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A FACILE SYNTHESIS OF 1,3-DICARBONYL COMPOUNDS FROM 1-ALKYNE AND ACID ANHYDRIDE PROMOTED BY DICHLORO-BIS(TRIFLUOROMETHANESULFONATO)TITANIUM(IV)

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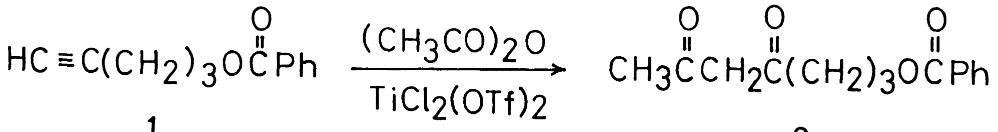
1,3-Dicarbonyl compounds are prepared in high yields by acylation of 1-alkyne derivatives with acid anhydride in the presence of dichloro-bis(trifluoromethanesulfonato)titanium(IV), followed by aqueous work up.

1,3-Dicarbonyl derivatives are considered to be useful intermediates in organic synthesis1) and are well known as a basic component for the generation of poly ketides in biogenetic condensation.2) Generally, 1,3-dicarbonyl compounds are prepared by the acylation of α-position of carbonyl compounds and their derivatives.1) In addition, it is known3) that the Friedel-Crafts type acylation of 1-alkyne by acid chloride in the presence of Lewis acid ($SnCl_4$, $AlCl_3$)4) affords β-chlorovinyl ketone which may be subsequently saponified to 1,3-dicarbonyl compound. This reaction, however, generally proceeds in poor yield and is not applicable to 1-alkyne containing labile functional groups such as ketone and 3- or 4-acyloxy group.

From the standpoint that metal triflate systems are powerful reagents to generate carbocationic species,5) we have studied on carbon-carbon bond forming reactions mediated by dichloro-bis(trifluoromethanesulfonato)titanium(IV) (=titanium(IV) bistriflate) such as the Claisen type ester condensation.6) Now, we investigated the application of titanium(IV) bistriflate as an effective Lewis acid to promote the acylation reaction of 1-alkynes.

In this communication, we wish to report on a facile one pot procedure for the synthesis of 1,3-dicarbonyl compounds by the acylation of 1-alkyne derivatives containing a variety of functional groups with acid anhydride in the presence of titanium(IV) bistriflate.

In the first place, we screened the molar ratio and the reaction conditions to optimize the yield taking the reaction of 5-benzoyloxy-1-pentyne (1) with acetic anhydride as a model. As shown in Table 1, combined use of 1.7 equiv. of titanium (IV) bistriflate and 3.7 equiv. of acetic anhydride gave the best result.



$$\mathrm{HC{\equiv}C(CH_2)_3O\overset{O}{\overset{\|}{C}}Ph} \xrightarrow[\mathrm{TiCl_2(OTf)_2}]{\mathrm{(CH_3CO)_2O}} \mathrm{CH_3\overset{O}{\overset{\|}{C}}CH_2\overset{O}{\overset{\|}{C}}(CH_2)_3O\overset{O}{\overset{\|}{C}}Ph}$$

1 2

A typical procedure is described as follows; to a suspension of titanium(IV) bistriflate (141 mg, 0.338 mmol) in 0.7 ml of dichloromethane was added acetic anhydride (76 mg, 0.744 mmol) in 1.0 ml of dichloromethane at 0 °C under argon atmosphere with stirring. The reaction mixture was stirred at 0 °C for 15 min and kept standing at room temperature for an additional 30 min. At this point the reaction mixture turned to yellow solution, and 5-benzoyloxy-1-pentyne (38 mg, 0.203 mmol) was added dropwise at 0 °C. And the reaction mixture was stirred for 5 h at room temperature. Then phosphate buffer of pH 7.0 was added to the reaction mixture with vigorous stirring. After cerite filtration of the mixture, the aqueous layer was extracted with dichloromethane two times, then the combined organic layer was dried over Na_2SO_4. After concentration in vacuo, the resulted oil was purified by preparative thin layer chromatography (hexane : ethyl acetate = 5 : 1) to yield 7-benzoyloxy-2,4-heptanedione (43 mg, 85%).

