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PAPER

Direct allenol-based stereocontrolled access to substituted (*E*)-1,3-enynes†

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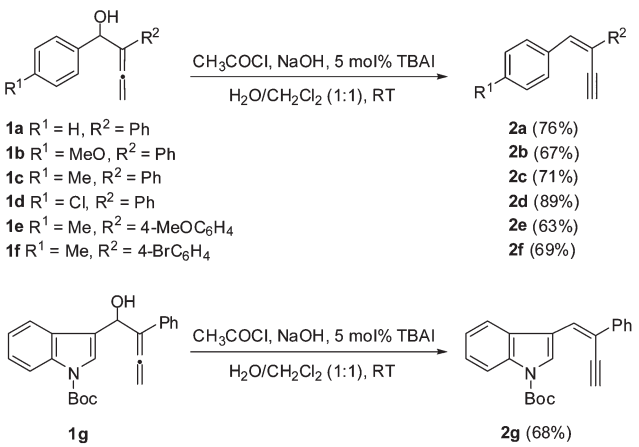
A stereoselective synthesis of 1-substituted (*E*)-2-aryl-but-1-en-3-ynes, including tetrasubstituted alkenes, has been developed from aryl-substituted α-allenols by treatment with the AcCl–NaOH (aqueous) system. This transformation might be explained through the elimination of acetic acid, made up of a δ-hydrogen and the acetate group in the initially formed α-allenic acetate.

Introduction

The important medicinal properties of compounds containing the 1,3-enyne moiety, in addition to the use of functionalized 1,3-enynes as building blocks for the preparation of bioactive molecules or organic electronic material, are now well established.[1,2] On the other hand, during the past decades the allene group has developed from almost a rarity to an established member of the weaponry utilized in modern organic synthetic chemistry.[3] In particular, transformations involving allenols have been pursued with renewed interest.[4] However, surprisingly, the direct preparation of 1,3-enynes from allenolic moieties has not been mentioned in the literature; only Lee and Ma have independently reported two-step procedures starting from very activated allenols, namely, 2-(methoxycarbonyl)-2,3-allenols.[5] We now report direct stereocontrolled access to the (*E*)-1,3-enyne moiety from aryl-substituted α-allenols.

Results and discussion

Starting materials for enyne formation, aryl-substituted α-allenols **1**, were readily prepared in good yields from the corresponding aldehyde *via* the regiocontrolled indium-mediated Barbier-type carbonyl-allenylation reaction using our previously described methodology.[6] Water-based organic reactions have been gaining in popularity because of their synthetic advantages (many reactive functional groups, such as hydroxy, amine, and carboxylic functions, do not require the protection–deprotection protocol in such reactions, and many water soluble compounds do not need to be converted into their derivatives and can be reacted directly), as well as unique reactivity and selectivity that are not often attained under dry conditions.[7] In this context, efforts were directed towards a direct approach for the stereoselective synthesis of functionalized 1,3-enynes **2** by reaction of aryl-substituted α-allenols **1** in an aqueous medium. Initial experiments were carried out using as a model substrate allenol **1a** just by the addition of acetyl chloride and aqueous NaOH. We observed that the reaction did not proceed "on water", probably because substrate **1a** is completely insoluble in aqueous media. After some experimentation, it was found that the use of a biphasic water–dichloromethane mixture was necessary for the reaction to occur. When phenyl-substituted allenol **1a** was treated with acetyl chloride and aqueous NaOH–dichloromethane (1 : 1) at room temperature, the 1,2-diphenyl (*E*)-1,3-enyne **2a** was directly formed in 76% yield after 24 h (Scheme 1). Thus, allenol **1a** undergoes elimination of water, made up of a δ-hydrogen and the hydroxyl group.[8] Having established the optimal reaction conditions, we explored the scope of the



Scheme 1 Direct synthesis of arene-tethered (*E*)-1,3-enynes **2a–g** from allenols **1a–g**.

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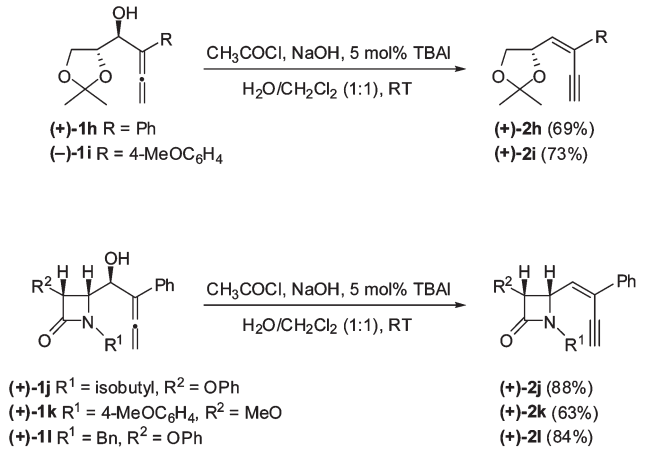
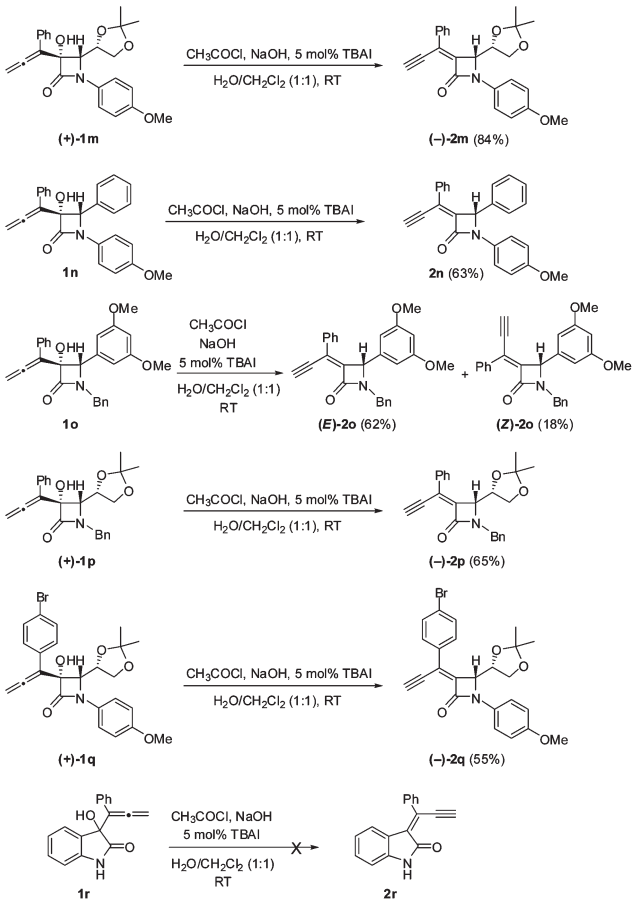


Scheme 2 Direct synthesis of enantiopure (*E*)-1,3-enynes **2h–l** from allenols **1h–l**.

