Efficient Homologation of Acetylenes to Allenes

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Summary A general route for the synthesis of allenes from acetylenes is reported and appropriate reaction conditions are described for the preparation of substituted allenes and allenols, including optically active allenols.

Recently, we have reported an unusual transformation of some ethynyl A-nor steroids to the corresponding allenic compounds.[1] We now report results which confirm this one-step conversion of acetylenes into allenes to be both general and versatile. In essence, the reaction conditions involve heating a solution containing an acetylene, formaldehyde, and an amine in the presence of an inorganic salt.

Firstly, we prepared the Mannich base of the acetylenic compounds (**1**)—(**4**) in order to investigate the optimal conditions for the transformation into the corresponding allenes (**9**)—(**12**). The reactions performed on the Mannich bases with formaldehyde alone (no free amine present) gave only the starting materials. Conversely, treatment of the Mannich base, in dioxan or tetrahydrofuran (THF) solution, in the presence of copper bromide afforded the highest yields of allenes.

We then studied the direct conversion of the acetylenic compounds (**1**)—(**7**) into the homologous allenes (**9**)—(**15**). The acetylenic compounds were mixed with formaldehyde, various secondary amines, and inorganic salts, in different solvents, until the starting material disappeared. A careful investigation of this reaction has permitted the definition of a number of factors which lead to the desired allene (see Table).

Typical reaction conditions are as follows. The acetylenic compounds were heated with formaldehyde (1·6 equiv.), di-isopropylamine (1·2 equiv.), and copper bromide (0·33 equiv.) under reflux in dioxan or tetrahydrofuran solution for several hours. The mixture was cooled and extraction by the usual procedure, followed by chromatography, led to the homologous allenes. Although it seems clear that the reaction involves the Mannich base as an intermediate, it does not have to be isolated. Moreover, surprisingly there is no need to prepare the quaternary salt, since this conversion of acetylenes into allenes is essentially a one-step reaction.

It is apparent from the Table that copper bromide is an appropriate salt to catalyse the conversion of acetylenes into allenes. Di-isopropylamine seems to be the best amine in terms of yields and reaction rates. Among the various solvents which have been investigated thus far (for their dielectric constant, polarity, or b.p.), tetrahydrofuran and dioxan seem to give satisfactory results. It is not merely a question of temperature, as the reaction rate is faster in toluene, but slower in acetonitrile.

It is of interest to note that this conversion can be performed on prop-2-ynylic alcohols (**1**)—(**3**), ethers (**6**), and

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Table. Preparation of the allenes $RCH{=}C{=}CH_2$ (**9**)—(**16**) from the acetylenes $RC{\equiv}CH$ (**1**)—(**8**).[a]

R	Acetylene	Time/h	Allene	% Yield
$Me[CH_2]_4CH(OH)-$	(**1**)	2	(**9**)	97[b]
$PhCH(OH)-$	(**2**)	1·5	(**10**)	67
$CH_2[CH_2]_3C(OH)-$	(**3**)	4	(**11**)	50
$Me[CH_2]_5-$	(**4**)	5	(**12**)	26
$Me[CH_2]_7-$	(**5**)	7	(**13**)	65
$O[CH_2]_4CH{-}O-$	(**6**)	5	(**14**)	46
$HOCH_2[CH_2]_3-$	(**7**)	23	(**15**)	26[c]
$Me[CH_2]_4CH(OAc)-$	(**8**) ($[\alpha]_D$ − 69°)	6	(**16**) ($[\alpha]_D$ − 104°)	41

[a] Unless otherwise stated conditions were as follows: the acetylene (1 equiv.), formaldehyde (1·6 equiv.), CuBr (0·33 equiv.), and $HNPr^i_2$ (1·2 equiv.), were heated in refluxing dioxan until all the starting material had disappeared. Yields were determined by g.l.c. (10% Carbowax 20 M; 2·5 m × 2 mm) and have not yet been optimized. [b] Variation with metal salt (2 h in refluxing dioxan with $HNPr^i_2$): 34% with $AgNO_3$; 18% with $CuCl_2.2H_2O$; only traces with Cu or $FeCl_3$; 0% with $CeCl_3$ and $FeSO_4$; 0·03 equiv. of CuBr led to incomplete conversion after 8 h, while 10 equiv. led to a 40% yield and decomposition products after 2 h. Variation with amine (1·2 equiv. of amine for 2 h in refluxing dioxan unless noted otherwise): 35% with $HNBu^n_2$ after 23 h; 7% with $HNEt_2$; 0% with 2,2,6,6-tetramethylpyridine. Variation with solvent (1·2 equiv. of $HNPr^i_2$): 54% in THF after 7 h; 48% in 1,2-dimethoxyethane after 5 h; 37% in benzene after 5 h; 33% in MeCN after 5 h; 56% in refluxing toluene after 1 h. [c] Low yield attributed to high volatility of product.

acetates (**8**), as well as on plain acetylenic compounds (**4**), (**5**), and (**7**) thus showing the reaction to be of general applicability for the homologation of acetylenes to allenes. Thus far, the best yields have been obtained with prop-2-ynylic alcohols, ethers, and esters, which seems to indicate that the reaction rate is improved by vicinal participation of the oxygen group for the transfer of hydrogen to the acetylenic unit. However, this participation does not affect the C–O bond, since the optically active prop-2-ynylic acetate (**8**) provided the optically active allene (**16**),‡ *i.e.*, optical activity is preserved during homologation.

At present, there is no basis for mechanistic conclusions, especially with regard to whether the newly introduced hydrogen on the allene originates from the amine, formaldehyde, or the solvent. Of great significance is the straightforward formation of allenes under these mild conditions, which is a novel process.

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‡ All substances had spectroscopic properties consistent with the assigned structures.

[1] P. Crabbé, D. André, and H. Fillion, *Tetrahedron Letters*, 1979, 893.