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SELECTIVE HYDROESTERIFICATION OF ALKYNES TO MONO- OR DIESTERS

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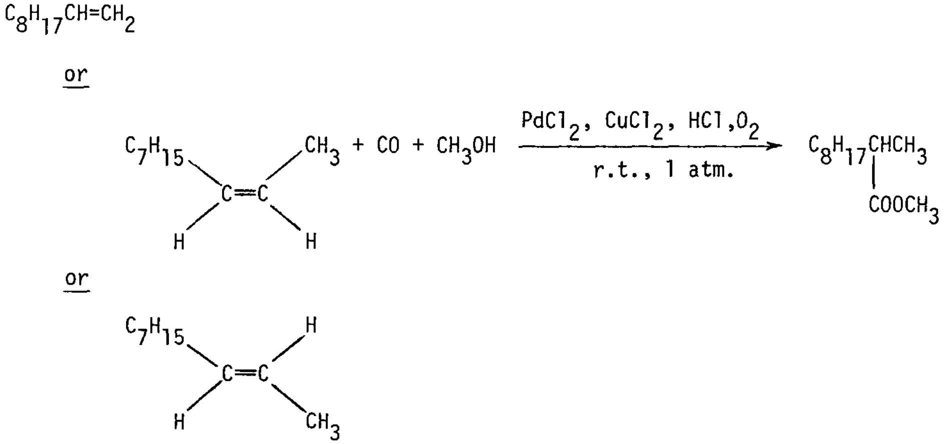
Summary: *Terminal alkynes (including acetylene) undergo regioselective hydroesterification to unsaturated* <u>*cis*</u>*-diesters using $PdCl_2$, $CuCl_2$, HCl, alcohol, carbon monoxide, and oxygen;* <u>*cis*</u>*-monoesters are formed from internal alkynes. These reactions are complete within two hours at room temperature and atmospheric pressure.*

Recently, we described the rapid, regiospecific hydroesterification of olefins under remarkably mild conditions using palladium chloride as the catalyst. For example, treatment of 1-decene or <u>cis</u>-or <u>trans</u>-2-decene with carbon monoxide and oxygen, methanol, hydrochloric acid, and catalytic amounts of palladium and copper chlorides, at room temperature and atmospheric pressure, afforded methyl 2-methyldecanoate as the only product in excellent yield.[1]



It was of interest to learn whether alkynes would react in a similar fashion to give α,β-unsaturated monoesters, some of which are important industrial chemicals. We now wish to report that alkynes react in a regioselective manner to give monoesters or diesters, subject to the nature of the organic substrate.

Exposure of acetylene (<u>1</u>,R=H) to the reaction conditions described above afforded dimethyl maleate (<u>2</u>,R=H,R'=CH_3) and dimethyl fumarate (<u>3</u>,R=H,R'=CH_3) in quantitative yield. The ratio of <u>2</u>/<u>3</u> was 6.1/1.0. A series of monosubstituted alkynes also reacted in a regioselective

Table 1

Products Obtained from the Hydroesterification of Alkynes

Alkyne[a]	Alcohol[b]	Product	Yield, %[c]
1,R=H	A	2,R=H,R'=CH_3	86[d]
		3,R=H,R'=CH_3	14
1,R=C_3H_7	A	2,R=C_3H_7,R'=CH_3	78[e]
		3,R=C_3H_7,R'=CH_3	22
1,R=C_4H_9	A	2,R=C_4H_9,R'=CH_3	76[d]
		3,R=C_4H_9,R'=CH_3	22
1,R=C_6H_{13}	A	2,R=C_6H_{13},R'=CH_3	80[e]
		3,R=C_4H_9,R'=CH_3	20
1,R=Cyclohexyl	A	2,R=C_6H_{11},R'=CH_3	89[f]
		3,R=C_6H_{11},R'=CH_3	11
1,R=Cyclohexyl	B	2,R=C_6H_{11},R'=C_2H_5	86[d]
		3,R=C_6H_{11},R'=C_2H_5	13
1,R=$PhCH_2CH_2$	A	2,R=$PhCH_2CH_2$,R'=CH_3	74[e]
		3,R=$PhCH_2CH_2$,R'=CH_3	26
1,R=$C_2H_5CH(CH_3)$	A	2,R=$C_2H_5CH(CH_3)$R'=CH_3	84[e]
		3,R=$C_2H_5CH(CH_3)$,R'=CH_3	16
4,R=C_4H_9	A	5,R=C_4H_9,R'=CH_3	72[d]
4,R=C_4H_9	C	5,R=C_4H_9,R'=C_3H_7	76[d]
4,R=C_6H_{13}	A	5,R=C_6H_{13},R'=CH_3	65[d]
4,R=$(CH_3)_2CHCH_2$	A	5,R=$(CH_3)_2CHCH_2$,R'=CH_3	75[d]
2,9-Dimethyl-5-decyne	A	cis-$(CH_3)_2CHCH_2CH_2CH{=}C(COOCH_3)CH_2CH_2CH(CH_3)_2$	70[d]