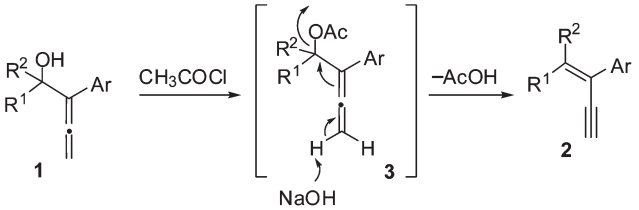
methodology by subjecting a range of aryl-substituted α-allenols **1b–g** to dehydration/rearrangement and the results are shown in Scheme 1. In each case, the crude reaction mixtures are extremely clean and (*E*)-1,3-enynes **2b–g** are the only products detected (Scheme 1).[9] Besides, as revealed in Scheme 1, various aryl-substituted allenols were suitable for such a reaction. For example, phenyl, *p*-methoxyphenyl, and *p*-bromophenyl substituents at the allene side were tolerated. Next, we decided to use heteroaromatic α-allenol derivatives as the reactants. Tolerance toward this type of substituent at the alkene end was demonstrated by the obtention of the corresponding indole derivative **2g** in fair yield.

Satisfied with the above results, we set out to evaluate the reaction for substrates that contain stereocenters. Thus, a series of aliphatic enantiopure α-allenol derivatives were tested (Scheme 2). Allenols **1h** and **1i** were smoothly converted into the desired 1,3-enynes **2h** and **2i**. To assess scope, the even more challenging enantiopure 2-azetidinone-tethered allenols **1j–l** were tested as precursors. Similarly, the aliphatic chain bearing a β-lactam moiety also afforded the expected (*E*)-1,3-enynes **2j–l** as single isomers. These results indicate that the stereochemical integrity at the heterocyclic stereocenters was retained in the course of the reaction.

Despite Lee's and Ma's statement that tetrasubstituted alkenes bearing ethynyl groups could not be prepared because acylation of the corresponding tertiary allenolic moiety did not work,[5] we decided to test our method with highly hindered allenols **1m–r**. To our delight, when the allene substituent was moved in the 2-azetidinone ring from position C4 to C3, as in (3*R*,4*S*)-3-hydroxy-3-(1-phenylpropa-1,2-dienyl)azetidin-2-ones **1m–q**, it furnished the corresponding enyne β-lactams **2m–q** in fair yields in its reaction with the AcCl–NaOH (aqueous) system. Whereas the reaction of allenols **1m**, **1n**, **1p**, and **1q** did take place with complete stereoselectivity, thus forming adducts (*E*)-**2m**, (*E*)-**2n**, (*E*)-**2p**, and (*E*)-**2q**, the dehydration/rearrangement of its dimethoxyaryl homologue **1o** gave 1,3-enynes **2o** with the absence of total stereoselectivity [(*E*)-**2o**/(*Z*)-**2o** = 78 : 22]. Fortunately, the isomeric 1,3-enynes (*E*)-**2o** and (*Z*)-**2o** were easily separated by column chromatography. Remarkably, Scheme 3 shows how the mild conditions of the process allow the



Scheme 3 Direct synthesis of tetrasubstituted 1,3-enynes **2m–q** from tertiary allenols **1m–q**.



Scheme 4 Proposed mechanism for the direct formation of 1,3-enynes **2** from allenols **1**.

stereoselective formation of tetrasubstituted enyne β-lactams without harming the sensitive four-membered ring. However, when the tether for the tetrasubstituted enyne formation is an *NH*-oxindole ring, *e.g.* **1r**, the reaction did not give the expected product **2r**, instead, an unidentified mixture was formed (Scheme 3).

A possible reaction course for the dehydration/rearrangement process is shown in Scheme 4. Initially, the reaction of allenols **1** with acetyl chloride affords the non-isolable allenic acetates **3**. Next, sodium hydroxide abstracts the distal allenic proton of intermediates **3**, which evolve to (*E*)-1,3-enynes **2** through subsequent triple bond generation with concomitant acetate elimination.

Conclusions

In conclusion, we have successfully accomplished a very attractive strategy for the direct stereoselective synthesis of the chemically and biologically relevant 1,3-enyne moiety from readily available aryl-substituted α-allenols.

Experimental section

^{1}H NMR and ^{13}C NMR spectra were recorded on a Bruker Avance AVIII-700 with a cryoprobe, a Bruker Avance-300, a Varian VRX-300S or a Bruker AC-200. NMR spectra were recorded in $CDCl_3$ solutions, unless otherwise stated. Chemical shifts are given in ppm relative to TMS (^{1}H, 0.0 ppm) or $CDCl_3$ (^{13}C, 76.9 ppm). Low and high resolution mass spectra were taken on an AGILENT 6520 Accurate-Mass QTOF LC/MS spectrometer using the electronic impact (EI) or electrospray modes (ES) unless otherwise stated. Specific rotation $[\alpha]_D$ is given in 10^{-1} deg cm^2 g^{-1} at 20 °C, and the concentration (c) is expressed in g per 100 mL. All commercially available compounds were used without further purification.

