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Convenient Syntheses of Methyl 2-Bromo- and 2-Iodo-2,3-butadienoates

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CONVENIENT SYNTHESES OF METHYL 2-BROMO- AND 2-IODO-2,3-BUTADIENOATES

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Abstract: Syntheses of methyl 2-bromo- and 2-iodo-2,3-butadienoates **3** and **6** from readily available starting materials are described. **3** and **6** will be valuable building blocks for the synthesis of 2-aryl and 2-alkenyl substituted alka-2,3-dienoates via Palladium-catalyzed cross-coupling reactions.

Allene carboxylates constitute a class of synthetically valuable compounds. Due to the electron-withdrawing character of the ester functional group, they show an enhanced reactivity towards nucleophiles and can also serve as dienophiles in Diels-Alder reactions. As a consequence, they are useful in a variety of synthetic manipulations leading to both acyclic and carbo- or heterocyclic molecules.[1]

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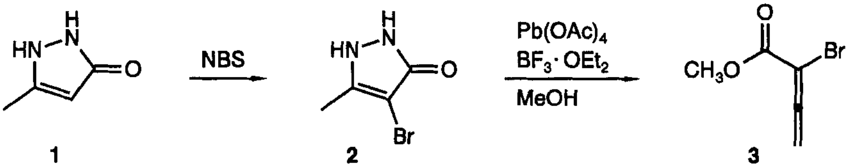
Several methods for the preparation of allenic esters are known,[2-8] however, they seem to lack generality as far as 2-aryl or 2-alkenyl substituted analogs are concerned. To achieve formation of carbon-carbon bonds between sp^2-carbons, Pd-catalyzed coupling reactions[9] are established as a powerful tool. While suitable aryl and alkenyl organometallics are readily accessible, the requisite allenic coupling partners, 2-halo-substituted derivatives **3** and **6**, are hitherto unknown.[10] Convenient procedures for their preparation are presented below.

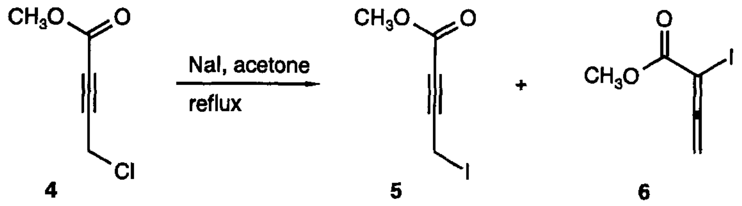
Bromination of heterocycle **1**[11] with NBS leads to the bromo derivative **2** in 73% yield.[12] Subsequent transformation of **2** by a literature procedure[4] affords **3** in 59% yield.



1 **2** **3**

This way of preparation cannot be extended to the iodo derivative **6**. While iodination of **1** is accomplished simply by reaction with iodine, the resulting heterocycle rapidly decomposes when coming into contact with protic solvents, thus precluding any further manipulation in methanol.

As a workable alternative, reaction of sodium iodide with methyl 4-chloro-2-butynoate (**4**)[13] in acetone leads, in part, to an S_N2' displacement of halide to afford a mixture of **5** and **6** from which **6** can be separated by sublimation.



In summary, methyl 2-bromo- and 2-iodo-2,3-butadienoates **3** and **6** were conveniently prepared from readily available starting materials. These compounds will be valuable substrates for the Palladium-catalyzed cross-coupling with aryl and alkenyl organometallics.[14]

Experimental Section

Melting points: Leitz Heiztischmikroskop HM-Lux, uncorrected. Microanalyses: CH-Analyzer Labormatic Wösthoff and CHN-Autoanalyzer 185 Hewlett-Packard. MS: Vacuum Generators 7070 H; IR: Hitachi 270-30 and Nicolet 510 P (FT-IR). NMR: JNM-FX-100 and JNM-GX-400 (Jeol). Analytical gas chromatography: Kipp Analytica 8200, 47 m x 0.25 mm capillary column with SE 54, 1.6 bar N_2.