Table 1. The reaction of 5-benzoyloxy-1-pentyne with acetic anhydride [a)]

$TiCl_2(OTf)_2$ (equiv.)	Ac_2O (equiv.)	Reaction conditions	Product yield / %
1.1	1.1	0 °C 1 h	13
1.3	1.1	0 °C - r.t. 10 h	30
1.7	1.7	0 °C - r.t. 10 h	52
1.7	2.5	0 °C - r.t. 5 h	69
1.7	3.7	0 °C - r.t. 5 h	85

a) The reaction was carried out in dichloromethane solvent.

Next, the combination of various 1-alkynes and acid anhydrides under the present reaction conditions were studied, and the results are shown in Table 2.

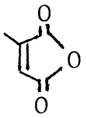
1-Alkynes containing various functional groups such as halogen atom or ester, cyano, 3-acyloxy, 4-methoxycarbonyloxy, and ketone groups gave the corresponding 1,3-dicarbonyl compounds without the loss of these functionalities.

The present method could be successfully demonstrated (Table 2, entries 18-22) in the synthesis of 1,3,6-triketone derivatives whose general preparations have been required a number of steps.[7)]

Several acid anhydrides can be employed in the reaction, except in the case of the cyclic acid anhydride, for example, citraconic anhydride was not suitable (Table 2, entry 5).

Table 2. The reaction of various types of 1-alkynes and acid anhydrides [a)]

Entry	1-Alkyne	Acid anhydride (equiv.)	Product	Yield / %
1	$HC\equiv C(CH_2)_3OOCPh$	$(MeCO)_2O$ (3.7)	$CH_3COCH_2CO(CH_2)_3OOCPh$	85
2	$HC\equiv C(CH_2)_3OOCPh$	$(EtCO)_2O$ (3.7)	$CH_3CH_2COCH_2CO(CH_2)_3OOCPh$	83

3	$HC\equiv C(CH_2)_3OOCPh$	$(PhCO)_2O$ (2.5)	$PhCOCH_2CO(CH_2)_3OOCPh$	87
4	$HC\equiv C(CH_2)_3OOCPh$	( $CO)_2O$ (3.7)	 $COCH_2CO(CH_2)_3OOCPh$	75
5	$HC\equiv C(CH_2)_3OOCPh$	 (3.7)	No Reaction	0
6	$HC\equiv C(CH_2)_3CH_3$	$(MeCO)_2O$ (3.7)	$CH_3COCH_2CO(CH_2)_3CH_3$	82
7	$HC\equiv C(CH_2)_3CH_3$	$(PhCO)_2O$ (2.5)	$PhCOCH_2CO(CH_2)_3CH_3$	83
8	$HC\equiv CPh$	$(MeCO)_2O$ (large excess)	$PhCOCH_2COCH_3$	71
9	$HC\equiv C(CH_2)_3OAc$	$(MeCO)_2O$ (3.7)	$CH_3COCH_2CO(CH_2)_3OAc$	80
10	$HC\equiv C(CH_2)_3Br$	$(MeCO)_2O$ (3.7)	$CH_3COCH_2CO(CH_2)_3Br$	83
11	$HC\equiv C(CH_2)_3CN$	$(MeCO)_2O$ (3.7)	$CH_3COCH_2CO(CH_2)_3CN$	67
12	$HC\equiv CCH_2OOCPh$	$(MeCO)_2O$ (3.7)	$CH_3COCH_2COCH_2OOCPh$	73
13	$HC\equiv C\underset{OAc}{\underset{\mid}{C}}H(CH_2)_2Ph$	$(MeCO)_2O$ (3.7)	$CH_3COCH_2CO\underset{OAc}{\underset{\mid}{C}}H(CH_2)_2Ph$	51
14	$HC\equiv C\underset{OCO_2CH_3}{\underset{\mid}{C}}H(CH_2)_7CH_3$	$(MeCO)_2O$ (3.7)	$CH_3COCH_2CO\underset{OCO_2CH_3}{\underset{\mid}{C}}H(CH_2)_7CH_3$	72
15	$HC\equiv CCH_2\underset{OAc}{\underset{\mid}{C}}H(CH_2)_2Ph$	$(MeCO)_2O$ (3.7)	$CH_3COCH_2COCH_2\underset{OAc}{\underset{\mid}{C}}H(CH_2)_2Ph$	27[c]
16	$HC\equiv C(CH_2)_2OCO_2CH_3$	$(MeCO)_2O$ (3.7)	$CH_3COCH_2CO(CH_2)_2OCO_2CH_3$	82
17	$HC\equiv CCH_2\underset{OCO_2CH_3}{\underset{\mid}{C}}H(CH_2)_2Ph$	$(MeCO)_2O$ (3.7)	$CH_3COCH_2COCH_2\underset{OCO_2CH_3}{\underset{\mid}{C}}H(CH_2)_2Ph$	73
18	$HC\equiv C(CH_2)_2COCH_3$	$(MeCO)_2O$ (3.7)	$CH_3COCH_2CO(CH_2)_2COCH_3$	62[d][e]
19	$HC\equiv C(CH_2)_2COCH_3$	$(PhCO)_2O$ (3.7)	$PhCOCH_2CO(CH_2)_2COCH_3$	75[d][e]
20	$HC\equiv C(CH_2)_2CO(CH_2)_2CH_3$	$(MeCO)_2O$ (3.7)	$CH_3COCH_2CO(CH_2)_2CO(CH_2)_2CH_3$	66[d]
21	$HC\equiv C(CH_2)_2COCH_2CO_2CH_3$	$(PhCO)_2O$ (2.5)	$PhCOCH_2CO(CH_2)_2COCH_2CO_2CH_3$	63[d]
22	$HC\equiv C(CH_2)_2COPh$	$(MeCO)_2O$ (2.5)	$CH_3COCH_2CO(CH_2)_2COPh$	35[d]