Indium-promoted reaction between 3-substituted prop-2-ynyl bromides and aldehydes; general procedure for the synthesis of α-allenic alcohols 1a–o

1-Bromo-3-phenyl-2-propyne, 1-bromo-3-(*p*-methoxyphenyl)-2-propyne, or 1-bromo-3-(*p*-bromophenyl)-2-propyne (3.0 mmol) was added to a well stirred suspension of the corresponding aldehyde (1.0 mmol) and indium powder (6.0 mmol) in THF–NH_4Cl (aq. sat.) (1 : 5, 5 mL) at 0 °C. After disappearance of the starting material (TLC) the mixture was extracted with ethyl acetate (3 × 5 mL). The organic extract was washed with brine, dried ($MgSO_4$) and concentrated under reduced pressure. Chromatography of the residue using ethyl acetate–hexanes mixtures gave analytically pure compounds. Spectroscopic and analytical data for previously unreported α-allenic alcohols **1** follow.

α-Allenic alcohol 1e

From 250 mg (2.08 mmol) of *p*-anisaldehyde and after chromatography of the residue using hexanes–ethyl acetate (6 : 1) as the eluent, we obtained compound **1e** (374 mg, 68%) as a colorless oil; ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C): δ = 7.35 (d, 2H, J = 8.0 Hz), 7.29 (d, 2H, J = 9.0 Hz), 7.15 (d, 2H, J = 7.9 Hz), 6.81 (d, 2H, J = 8.9 Hz), 5.64 (br s, 1H), 5.34 (dd, 1H, J_{AB} = 11.9, 2.6 Hz), 5.29 (dd, 1H, J_{AB} = 11.9, 2.6 Hz), 3.77 (s, 3H), 2.34 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$, 25 °C): δ = 207.2, 158.7, 139.1, 137.5, 133.0, 129.1 (2C), 128.1 (2C), 126.9 (2C), 113.9 (2C), 109.5, 81.3, 72.3, 55.2, 21.1; IR ($CHCl_3$): ν = 3365, 2990, 1944 cm^{-1}; HRMS (ES): calcd for $C_{18}H_{18}O_2$ $[M]^+$: 266.1307; found: 266.1304.

α-Allenic alcohol 1f

From 290 mg (0.92 mmol) of *p*-bromobenzaldehyde and after chromatography of the residue using hexanes–ethyl acetate (10 : 1) as the eluent, we obtained compound **1f** (191 mg, 69%) as a colorless oil; ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C): δ = 7.40 (d, 2H, J = 8.6 Hz), 7.35 (d, 2H, J = 8.1 Hz), 7.26 (d, 2H, J = 8.6 Hz), 7.17 (d, 2H, J = 8.0 Hz), 5.64 (t, 1H, J = 2.2 Hz), 5.32 (dd, 1H, J_{AB} = 12.3, 2.5 Hz), 5.26 (dd, 1H, J_{AB} = 12.3, 2.5 Hz), 2.57 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$, 25 °C): δ = 207.6, 138.6, 137.6, 132.9, 131.4 (2C), 129.1 (2C), 128.5 (2C), 126.7 (2C), 120.8, 109.0, 81.5, 72.1, 21.1; IR ($CHCl_3$): ν = 3360, 2992, 1941 cm^{-1}; HRMS (ES): calcd for $C_{17}H_{15}{}^{79}BrO$ $[M]^+$: 314.0306; found: 314.0303.

α-Allenic alcohol (−)-1i

From 397 mg (3.05 mmol) of (*R*)-2,3-*O*-isopropylideneglyceraldehyde and after chromatography of the residue using hexanes–ethyl acetate (6 : 1) as the eluent, we obtained compound (−)-**1i** (505 mg, 60%) as a colorless oil; $[\alpha]_D$ = −10.0 (c 0.2, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C): δ = 7.39 (d, 2H, J = 8.9 Hz), 6.91 (d, 2H, J = 8.9 Hz), 5.30–5.28 (m, 2H), 4.90 (dd, 1H, J = 6.3, 2.6 Hz), 4.36 (td, 1H, J = 6.6, 3.8 Hz), 4.13 (dd, 1H, J = 13.7, 7.2 Hz), 4.06 (dd, 1H, J = 12.4, 6.6 Hz), 3.94–3.92 (m, 1H), 3.84 (s, 3H), 1.51 (s, 3H), 1.39 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$, 25 °C): δ = 207.5, 158.9. 133.0, 127.8 (2C), 126.0, 114.1 (2C), 109.2, 80.9, 77.2, 69.4, 64.5, 55.3, 26.4, 24.9; IR ($CHCl_3$): ν = 3362, 2994, 1942 cm^{-1}; HRMS (ES): calcd for $C_{16}H_{20}O_4$ $[M]^+$: 276.1362; found: 276.1362.

α-Allenic alcohol (+)-1j

From 500 mg (2.01 mmol) of the corresponding β-lactam carbaldehyde and after chromatography of the residue using hexanes–ethyl acetate (4 : 1) as the eluent, we obtained compound (+)-**1i** (431 mg, 59%) as a colorless oil; $[\alpha]_D$ = +43.3 (c 0.4, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C): δ = 7.46–7.40 (m, 2H), 7.40–7.35 (m, 2H), 7.33–7.31 (m, 1H), 7.29–7.22 (m, 2H), 7.02–6.95 (m, 3H), 5.22 (d, 1H, J = 5.0 Hz), 5.23–5.18 (m, 1H), 5.12–5.08 (m, 1H), 5.06 (br s, 1H), 4.18 (dd, 1H, J = 6.6, 5.0 Hz), 3.36 (dd, 1H, J = 13.7, 8.5 Hz), 3.19 (dd, 1H, J = 13.7, 6.6 Hz), 2.22 (br s, 1H), 2.07–1.98 (m, 1H), 0.96 (d, 3H, J = 6.7 Hz), 0.92 (d, 3H, J = 6.6 Hz); ^{13}C NMR (75 MHz, $CDCl_3$, 25 °C): δ = 207.8, 166.6, 157.7, 134.0, 129.4 (2C), 128.8 (2C), 127.5, 126.8 (2C), 122.4, 116.0 (2C), 107.2, 80.6, 80.3, 69.8, 60.5, 49.6, 27.0, 20.4, 20.2; IR ($CHCl_3$): ν = 3364, 2991, 1943, 1744 cm^{-1}; HRMS (ES): calcd for $C_{23}H_{25}NO_3$ $[M]^+$: 363.1834; found: 363.1839.

