General Synthesis of 2-Acyloxy-1,3-dienes in One Step from Carboxylic Acids and Butenyne Derivatives

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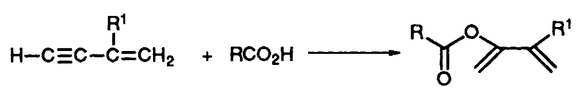
2-Acyloxy-1,3-dienes are obtained by regioselective addition of carboxylic acids and *N*-protected amino acids to vinylacetylene derivatives, with (arene)(phosphine)ruthenium(II) complexes as catalysts.

Functional buta-1,3-diene derivatives have been shown to be valuable reagents in synthesis *via* Diels–Alder reactions: examples include 2-silyloxy-,[1] 2-morpholino-,[2] or 1-acyloxy-[3] compounds. Whereas 1,3-dien-1-yl acetates can be prepared easily by reaction of isopropenyl acetate with α,β-unsaturated aldehydes or ketones and lead to Diels–Alder products,[3,4] the access to 1,3-dien-2-yl carboxylates is not straightforward: they have been obtained from vinylacetylene and carboxylic acids in the presence of mercury salts but in very low yields due to polymerization.[5]

We report here a general method for the regioselective synthesis of 2-acyloxy-1,3-dienyl carboxylates from ruthenium–phosphine complex-catalysed addition of carboxylic acids and *N*-protected amino acids to the easily accessible 2-methylbutenyne (**a**) and vinylacetylene (**b**).[6] It is based on our previous observation that carboxylic acids regioselectively add to prop-2-ynyl alcohol derivatives, in the presence of a ruthenium catalyst, to produce β-oxopropyl esters.[7]

The reaction of benzoic acid (1 equiv.) with a slight excess of the enyne (**a**) and $[RuCl_2(PMe_3)(p\text{-cymene})]$[8] (0.01 equiv.) in toluene at 80 °C for 24 h led to (**1a**). Gas chromatography of the crude product showed the presence of a small amount of its isomer $PhCO_2CH{=}CHC(Me){=}CH_2$, but distillation under reduced pressure (b.p. 24—26 °C, 13 mmHg), afforded pure (**1a**) in 84% yield† (Scheme 1). Similarly, the dienes (**2a**) (77%) and (**3a**) (76%) or (**2b**) (60%) and (**4b**) (70%)† were isolated, respectively from the butenynes (**a**) and (**b**), in their pure form after distillation.

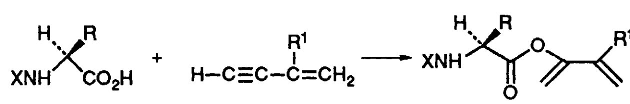
The reaction cannot be extended directly to amino acids. However, *N*-protected amino acids (**5**)—(**8**) regioselectively add in the presence of $[RuCl_2(PMe_3)(p\text{-cymene})]$ (0.01 equiv.) to butenyne derivatives (**a**) for 24 h and (**b**) for 15 h at 80 °C. Thus the optically active esters (**5a**) (65%), (**6a**) (68%), (**7a**) (64%), (**8a**) (87%), (**5b**) (62%), and (**8b**) (58%)† were isolated. It is noteworthy that the catalytic reaction proceeds without significant racemization of the amino acid derivatives, for hydrolysis in aqueous HCl (1 M) at 25 °C of (**7a**) $\{[\alpha]_D^{20}$ −40° (*c* 1, EtOH)$\}$, obtained from the pure, optically active amino acid (**7**) $\{[\alpha]_D^{20}$ +20 ± 2° (*c* 1, EtOH)$\}$ affords compound (**7**) with $[\alpha]_D^{20}$ +18 ± 2° (*c*, 1, EtOH).



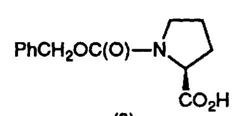
(**a**) R^1 = Me (**1**) – (**4**) (**1a**) – (**3a**)
(**b**) R^1 = H (**2b**), (**4b**)

(**1**) R = Ph
(**2**) R = Bu^t
(**3**) R = *trans*-MeCH=CH
(**4**) R = 2,6-$F_2C_6H_3$

Scheme 1. *General conditions*: the carboxylic acid (10 mmol), the enyne (**a**) or (**b**) (12 mmol), and the catalyst $[RuCl_2(PMe_3)(p\text{-cymene})]$, acid/catalyst = 100; toluene (10 ml) in an autoclave at 80 °C for 24 h. Yields are given in the text after reduced pressure distillation (10 mmHg).



