (Ph_3): Mp 236–237 °C (colorless needles from chloroform–hexane). IR: 3200–2400 (br), 1653, 1595, 1448, 1402, 1275, 700, 676 cm^{-1}. ^{1}H NMR: δ 6.53 (1H, s), 7.14–7.36 (11H, m), 7.41–7.43 (2H, m), 7.55–7.57 (2H, m), 12.02 (1H, broad s). ^{13}C NMR: δ 118.8 (s), 119.0 (d), 127.9 (d), 128.2 (d), 128.3 (d), 128.6 (d), 128.7 (d), 128.8 (d), 129.3 (d), 130.2 (d), 132.8 (s), 133.0 (d), 137.8 (s), 138.1 (s), 146.8 (s), 154.6 (s), 163.7 (s), 195.3 (s). Found: C, 82.26; H, 4.90; N, 3.97%. Calcd for $C_{24}H_{17}NO_2$: C, 82.03; H, 4.88; N, 3.99%.

19 (Ph, *i*-Pr, Ph): Mp 191–193.5 °C (colorless needles from chloroform–hexane). IR: 3200–2500 (br), 1703, 1645, 1593, 1493, 1458, 1396, 1259, 1209, 775, 702 cm^{-1}. ^{1}H NMR: δ 0.51 (6H, d, $J = 7.0$ Hz), 1.99 (1H, septet, $J = 7.0$ Hz), 6.43 (1H, s), 7.36 (5H, m), 7.5 (5H, m), 11.8 (1H, broad s). ^{13}C NMR: δ 17.8 (q), 42.2 (d), 119.1 (d), 121.0 (s), 128.4 (d), 128.5 (d), 128.6 (d), 128.9 (d), 129.3 (d), 130.4 (d), 133.0 (s), 138.0 (s), 145.2 (s), 153.5 (s), 163.1 (s), 207.8 (s). Found: C, 79.68; H, 6.12; N, 4.18%. Calcd for $C_{21}H_{17}NO_2$: C, 79.47; H, 6.03; N, 4.41%.

19 (Ph, *t*-Bu, Ph): Mp 162–163 °C (colorless needles from chloroform–hexane). IR: 3200–2400, 1693, 1649, 1603, 1589, 1493, 1263, 1190, 1051, 783, 702, 673 cm^{-1}. ^{1}H NMR: δ 0.37 (9H, s), 6.49 (1H, s), 7.39 (5H, s), 7.44–7.46 (3H, m), 7.53–7.55 (2H, m), 10.9–11.2 (1H, broad s). ^{13}C NMR: δ 27.1 (q), 45.2 (s), 118.8 (d), 121.2 (s), 128.5 (d), 128.8 (d), 129.1 (d), 129.5 (d), 129.9 (d), 130.4 (d), 133.3 (s), 138.0 (s), 142.4 (s), 152.6 (s), 163.2 (s), 213.1 (s). Found: C, 78.87; H, 6.29; N, 4.24%. Calcd for $C_{22}H_{21}NO_2/0.5H_2O$: C, 78.66; H, 6.45; N, 4.17%.

19 (2-furyl, *t*-Bu, Ph): Mp 264–265.5 °C (colorless needles from chloroform–hexane). IR: 3200–2400 (br), 1689, 1649, 1603, 1452, 1400, 1173, 781, 667, 577 cm^{-1}. ^{1}H NMR: δ 0.66 (9H, s), 1.8 (1H, br), 6.54 (2H, m), 7.17 (1H, d, $J = 3.5$ Hz), 7.40 (5H, s), 7.55 (1H, d, $J = 1.5$ Hz), 12.1 (1H, broad s). ^{13}C NMR: δ 27.3 (q), 45.8 (s), 112.6 (d), 114.3 (d), 118.3 (s), 119.3 (d), 128.5 (d), 129.1 (d), 129.5 (d), 132.7 (d), 138.2 (d), 144.5 (d), 145.5 (s), 152.8 (s), 163.2 (s), 212.1 (s). Found: C, 72.87; H, 5.82; N, 4.16%. Calcd for $C_{20}H_{19}NO_3/0.5H_2O$: C, 72.87; H, 5.82; N, 4.16%.