α-Allenic alcohol (+)-1l

From 463 mg (1.64 mmol) of the corresponding β-lactam carbaldehyde and after chromatography of the residue using hexanes–ethyl acetate (4 : 1) as the eluent, we obtained compound (+)-**1l** (283 mg, 44%) as a colorless oil; $[\alpha]_D$ = +14.5 (c 0.5, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C): δ = 7.28–7.22 (m, 9H), 7.18–7.13 (m, 3H), 6.94–6.85 (m, 3H), 5.11 (d, 1H, J = 5.0 Hz), 5.00–4.92 (m, 4H), 4.79 (d, 1H, J = 14.8 Hz), 4.37 (d, 1H, J = 14.8 Hz); ^{13}C NMR (75 MHz, $CDCl_3$, 25 °C): δ = 207.8, 166.5, 157.7, 135.9, 133.9, 129.4 (2C), 128.8 (2C), 128.7 (2C), 128.4 (2C), 127.8, 127.5, 126.7 (2C), 122.3, 116.0 (2C), 106.8, 80.6, 80.4, 70.2. 59.8, 45.8; IR ($CHCl_3$):

ν = 3361, 2988, 1940, 1741 cm^{-1}; HRMS (ES): calcd for $C_{26}H_{23}NO_3$ $[M]^+$: 397.1678; found: 397.1675.

α-Allenic alcohol 1n

From 110 mg (0.29 mmol) of the corresponding azetidine-2,3-dione and after chromatography of the residue using hexanes–ethyl acetate (2 : 1) as the eluent, we obtained compound **1n** (67 mg, 63%) as a colorless oil; ^1H NMR (300 MHz, $CDCl_3$, 25 °C): δ = 7.50 (d, 2H, J = 7.1 Hz), 7.36–7.17 (m, 10H), 6.70 (d, 2H, J = 9.1 Hz), 5.30 (d, 2H, J = 5.3 Hz), 5.24 (s, 1H), 3.66 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$, 25 °C): δ = 208.0, 164.9, 156.4, 133.5, 132.6, 130.4, 129.1, 129.0 (2C), 128.6 (2C), 128.2 (2C), 128.1 (2C), 127.7, 119.0 (2C), 114.3 (2C), 105.6, 86.0, 81.2, 67.9, 55.5; IR ($CHCl_3$): ν = 3371, 2998, 1946, 1749 cm^{-1}; HRMS (ES): calcd for $C_{25}H_{21}NO_3$ $[M]^+$: 383.1521; found: 383.1530.

α-Allenic alcohol 1o

From 215 mg (1.70 mmol) of the corresponding azetidine-2,3-dione and after chromatography of the residue using hexanes–ethyl acetate (2 : 1) as the eluent, we obtained compound **1o** (198 mg, 68%) as a colorless oil; ^1H NMR (300 MHz, $CDCl_3$, 25 °C): δ = 7.41 (d, 2H, J = 7.0 Hz), 7.24–7.15 (m, 6H), 7.03–6.99 (m, 2H), 6.40 (br s, 1H), 6.35 (s, 1H), 6.34 (s, 1H), 5.20 (d, 1H, J_{AB} = 12.6 Hz), 5.15 (d, 1H, J_{AB} = 12.6 Hz), 4.84 (d, 1H, J = 15.0 Hz), 4.57 (s, 1H), 3.81 (d, 1H, J = 15.0 Hz), 3.70 (s, 6H); ^{13}C NMR (75 MHz, $CDCl_3$, 25 °C): δ = 207.5, 168.3, 161.2, 136.0, 134.9, 132.5, 128.7 (2C), 128.4 (2C), 128.3 (2C), 128.1 (2C), 127.7, 127.5, 106.3 (2C), 105.3, 100.9, 87.2, 81.0, 77.1, 67.8, 55.4 (2Me), 44.0; IR ($CHCl_3$): ν = 3373, 3000, 1947, 1750 cm^{-1}; HRMS (ES): calcd for $C_{27}H_{25}NO_4$ $[M]^+$: 427.1784; found: 427.1792.

α-Allenic alcohol (+)-1q

From 150 mg (0.52 mmol) of the corresponding azetidine-2,3-dione and after chromatography of the residue using hexanes–ethyl acetate (3 : 1) as the eluent, we obtained compound (+)-**1q** (153 mg, 60%) as a colorless oil; $[\alpha]_D$ = +2.3 (c 0.2, $CHCl_3$); ^1H NMR (300 MHz, $CDCl_3$, 25 °C): δ = 7.57–7.55 (m, 4H), 7.46 (d, 2H, J = 9.0 Hz), 6.85 (d, 2H, J = 9.0 Hz), 5.31 (s, 2H), 4.63 (s, 1H), 4.55 (dd, 1H, J = 13.7, 6.7 Hz), 4.40 (d, 1H, J = 6.7 Hz), 4.30 (d, 1H, J = 8.9, 6.7 Hz), 3.80 (m, 4H), 1.47 (s, 3H), 1.38 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$, 25 °C): δ = 207.9, 166.2. 156.8, 131.7 (2C), 130.5, 130.0 (2C), 128.3, 121.9, 120.2 (2C), 114.1 (2C), 109.9, 105.3, 84.2, 81.3, 76.4, 66.8, 66.5, 55.5, 26.5, 25.2; IR ($CHCl_3$): ν = 3381, 3003, 1945, 1752 cm^{-1}; HRMS (ES): calcd for $C_{24}H_{24}{}^{79}BrNO_5$ $[M]^+$: 485.0838; found: 485.0829.