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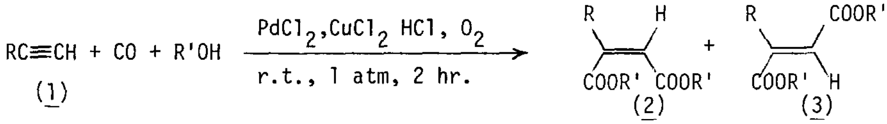
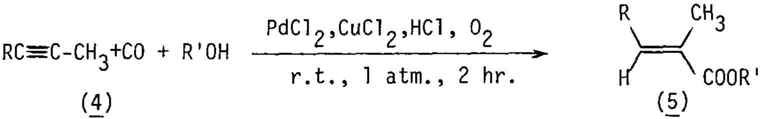
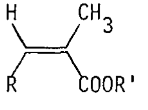
[a] R=C_3H_7,C_4H_9,C_6H_{13} refer to straight chain alkyl groups. [b] A=CH_3OH,B=C_2H_5OH,C=n-C_3H_7OH. [c] Yields are based on reactant alkyne. [d] Isolated yields. [e] Yield determined by nmr spectroscopy. [f] Yield determined by gas chromatography.

manner to give the *cis*-diester as the principal product with the *trans* isomer obtained as a by-product. The combined yields were quantitative and the products were identified by comparison of boiling points and spectral (ir, nmr, ms) results with literature data (comparison with authentic materials was made in five cases). In no case were α,β-unsaturated monoesters detected in these reactions. Methanol was usually employed as the alcohol although ethanol and propanol could also be used. The yields of the products obtained from these reactions are listed in Table 1, and are based on the amount of alkyne.



Interestingly, 2-alkynes (4), (i.e., internal alkynes) also react regioselectively but to give monoesters (5) and *not* diesters. Furthermore, the monoester which is formed is of *cis* stereochemistry. Compound 5 can be readily distinguished from the Z isomer (6) since the chemical shift for the vinylic proton of 5 occurs at δ6.50-7.00 while the corresponding proton of 6 gives a signal at δ5.60-6.10[2-8]. Compounds of structural type 5 are easily distinguished from 7 by virtue of the multiplicity of the vinylic hydrogen in the nmr spectrum, with a triplet appearing in the case of 5 and a quartet for 7[3,5,7-9]. A triplet was observed for the vinylic proton of the unsaturated esters obtained from 4 [e.g., 5,R=C_6H_{13},R'=CH_3,δ6.75(J=7.5Hz);R=C_4H_9, R'=C_3H_7,δ6.69(J=7.0Hz)]. Of course, the vinylic proton of the product formed from the symmetrical alkyne, 2,9-dimethyl-5-decyne, gave a triplet absorption[δ6.68,J=7.5Hz]. The unsaturated ester (5) could be converted to the saturated analog with L-selectride and t-butyl alcohol (e.g., 5,R=C_6H_{13},R'=CH_3)[10]. Vinyl ethers and an unidentified compound were obtained as by-products using internal alkynes as the substrates.

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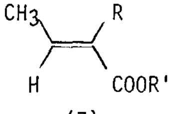
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The present methodology has several attractive features when compared with the very extensive primary and patent literature on alkyne hydroesterification[11,12]. For instance, Chiusoli and co-workers[13] described the dicarbomethoxylation of acetylene using palladium chloride and thiourea (no HCl and a small % of oxygen) to give not only 2 and 3 (R=H,R'=CH_3) but appreciable amounts of polymeric materials and isomeric muconate esters. In the present case, the reaction is a very facile and clean one. While diesters are the usual products of the hydroesterification of terminal and internal alkynes, the regioselectivity is variable, and chloroesters are often formed as well[12]. Here, only diesters are obtained from terminal alkynes, and with good *cis*-selectivity. In addition, the regiospecific formation of *cis*-monoesters from internal alkynes is of synthetic value, and the sensitivity of the reaction course (i.e., mono vs. diesterification) to the kind of alkyne substrate is, to our knowledge, unprecedented. Critical to the success of these reactions is the use of oxygen and acidic conditions. The mechanism of the reaction and, in particular, the role of acid and oxygen, is under investigation.

In conclusion, the exceedingly mild palladium(II) catalyzed hydroesterification of alkynes to mono or diesters can be achieved in high yields in a regioselective or regiospecific manner.

The following general procedure was used: palladium chloride is added to the alcohol through which is bubbling carbon monoxide. After one minute, concentrated hydrochloric acid (1 ml.) is added. Once the solution turns yellow ($PdCl_2$ is dissolved), copper(II) chloride (5-10/1 ratio of $CuCl_2/PdCl_2$) is added and oxygen is bubbled through the solution (as well as carbon monoxide). The alkyne (10-25/1 ratio of alkyne/$PdCl_2$) is now added, and the reaction mixture is stirred for two hours at room temperature. Treatment with hexane, followed by drying and rotary evaporation of the hexane gave the crude products which were purified by distillation or chromatography.

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