Deacylation of 5-Acyl-2-pyridone Derivatives 9 (R^4, R^5, R^3) to 21 (R^4, R^3) (Table 4, Run 21). To a solution of potassium hydroxide (0.84 g, 15 mmol) in ethanol (10 mL), 0.19 g (0.50 mmol) of **9** (Et, Ph, Ph) was added. The solution turned red-brown. The mixture was refluxed for 4 h, and then poured into ice water. The solution turned yellow, which was extracted with toluene, washed with brine, and dried over sodium sulfate. Removal of the solvent gave 0.13 g (0.49 mmol) of pure 6-ethyl-9,9-dimethyl-4-phenyl-7-oxa-1-azabicyclo[4.3.0]non-3-en-2-one, **21** (Et, Ph): Mp 98–99.5 °C (colorless prisms from hexane). IR: 2968, 1650, 1605, 1446, 1412, 1379, 1198, 1128, 881, 760, 717, 681 cm^{-1}. ^{1}H NMR: δ 0.91 (3H, t, $J = 7.5$ Hz), 1.56 (3H, s), 1.65 (3H, s), 1.76 (1H, qdd, $J = 7.5$, 14.7, and 1.6 Hz), 1.88 (1H, qd, $J = 7.5$ and 14.7 Hz), 2.72 (1H, ddd, $J =$ 16.6, 2.9, and 1.6 Hz), 3.17 (1H, d, $J = 16.6$ Hz), 3.85 (1H, d, $J = 8.9$ Hz), 3.89 (1H, d, $J = 8.9$ Hz), 6.20 (1H, d, $J = 2.9$ Hz), 7.36–7.44 (3H, m), 7.47–7.50 (2H, m). ^{13}C NMR: δ 8.5 (q), 25.1 (q), 25.3 (q), 27.2 (t), 35.9 (t), 59.7 (s), 77.1 (t), 96.2 (s), 121.3 (d), 125.9 (d), 128.8 (d), 129.5 (d), 137.5 (s), 146.3 (s), 162.3 (s). Found: C, 75.06; H, 7.80; N, 5.01%. Calcd for $C_{17}H_{21}NO_2$: C, 75.25; H, 7.80; N, 5.16%.

Similarly, **21** (Me, Ph) was obtained from **9** (Me, Ph, Ph): Colorless oil. IR: 1653, 1606, 1448, 1412, 1284, 766, 690 cm^{-1}. ^{1}H NMR: δ 1.45 (3H, s), 1.53 (3H, s), 1.62 (3H, s), 2.92 (2H, br s), 3.90 (2H, s), 6.20 (1H, t, $J = 1$ Hz), 7.4 (5H, m).

Dealkylation of 21 to 4,6-Disubstituted 2-Pyridone 20 (Table 4, Run 22). A solution of **21** (Me, Ph) (0.11 g, 0.43 mmol) and sulfuric acid (2.0 mL) in ethanol (20 mL) was refluxed for 30 h. The reaction mixture was poured into ice water, extracted with chloroform, washed with brine, and dried over sodium sulfate. 6-Methyl-4-phenyl-2-pyridone **20** (Me, Ph) (0.08 g) was obtained after removal of the solvent: Mp

210–210.5 °C (colorless needles from chloroform–hexane). IR: 3200–2500, 1655, 1637, 1529, 1466, 1248, 955, 866, 764, 702 cm^{-1}. ^{1}H NMR: δ 2.45 (3H, s), 6.36 (1H, s), 6.65 (1H, br s), 7.39–7.56 (3H, m), 7.57–7.65 (2H, m), 13.35 (1H, br s). ^{13}C NMR: δ 19.3 (q), 105.9 (d), 113.2 (d), 126.9 (d), 128.9 (d), 129.4 (d), 138.1 (s), 145.7 (s), 154.4 (s), 166.2 (s). Found: C, 77.68; H, 6.02; N, 7.46%. Calcd for $C_{12}H_{11}NO$: C, 77.81; H, 5.99; N, 7.56%.