General procedure for the synthesis of (*E*)-1,3-enynes 2a–o in aqueous media

Tetrabutyl ammonium iodide (cat), 50% aqueous sodium hydroxide (5 mL) and acetyl chloride (0.22 mmol) were sequentially added at room temperature to a solution of the appropriate α-allenol **1** (0.20 mmol) in dichloromethane (4 mL). The reaction was stirred for 24 h before being partitioned between dichloromethane and water. The aqueous phase was extracted with dichloromethane (3 × 10 mL). The organic extract was washed with water and brine, dried ($MgSO_4$) and concentrated under reduced pressure. Chromatography of the residue using ethyl acetate–hexanes mixtures gave analytically pure compounds. Spectroscopic and analytical data for compounds **2** follow.

(*E*)-1,3-Enyne 2a

From 200 mg (0.90 mmol) of α-allenol **1a** and after chromatography of the residue using hexanes–ethyl acetate (10 : 1) as the eluent, we obtained compound **2a** (139 mg, 76%) as a colorless oil; ^1H NMR (300 MHz, $CDCl_3$, 25 °C): δ = 8.03 (d, 2H, J = 7.3 Hz), 7.79 (d, 2H, J = 7.0 Hz), 7.48–7.43 (m, 4H), 7.37 (d, 2H, J = 7.3 Hz), 7.29 (s, 1H), 3.59 (d, 1H, J = 0.6 Hz); ^{13}C NMR (75 MHz, $CDCl_3$, 25 °C): δ = 139.2, 136.4, 136.2, 129.1 (2C), 128.6, 128.5 (2C), 128.3 (2C), 128.0, 126.4 (2C), 121.0, 85.3, 82.4; IR ($CHCl_3$): ν = 3285, 3020, 1600 cm^{-1}; HRMS (ES): calcd for $C_{16}H_{12}$ $[M]^+$: 204.0939; found: 204.0937.

(*E*)-1,3-Enyne 2b

From 200 mg (0.79 mmol) of α-allenol **1b** and after chromatography of the residue using hexanes–ethyl acetate (8 : 1) as the eluent, we obtained compound **2b** (125 mg, 67%) as a colorless oil; ^1H NMR (300 MHz, $CDCl_3$, 25 °C): δ = 7.88 (d, 2H, J = 8.8 Hz), 7.63 (d, 2H, J = 7.1 Hz), 7.33–7.17 (m, 3H), 7.10 (s, 1H), 6.85 (d, 2H, J = 8.8 Hz), 3.76 (s, 3H), 3.46 (s, 1H); ^{13}C NMR (75 MHz, $CDCl_3$, 25 °C): δ = 159.8, 139.4, 135.9, 130.6 (2C), 129.1, 128.6 (2C), 127.6, 126.2 (2C), 118.2, 113.7 (2C), 84.9, 82.8, 55.3; IR ($CHCl_3$): ν = 3286, 3021, 1599 cm^{-1}; HRMS (ES): calcd for $C_{17}H_{14}O$ $[M]^+$: 234.1045; found: 234.1037.

(*E*)-1,3-Enyne 2c

From 200 mg (0.85 mmol) of α-allenol **1c** and after chromatography of the residue using hexanes–ethyl acetate (5 : 1) as the eluent, we obtained compound **2c** (133 mg, 71%) as a colorless oil; ^1H NMR (300 MHz, $CDCl_3$, 25 °C): δ = 7.96 (d, 2H, J = 8.0 Hz), 7.80 (dd, 2H, J = 8.0, 1.3 Hz), 7.48–7.38 (m, 3H), 7.29–7.27 (m, 2H), 7.27 (s, 1H), 3.60 (d, 1H, J = 0.7 Hz), 2.46 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$, 25 °C): δ = 139.3, 138.7, 136.4, 133.4, 129.1 (2C), 129.0 (2C), 128.4 (2C), 127.8, 126.3 (2C), 119.6, 85.1, 82.6, 21.4; IR ($CHCl_3$): ν = 3288, 3016, 1601 cm^{-1}; HRMS (ES): calcd for $C_{17}H_{14}$ $[M]^+$: 218.1096; found: 234. 218.1087.

(*E*)-1,3-Enyne 2d

From 200 mg (0.78 mmol) of α-allenol **1d** and after chromatography of the residue using hexanes–ethyl acetate (6 : 1) as the eluent, we obtained compound **2d** (166 mg, 89%) as a colorless oil; ^1H NMR (300 MHz, $CDCl_3$, 25 °C): δ = 7.81 (d, 2H, J = 8.5 Hz), 7.62 (dd, 2H, J = 8.5, 1.0 Hz), 7.32–7.24 (m, 5H), 7.08

(s, 1H), 3.47 (d, 1H, J = 0.6 Hz); ^{13}C NMR (75 MHz, $CDCl_3$, 25 °C): δ = 138.8, 134.9, 134.6, 134.1, 130.3 (2C), 128.5 (4C), 128.2, 126.4 (2C), 121.3, 85.9, 82.1; IR ($CHCl_3$): ν = 3283, 3019, 1606 cm^{-1}; HRMS (ES): calcd for $C_{16}H_{11}Cl$ $[M]^+$: 238.0549; found: 238.0554.

(*E*)-1,3-Enyne 2e

From 315 mg (1.18 mmol) of α-allenol **1e** and after chromatography of the residue using hexanes–ethyl acetate (6 : 1) as the eluent, we obtained compound **2e** (187 mg, 63%) as a colorless oil; ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C): δ = 7.93 (d, 2H, J = 8.3 Hz), 7.73 (d, 2H, J = 8.9 Hz), 7.26 (d, 2H, J = 8.3 Hz), 7.20 (s, 1H), 6.98 (d, 2H, J = 8.9 Hz), 3.89 (s, 3H), 3.58 (d, 1H, J = 0.7 Hz), 2.44 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$, 25 °C): δ = 159.4, 138.3, 134.7, 133.6, 131.8, 128.9 (2C), 128.8 (2C), 127.4 (2C), 119.1, 113.8 (2C), 84.9, 82.7, 55.3, 21.4; IR ($CHCl_3$): ν = 3284, 3010, 1606 cm^{-1}; HRMS (ES): calcd for $C_{18}H_{16}O$ $[M]^+$: 248.1201; found: 248.1191.