4-Bromo-5-methyl-1,2-dihydro-pyrazol-3-one (2)

To a solution of 5-methyl-1,2-dihydro-pyrazol-3-one (**1**)[11] (9.8 g, 100 mmol) in chloroform (100 mL) were added N-bromosuccinimide (17.8 g, 100 mmol) and AIBN (1.1 g, 7 mmol) with stirring. The mixture was refluxed for 6 h; after 1 h an additional portion of AIBN (1.1 g; 7 mmol) was added. After being cooled to room temperature, the crude product was obtained by filtration. The resulting yellow solid was washed with chloroform (30 mL) and recrystallized from ethanol to afford a white solid (12.9 g, 73 %): mp 192 - 194 °C.[12] Anal. Calcd for $C_4H_5BrN_2O$: C, 27.15; H, 2.85; Br, 45.15; N, 15.83. Found: C, 27.14; H, 2.95; Br, 45,00; N, 15,77. MS m/z (%): 178 (M^+, ^{81}Br, 100), 177 (15), 176 (M^+, ^{79}Br, 100), 98

(47), 97 (52), 67 (24). IR (KBr): ν 3400-2000, 1594 cm^{-1}. ^{1}H-NMR (100 MHz, $CDCl_3$): δ 2.09 (s, 3 H, CH_3), 8-11 (bs, 2 H, NH). ^{13}C-NMR (100 MHz, $CDCl_3$): δ 10.3 (CH_3), 77.6 (C-Br), 138.0 (C-CH_3), 157.8 (C=O).

Methyl 2-bromo-2,3-butadienoate (3)

To a mixture of borontrifluoride etherate (2.0 mL, 16.3 mmol) and lead-(IV)-acetate (5.66 g, 12.8 mmol) in methanol (20 mL) at 0 °C was added 4-bromo-5-methyl-1,2-dihydro-pyrazol-3-one (**2**) (1.13 g, 6.4 mmol) in several portions during 10 min. After being stirred for another 15 min at 0 °C and a further 90 min at room temperature, water (30 mL) was added and the mixture was extracted three times with chloroform (30 mL each). The organic layer was dried ($MgSO_4$), filtered and concentrated. Flash chromatography (hexane/ethyl acetate = 19:1) yields white crystals of a lachrymator (0.67 g, 59 %): mp 51 - 53 °C. Anal. Calcd for $C_5H_5BrO_2$: C, 33.93; H, 2.85; Br, 45.14. Found: C, 34.06; H, 3.05; Br, 45.18. MS m/z (%): 178 (M^+, ^{81}Br, 83), 177 (7), 176 (M^+, ^{79}Br, 81), 149 (31), 147 (67), 145 (37), 119 (95), 117 (96), 68 (81), 67 (100), 66 (77), 59 (56). IR (KBr): ν 1953, 1899, 1719 cm^{-1}. ^{1}H-NMR (400 MHz, $CDCl_3$): δ 3.83 (s, 3 H, OCH_3), 5.31 (s, 2 H, =CH_2). ^{13}C-NMR (100 MHz, $CDCl_3$): δ 53.7 (OCH_3), 83.7 (CBr), 84.2 (=CH_2), 164.2 (C=O), 212.0 (=C=).

Methyl 2-iodo-2,3-butadienoate (6)

A solution of sodium iodide (1.65 g, 11 mmol) in acetone (10 mL) was added to a solution of methyl 4-chloro-2-butynoate (**4**)[13] (1.23 g, 9 mmol) in acetone (1 mL) with stirring. The mixture was refluxed for 1 h (when gas chromatographic analysis at 130 °C revealed that the ratio of **6** to **5** did no longer increase), then cooled to room temperature, and concentrated. Water (10 mL) was added and the organic material was extracted with two 30 mL portions of ether. The combined organic layers were washed with 10% aqueous sodium thiosulfate (10 mL) and water (10 mL), then dried ($MgSO_4$), filtered and concentrated to give a brown oil which solidified on standing. Sublimation (40 °C, 0.1 mm Hg) of the crude afforded a yellow solid that was recrystallized from pentane to give slightly yellow crystals of a lachrymator (0.79 g, 39%): mp 47-49 °C. Anal. Calcd for $C_5H_5IO_2$: C, 26.81; H, 2.25. Found: C, 26.86, H 2.36. MS m/z (%): 224 (M^+, 100), 193 (21), 165 (50), 127 (29), 67 (93), 66 (54). IR (KBr): ν 3060, 1944, 1899, 1722 cm^{-1}. ^1H-NMR (400 MHz, $CDCl_3$): δ 3.82 (s, 3 H, OCH_3), 5.04 (s, 2 H, $=CH_2$). ^{13}C-NMR (100 MHz, $CDCl_3$): δ 51.5 (*C*-I), 54.0 (O*C*H_3), 79.6 (=*C*H_2), 162.4 (*C*=O), 215.4 (=*C*=).

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