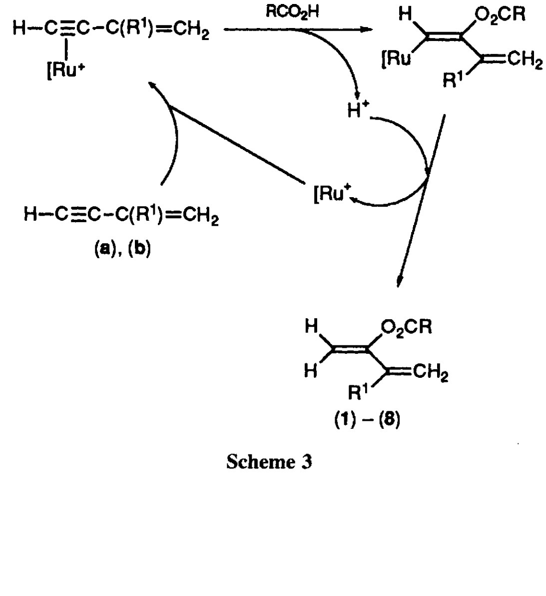
(**5**) – (**7**) (**a**) R^1 = Me (**5a**) – (**8a**)
(**b**) R^1 = H (**5b**), (**8b**)



(**8**)

(**5**) X = Bu^tOCO, R = Me
(**6**) X = Bu^tOCO, R = Pr^i
(**7**) X = Bu^tOCO, R = CH_2Ph

Scheme 2. *General conditions*: the *N*-protected amino acid (10 mmol), the enyne (**a**) or (**b**) (12 mmol), and the catalyst $[RuCl_2(PMe_3)(p\text{-cymene})]$ acid/catalyst = 100; in toluene (10 ml) in an autoclave at 80 °C for 24 h for (**a**) and for 15 h for (**b**). The dienes were purified on a silica gel column [(**8a**) and (**8b**)] or by crystallization from ether–hexane (1 : 5) [(**5a**), (**6a**), and (**7a**)].

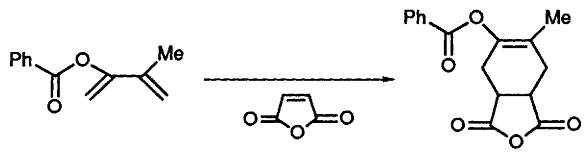


Scheme 3

† Satisfactory elemental analyses and high resolution mass spectrum analyses were obtained for dienes (**1a**)—(**8b**). Selected spectroscopic data: (**1a**): ^1H NMR ($CDCl_3$; 80 MHz): δ 5.21 [s, $OC(=CH_2)$], 5.02 [s, $Me\text{-}C(=CH_2)$], and 2.00 (s, MeC=); IR (film): $\nu_{max.}$ 1750 (C=O) and 1615 (C=C) cm^{-1}.

(**7a**): ^1H NMR ($CDCl_3$; 80 MHz): δ 4.96 (m, 5H, $2CH_2{=},CHNH$), 3.14 (d, $PhCH_2CH$, $^3J_{HH}$ 5.12 Hz), 1.90 [s, $MeC(=CH_2)$], and 1.41 (s, Me_3C); IR (film): $\nu_{max.}$ 1750 (CO amide), 1715 (CO ester), and 1610 (C=C) cm^{-1}.

(**9**): ^1H NMR ($CDCl_3$; 80 MHz): δ 8.08 (m, 2H, Ph), 7.55 (m, 3H, Ph), 3.49 (m, 2H, CHCH), 2.71 (m, 4H, CH_2CH), and 1.70 (s, MeC=); IR (KBr): $\nu_{max.}$ 1800 (CO anhydride) and 1750 (CO ester) cm^{-1}.



(1a) (9)

Scheme 4. *Conditions*: tetrahydrofuran, 60 °C.

The derivatives (**1b**)—(**8b**) of vinylacetylene polymerize in a few hours at room temperature whereas the esters (**1a**)—(**8a**) are more stable and polymerize at 25 °C only after a few days. However, all the diene derivatives of types (**a**) and (**b**) can be stored in dichloromethane solution at −20 °C at least for one month without polymerization.

Complexes of type [$RuCl_2(PR_3)$(arene)], especially those containing the basic PMe_3 ligand, appear to give the best yield and the highest selectivity for formation of 2-dienyl esters. The mechanism of the reaction may involve the activation, towards the carboxylate, of the ruthenium η^2-co-ordinated alkyne bond, the addition of the carboxylate group at the C(2), rather than the C(1) alkyne, carbon atom being favoured by electron-releasing phosphine ligands (Scheme 3).

The functional diene (**1a**) in tetrahydrofuran reacts with maleic anhydride at 60 °C and gives after 24 h a 60% yield of the cycloaddition product (**9**). The transformation (**1**) → (**1a**) → (**9**) can be achieved in one flask. When 1.5 equiv. of maleic anhydride was added to the catalytic mixture of $PhCO_2H$, isopropenylacetylene, and 0.01 equiv. of the ruthenium catalyst in toluene, after 24 h at 80 °C compound (**9**) was isolated in 40% yield (Scheme 4).

This preliminary study shows that the one-step regioselective synthesis of 2-acyloxy-1,3-dienes is general and has potential for the access to Diels–Alder reaction products.

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