(*E*)-1,3-Enyne 2f

From 290 mg (0.92 mmol) of α-allenol **1f** and after chromatography of the residue using hexanes–ethyl acetate (10 : 1) as the eluent, we obtained compound **2f** (191 mg, 69%) as a colorless oil; ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C): δ = 7.76 (d, 2H, J = 8.0 Hz), 7.47 (d, 2H, J = 8.8 Hz), 7.38 (d, 2H, J = 8.8 Hz), 7.09 (d, 2H, J = 8.0 Hz), 7.07 (s, 1H), 3.42 (d, 1H, J = 0.6 Hz), 2.27 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$, 25 °C): δ = 139.0, 138.2, 136.6, 133.1, 131.4 (2C), 129.1 (2C), 129.0 (2C), 127.8 (2C), 121.7, 118.4, 85.5, 82.1, 21.4; IR ($CHCl_3$): ν = 3290, 3027, 1598 cm^{-1}; HRMS (ES): calcd for $C_{17}H_{13}{}^{79}Br$ $[M]^+$: 296.0201; found: 296.0205.

(*E*)-1,3-Enyne 2g

From 50 mg (0.14 mmol) of α-allenol **1g** and after chromatography of the residue using hexanes–ethyl acetate (4 : 1) as the eluent, we obtained compound **2g** (33 mg, 68%) as a colorless oil; ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C): δ = 8.09 (d, 1H, J = 8.0 Hz), 7.65–7.62 (m, 1H), 7.28–7.25 (m, 7H), 7.21 (s, 1H), 6.24 (t, 1H, J = 6.7 Hz), 3.13–2.97 (m, 1H), 1.59 (s, 9H); ^{13}C NMR (75 MHz, $CDCl_3$, 25 °C): δ = 170.2, 138.1, 131.6 (2C), 128.2 (2C), 127.9 (2C), 127.8, 126.1, 124.7, 124.1, 123.1, 122.8, 119.8, 118.7, 115.5, 85.1, 83.0, 28.1, 28.2 (3C); IR ($CHCl_3$): ν = 3281, 3007, 1707, 1602 cm^{-1}; HRMS (ES): calcd for $C_{23}H_{21}NO_2$ $[M]^+$: 343.1572; found: 343.1580.

(*E*)-1,3-Enyne (+)-2h

From 135 mg (0.55 mmol) of α-allenol (+)-**1h** and after chromatography of the residue using hexanes–ethyl acetate (7 : 1) as the eluent, we obtained compound (+)-**2h** (88 mg, 69%) as a colorless oil; $[\alpha]_D$ = +30.0 (c 0.5, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C): δ = 7.55 (dd, 2H, J = 8.2, 1.6 Hz), 7.28–7.23 (m, 3H), 6.39 (d, 1H, J = 8.2 Hz), 5.18 (dd, 1H, J = 14.5, 7.2 Hz), 4.21 (dd, 1H, J = 8.2, 6.3 Hz), 3.62 (dd, 1H, J = 8.2, 7.2 Hz), 3.34 (s, 1H), 1.41 (s, 3H), 1.37 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$, 25 °C): δ = 136.5, 136.4, 128.4 (3C), 126.1 (2C), 125.3, 109.6, 84.8, 19.6, 75.1, 68.9, 26.7, 25.8; IR ($CHCl_3$): ν = 3298, 3080, 1610 cm^{-1}; HRMS (ES): calcd for $C_{15}H_{16}O_2$ $[M]^+$: 228.1150; found: 228.1143.

(*E*)-1,3-Enyne (+)-2i

From 120 mg (0.43 mmol) of α-allenol (−)-**1i** and after chromatography of the residue using hexanes–ethyl acetate (4 : 1) as the eluent, we obtained compound (+)-**2i** (82 mg, 73%) as a colorless oil; $[\alpha]_D$ = +18.3 (c 0.6, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C): δ = 7.57 (d, 2H, J = 9.1 Hz), 6.89 (d, 2H, J = 9.1 Hz), 6.35 (dd, 1H, J = 8.3, 0.6 Hz), 5.31–5.22 (m, 1H), 4.28 (dd, 1H, J = 8.3, 6.2 Hz), 3.83 (s, 3H), 3.69 (dd, 1H, J = 8.3, 7.3 Hz), 3.40 (d, 1H, J = 0.6 Hz), 1.49 (s, 3H), 1.45 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$, 25 °C): δ = 159.9, 134.2, 129.0, 127.4 (2C), 124.8, 113.8 (2C), 109.5, 84.6, 79.8, 75.2, 68.9, 55.3, 26.7, 25.8; IR ($CHCl_3$): ν = 3296, 3084, 1611 cm^{-1}; HRMS (ES): calcd for $C_{16}H_{18}O_3$ $[M]^+$: 258.1256; found: 258.1251.

(*E*)-1,3-Enyne (+)-2j

From 155 mg (0.43 mmol) of α-allenol (+)-**1j** and after chromatography of the residue using hexanes–ethyl acetate (3 : 1) as the eluent, we obtained compound (+)-**2j** (131 mg, 88%) as a colorless oil; $[\alpha]_D$ = +72.7 (c 1.5, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C): δ = 7.43–7.39 (m, 2H), 7.25–7.22 (m, 3H), 7.18–7.14 (m, 2H), 6.93–6.88 (m, 3H), 6.41 (dd, 1H, J = 9.6, 0.6 Hz), 5.34 (d, 1H, J = 4.4 Hz), 5.09 (dd, 1H, J = 9.6, 4.4 Hz), 3.40 (d, 1H, J = 0.6 Hz), 3.14 (dd, 1H, J = 13.9, 7.7 Hz), 2.85 (dd, 1H, J = 13.9, 6.7 Hz), 1.97–1.85 (m, 1H), 0.89 (t, 6H, J = 6.7 Hz); ^{13}C NMR (75 MHz, $CDCl_3$, 25 °C): δ = 165.7, 157.3, 136.4, 131.3, 129.5 (2C), 129.4, 128.9, 128.5 (2C), 126.3 (2C), 122.3, 115.5 (2C), 85.0, 81.9, 79.8, 59.2, 48.7, 27.5. 20.4 (2C); IR ($CHCl_3$): ν = 3290, 3033, 1734, 1606 cm^{-1}; HRMS (ES): calcd for $C_{23}H_{23}NO_2$ $[M]^+$: 345.1729; found: 345.1735.