Similarly, **20** (Et, Ph) was obtained from **21** (Et, Ph): Mp 155–156 °C (colorless needles from chloroform–hexane). IR: 3200–2600, 1653, 1581, 1531, 1470, 768, 694, 567 cm^{-1}. ^{1}H NMR: δ 1.37 (3H, t, $J = 7.5$ Hz), 2.77 (2H, q, $J = 7.5$ Hz), 6.41 (1H, s), 6.70 (1H, s), 7.42–7.48 (3H, m), 7.59–7.61 (2H, m), 13.4 (1H, broad). ^{13}C NMR: δ 12.9 (q), 26.5 (t), 104.6 (d), 113.2 (d), 126.9 (d), 129.0 (d), 129.5 (d), 138.1 (s), 151.6 (s), 154.6 (s), 165.9 (s). Found: C, 76.01; H, 6.50; N, 6.68%. Calcd for $C_{13}H_{13}NO/1/3H_2O$: C, 76.07; H, 6.71; N, 6.82%.

References

1 R. M. Acheson, *Acc. Chem. Res.* **1971**, *4*, 177.

2 N. E. Holden, A. Lapworth, *J. Chem. Soc.* **1931**, 2368; G. A. Swan, *J. Chem. Soc.* **1955**, 1039; K. Buggle, G. P. Hughes, E. M. Philbin, *Chem. Ind. (London)* **1969**, 77.

3 M. M. Abou-Elzahab, S. N. Ayyad, M. T. Zimaity, *Z. Naturforsch., B: Chem. Sci.* **1986**, *41*, 363; A. J. Frew, G. R. Proctor, *J. Chem. Soc., Perkin Trans. 1* **1980**, 1245.

4 A. J. Frew, G. R. Proctor, J. V. Silverton, *J. Chem. Soc., Perkin Trans. 1* **1980**, 1251.

5 S. M. Ruder, V. R. Kulkarni, *J. Org. Chem.* **1995**, *60*, 3084.

6 M. Higo, T. Sakashita, M. Toyoda, T. Mukaiyama, *Bull. Chem. Soc. Jpn.* **1972**, *45*, 250.

7 L. A. Paquette, T. Morwick, *J. Am. Chem. Soc.* **1995**, *117*, 1451; J. L. Dillon, Q. Gao, *J. Org. Chem.* **1994**, *59*, 6868.

8 a) J. J. Fitzgerald, A. R. Pagano, V. M. Sakoda, R. A. Olofson, *J. Org. Chem.* **1994**, *59*, 4117. b) L. Deloux, M. Srebnik, *J. Org. Chem.* **1994**, *59*, 6871. c) U. K. Tambar, B. M. Stoltz, *J. Am. Chem. Soc.* **2005**, *127*, 5340.

9 Y. Tohda, T. Yanagidani, S. Hiramatsu, N. Nishiwaki, K. Tani, K. Imagawa, M. Ariga, *Bull. Chem. Soc. Jpn.* **1997**, *70*, 2781.

10 Z.-T. Huang, X. Shi, *Synthesis* **1990**, 162; Z.-T. Huang, P.-C. Zhang, *Chem. Ber.* **1989**, *122*, 2011.

11 Y. Tohda, T. Kawashima, M. Ariga, R. Akiyama, H. Shudoh, Y. Mori, *Bull. Chem. Soc. Jpn.* **1984**, *57*, 2329.

12 Y. Tohda, M. Morikawa, T. Kawashima, M. Ariga, Y. Mori, *Chem. Lett.* **1986**, 273.

13 K. Sonogashira, Y. Tohda, N. Hagihara, *Tetrahedron Lett.* **1975**, *16*, 4467; R. Rossi, A. Carpita, F. Bellina, *Org. Prep. Proced. Int.* **1995**, *27*, 127; K. R. Buszek, Y. Jeong, *Tetrahedron Lett.* **1995**, *36*, 5677.

14 Y. Tohda, K. Sonogashira, N. Hagihara, *Synthesis* **1977**, 777.

15 L. Palombi, L. Arista, A. Lattanzi, F. Bonadies, A. Scettri, *Tetrahedron Lett.* **1996**, *37*, 7849; J. Bach, R. Berenguer, J. Garcia, T. Loscertales, J. Manzanal, J. Vilarrasa, *Tetrahedron Lett.* **1997**, *38*, 1091.

16 P. Allen, Jr., J. Ginos, *J. Org. Chem.* **1963**, *28*, 2759.