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a) The reaction was carried out in dichloromethane solvent.

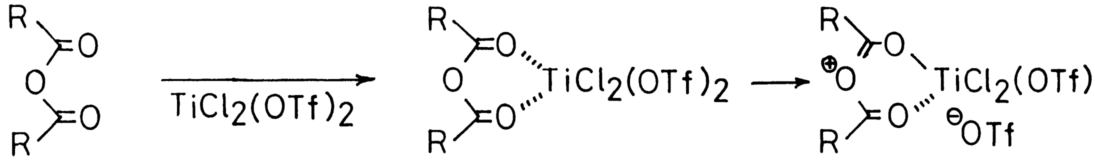
b) Isolated yield. These products were purified with preparative thin layer chromatography except entries 16-20.

c) 1-Phenyl-3-octen-5,7-dione was obtained in 44% yield as a by-product.
d) These products were purified by flash column chromatography (hexane : ethyl acetate = 5 : 1).
e) IR, ^{1}H-NMR and MS spectrum data were coincident with those of literature.$^{7,8)}$

Also, it is noted that when acid chloride was used in place of acid anhydride in the above reaction, complex mixtures resulted.

The combination of acid anhydride and the other Lewis acids such as $AlCl_3$, $TiCl_4$ and $Sn(OTf)_2$ showed that the desired reaction did not proceed under the same reaction conditions. Only a trace amount of the desired product was isolated, when $SnCl_4$ or trifluoromethanesulfonic acid was used as a promoter.

The order of the addition of reagents influences on the yield and the best yield was attained when 1-aklyne was added to the mixture of acid anhydride and titanium(IV) bistriflate. The result indicates that an initial formation of a complex (3) between titanium(IV) bistriflate and acid anhydride is critical for the acylation step.



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Thus, the convenient and useful method for the preparation of 1,3-dicarbonyl compounds containing various functional groups, which are especially labile under basic conditions, have been developed. Further investigations directed towards new type of carbon-carbon bond forming reaction utilizing characteristic property of titanium(IV) bistriflate are currently in progress.

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