(*E*)-1,3-Enyne (+)-2k

From 91 mg (0.26 mmol) of α-allenol (+)-**1k** and after chromatography of the residue using hexanes–ethyl acetate (3 : 1) as the eluent, we obtained compound (+)-**2k** (55 mg, 63%) as a colorless oil; $[\alpha]_D$ = +23.3 (c 1.5, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C): δ = 7.59 (dd, 2H, J = 8.0, 1.9 Hz), 7.34 (d, 2H, J = 9.0 Hz), 7.30–7.26 (m, 3H), 6.78 (d, 2H, J = 9.0 Hz), 6.54 (d, 1H, J = 9.6 Hz), 5.31 (dd, 1H, J = 9.6, 4.8 Hz), 4.74 (d, 1H, J = 4.8 Hz), 3.69 (s, 3H), 3.54 (s, 1H), 3.45 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$, 25 °C): δ = 163.3, 156.5, 147.0, 136.1, 132.3, 131.0, 128.9, 128.8 (2C), 126.3 (2C), 118.5 (2C), 114.5 (2C), 86.0, 85.0, 75.9, 59.0, 58.5, 55.5; IR ($CHCl_3$): ν = 3292, 3030, 1731, 1603 cm^{-1}; HRMS (ES): calcd for $C_{21}H_{19}NO_3$ $[M]^+$: 333.1365; found: 333.1371.

(*E*)-1,3-Enyne (+)-2l

From 75 mg (0.19 mmol) of α-allenol (+)-**1l** and after chromatography of the residue using hexanes–ethyl acetate (3 : 1) as the eluent, we obtained compound (+)-**2l** (61 mg, 84%) as a

colorless oil; $[\alpha]_D$ = +50.0 (*c* 1.9, $CHCl_3$); ^1H NMR (300 MHz, $CDCl_3$, 25 °C): δ = 7.26–7.13 (m, 12H), 6.89–6.86 (m, 3H), 6.26 (dd, 1H, *J* = 9.8, 0.6 Hz), 5.30 (d, 1H, *J* = 4.4 Hz), 5.00 (dd, 1H, *J* = 9.8, 4.4 Hz), 4.53 (d, 1H, *J* = 14.7 Hz), 4.16 (d, 1H, *J* = 14.7 Hz), 3.26 (d, 1H, *J* = 0.6 Hz); ^{13}C NMR (75 MHz, $CDCl_3$, 25 °C): δ = 164.9, 157.2, 136.3, 135.3, 131.0 (2C), 129.5 (2C), 129.2, 128.8 (4C), 128.4 (2C), 127.9 (2C), 126.2, 122.2, 115.4 (2C), 85.1, 82.1, 79.6, 58.3, 45.0; IR ($CHCl_3$): ν = 3288, 303q, 1735, 1605 cm^{-1}; HRMS (ES): calcd for $C_{26}H_{21}NO_2$ $[M]^+$: 379.1572; found: 379.1578.

(*E*)-1,3-Enyne (−)-2m

From 105 mg (0.26 mmol) of α-allenol (+)-**1m** and after chromatography of the residue using hexanes–ethyl acetate (2 : 1) as the eluent, we obtained compound (−)-**2m** (85 mg, 84%) as a colorless oil; $[\alpha]_D$ = −126.9 (*c* 2.6, $CHCl_3$); ^1H NMR (300 MHz, $CDCl_3$, 25 °C): δ = 8.08 (dd, 2H, *J* = 8.0, 1.9 Hz), 7.57 (d, 2H, *J* = 9.1 Hz), 7.44–7.41 (m, 3H), 6.90 (d, 2H, *J* = 9.1 Hz), 4.82 (d, 1H, *J* = 5.6 Hz), 4.60 (dd, 1H, *J* = 12.6, 6.7 Hz), 4.21 (d, 2H, *J* = 6.7 Hz), 3.81 (s, 3H), 3.51 (s, 1H), 1.44 (s, 3H), 1.35 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$, 25 °C): δ = 158.5, 156.6, 142.1, 133.3, 131.2, 129.9, 129.2 (2C), 128.2 (2C), 123.1, 120.0 (2C), 114.1 (2C), 109.7, 85.5, 80.8, 77.2, 67.0, 61.8, 55.4, 26.4, 25.5; IR ($CHCl_3$): ν = 3285, 3044, 1726, 1598 cm^{-1}; HRMS (ES): calcd for $C_{24}H_{23}NO_4$ $[M]^+$: 389.1627; found: 389.1629.

(*E*)-1,3-Enyne 2n

From 110 mg (0.29 mmol) of α-allenol **1n** and after chromatography of the residue using hexanes–ethyl acetate (2 : 1) as the eluent, we obtained compound **2n** (67 mg, 63%) as a colorless oil; ^1H NMR (300 MHz, $CDCl_3$, 25 °C): δ = 8.09 (dd, 2H, *J* = 8.4, 1.6 Hz), 7.43–7.40 (m, 2H), 7.33–7.23 (m, 8H), 6.71 (d, 2H, *J* = 9.1 Hz), 5.38 (s, 1H), 3.64 (s, 3H), 3.13 (s, 1H); ^{13}C NMR (75 MHz, $CDCl_3$, 25 °C): δ = 158.8, 156.8, 147.0, 136.2, 133.8, 131.4, 130.3, 129.3 (2C), 129.2, 129.1 (2C), 128.8 (2C), 128.5 (2C), 123.5, 118.9 (2C), 114.9 (2C), 86.3, 79.7, 63.7, 55.8; IR ($CHCl_3$): ν = 3284, 3064, 1728, 1596 cm^{-1}; HRMS (ES): calcd for $C_{25}H_{19}NO_2$ $[M]^+$: 365.1416; found: 365.1412.

Reaction of allenol 1o. Preparation of (*E*)-1,3-enyne 2o and (*Z*)-1,3-enyne 2o

From 65 mg (0.15 mmol) of α-allenol **1o** and after chromatography of the residue using hexanes–ethyl acetate (5 : 1) as the eluent, 38 mg (62%) of the less polar compound (*E*)-**2o** and 11 mg (18%) of the more polar compound (*Z*)-**2o** were obtained.

(*E*)-1,3-Enyne 2o

Colorless oil; ^1H NMR (300 MHz, $CDCl_3$, 25 °C): δ = 8.09 (dd, 2H, *J* = 8.2, 1.6 Hz), 7.33–7.11 (m, 8H), 6.40–6.36 (m, 3H), 4.83 (d, 1H, *J* = 15.1 Hz), 4.79 (s, 1H), 3.88 (d, 1H, *J* = 15.1 Hz), 3.69 (s, 6H), 3.04 (s, 1H); ^{13}C NMR (75 MHz, $CDCl_3$, 25 °C): δ = 161.5, 160.9, 147.4, 138.0, 135.3, 133.3, 129.7, 128.8 (2C), 128.7 (2C), 128.6 (2C), 128.3 (2C), 127.8, 122.5, 106.3 (2C), 100.6, 85.1, 79.2, 77.1, 62.3, 55.4 (2C), 44.5; IR ($CHCl_3$): ν = 3282, 3066, 1726, 1595 cm^{-1}; HRMS (ES): calcd for $C_{27}H_{23}NO_3$ $[M]^+$: 409.1678; found: 365.409.1697.

(*Z*)-1,3-Enyne 2o

Colorless oil; ^1H NMR (300 MHz, $CDCl_3$, 25 °C): δ = 7.31 (dd, 2H, *J* = 7.4, 1.9 Hz), 7.25–7.19 (m, 4H), 7.15–7.11 (m, 4H), 6.27–6.24 (m, 3H), 4.97 (s, 1H), 4.86 (d, 1H, *J* = 15.1 Hz), 3.78 (d, 1H, *J* = 15.1 Hz), 3.62 (s, 6H), 3.51 (s, 1H); ^{13}C NMR (75 MHz, $CDCl_3$, 25 °C): δ = 162.8, 161.1, 147.3, 137.5, 135.4, 133.8, 129.3, 128.8 (2C), 128.6 (2C), 128.2 (2C), 128.1 (2C), 127.9, 127.8, 118.9, 105.8 (2C), 101.1, 85.2, 79.2, 63.7, 55.4 (2C), 44.4; IR ($CHCl_3$): ν = 3283, 3060, 1726, 1597 cm^{-1}; HRMS (ES): calcd for $C_{27}H_{23}NO_3$ $[M]^+$: 409.1678; found: 409.1683.

(*E*)-1,3-Enyne (−)-2p

From 390 mg (1.03 mmol) of α-allenol (+)-**1p** and after chromatography of the residue using hexanes–ethyl acetate (2 : 1) as the eluent, we obtained compound (−)-**2p** (252 mg, 65%) as a colorless oil; $[\alpha]_D$ = −16.0 (*c* 0.3, $CHCl_3$); ^1H NMR (300 MHz, $CDCl_3$, 25 °C): δ = 8.15 (d, 1H, *J* = 8.2 Hz), 8.14 (d, 1H, *J* = 7.8 Hz), 7.46–7.34 (m, 8H), 5.10 (d, 1H, *J* = 14.9 Hz), 4.54 (dd, 1H, *J* = 12.5, 6.0 Hz), 4.40 (d, 1H, *J* = 14.9 Hz), 4.23 (dd, 1H, *J* = 8.9, 6.6 Hz), 4.10 (d, 1H, *J* = 6.0 Hz), 4.00 (dd, 1H, *J* = 8.9, 6.0 Hz), 3.39 (s, 1H), 1.50 (s, 3H), 1.41 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$, 25 °C): δ = 161.4, 143.8, 135.9, 133.3, 129.8, 129.1 (2C), 128.8 (2C), 128.6 (2C), 128.4, 128.3 (2C), 127.8, 122.2, 109.7, 84.5, 80.5, 67.3, 61.0, 45.7, 26.5, 25.3; IR ($CHCl_3$): ν = 3280, 3039, 1723, 1595 cm^{-1}; HRMS (ES): calcd for $C_{24}H_{23}NO_3$ $[M]^+$: 373.1678; found: 373.1677.

(*E*)-1,3-Enyne (−)-2q

From 145 mg (0.30 mmol) of α-allenol (+)-**1q** and after chromatography of the residue using hexanes–ethyl acetate (2 : 1) as the eluent, we obtained compound (−)-**2q** (77 mg, 55%) as a colorless oil; $[\alpha]_D$ = −2.4 (*c* 0.1, $CHCl_3$); ^1H NMR (300 MHz, $CDCl_3$, 25 °C): δ = 8.00 (d, 2H, *J* = 8.8 Hz), 7.58 (d, 2H, *J* = 8.8 Hz), 7.57 (d, 2H, *J* = 9.0 Hz), 6.93 (d, 2H, *J* = 9.0 Hz), 4.83 (d, 1H, *J* = 5.3 Hz), 4.66–4.59 (m, 1H), 4.22 (d, 1H, *J* = 6.3 Hz), 4.21 (d, 1H, *J* = 7.1 Hz), 3.84 (s, 3H), 3.55 (s, 1H), 1.45 (s, 3H), 1.37 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$, 25 °C): δ = 158.4, 156.8, 142.6, 132.3, 131.4 (2C), 131.1, 130.8 (2C), 124.5, 121.9, 119.8 (2C), 114.2 (2C), 109.8, 85.9, 80.3, 76.9, 66.9, 61.9, 55.5, 26.4, 25.5; IR ($CHCl_3$): ν = 3280, 3046, 1726, 1597 cm^{-1}; HRMS (ES): calcd for $C_{24}H_{22}{}^{79}BrNO_4$ $[M]^+$: 467.0732; found: 467.0751.

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