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SYNTHESIS OF 5-BROMO-2,4-DIMETHYL-OXAZOLE BY FLASH-VACUUM PYROLYSIS OF 2-ACETYL-4-BROMO-3-METHYLISOXA-ZOL-5(2H)-ONE

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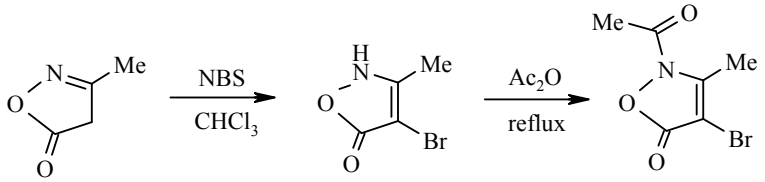
The photochemical or thermal loss of nitrogen and carbon dioxide from triazoles and isoxazol-5-ones, respectively, has been reported [1].

The photolysis [2] or pyrolysis [3, 4] of l-acyltriazoles leads to low yields of oxazoles as well as other products. However, Williams [5] has reported a new procedure for the thermal rearrangement of a number of acyltriazoles to oxazoles in good yields, although the procedure appears to be capable of variation only in the substituent at C-2.

Since isoxazol-5-ones are readily prepared from β-keto esters and their equivalents [6, 7], the procedures described herein should represent a useful additional method for the preparation of oxazoles. The bromination of 3-methylisoxazol-5(4H)-one (**1**) with N-bromosuccinimide at room temperature gave 4-bromo-3-methylisoxazol-5(2H)-one (**2**), which was converted to its N-acetyl derivative (**3**).



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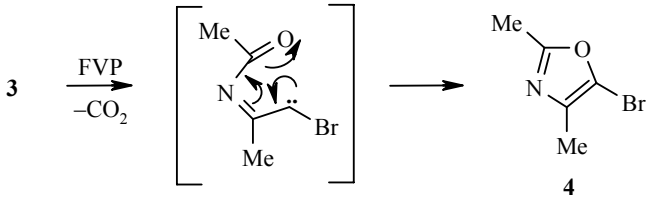
2-Acetyl-4-bromo-3-methylisoxazol-5(2H)-one (**3**) loses carbon dioxide under flash-vacuum pyrolysis conditions affording iminocarbene, which undergoes intramolecular cyclization through the oxygen of the acyl group to give 5-bromo-2,4-dimethyloxazole (**4**) according to the mechanism shown below.



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^{1}H and ^{13}C NMR spectra were recorded with a Bruker UltraShield spectrometer at 300 and 75.5 MHz, respectively. The spectra were measured in $CDCl_3$, using TMS as the internal standard. Infrared spectra were recorded on a Thermonicolet (Nexus 670) FT-infrared spectrometer, using sodium chloride cells and measured as a film or KBr disks. Mass spectra were recorded on a Varian Matt 311 spectrometer.

3-Methylisoxazol-5(4H)-one (**1**). The title compound was synthesized by a procedure adapted from the work by Jacquire [8].

4-Bromo-3-methylisoxazol-5(2H)-one (**2**). 3-Methylisoxazol-5(4H)-one (0.99 g, 10 mmol) was dissolved in chloroform (60 ml). N-Bromosuccinimide (1.95 g, 11 mmol) in carbon tetrachloride (50 ml) was added, and the solution was stirred at room temperature for 1 h, after which succinimide was observed to float to the surface, indicating the completion of the reaction. After filtration the resulting solution was extracted with water (5 × 100 ml) to remove any remaining dissolved impurities. The solution was dried (Na_2SO_4) and recrystallized from benzene/light petroleum giving 4-bromo-3-methylisoxazol-5(2H)-one as a pale yellow solid (1.54 g, 86%); mp 78-80°C. FT-IR spectrum (KBr), ν, cm^{-1}: 3433, 1813, 1437, 1386, 1168, 960, 868, 814, 653. ^{1}H NMR spectrum, δ, ppm: 2.27 (3H, s, CH_3); 4.88 (1H, s). ^{13}C NMR spectrum, δ, ppm: 11.72, 34.34, 162.16, 170.23. Mass spectrum (EI, 70 eV), *m/z* (I_{rel} , %): 179 $[M+2]^+$ (11), 177 $[M]^+$ (11), 151 (26), 149 (26), 134 (26), 132 (26), 67 (72), 44 (100). Found: *m/z* 178.9413 $[M+2]^+$, 176.9426 $[M]^+$. $C_4H_4BrNO_2$. Calculated: M = 178.9406, 176.9426.

2-Acetyl-4-bromo-3-methylisoxazol-5(2H)-one (**3**). A sample (890 mg) of 4-bromo-3-methyl-isoxazole-5(2H)-one was heated in acetic anyhydride (10 ml) for 2 h at 100°C. Removal of the solvent and recrystallization of the residue from diethyl ether/light petroleum gave the title compound as white needles (912 mg, 83%); mp 96–97°C. FT-IR spectrum (KBr), ν, cm^{-1}. 1820, 1770, 1724, 1587, 1396, 1374, 1357, 1285, 956. ^{1}H NMR spectrum, δ, ppm: 2.45 (3H, s, CH_3); 2.65 (3H, s, CH_3). ^{13}C NMR spectrum, δ, ppm: 15.06, 22.22, 88.34, 155.55, 162.55, 164.56**.** Mass spectrum (EI, 70 eV), *m/z* (I_{rel}, %): 221 $[M+2]^+$ (6), 219 $[M]^+$ (6), 179 (3), 177 (3), 140 (1), 138 (1), 108 (1), 106 (1), 67 (6), 51 (2), 43 (100).

5-Bromo-2,4-dimethyloxazole (**4**). Pyrolysis (580°C, 0.01 mm Hg, sublimation flask 110°C, 20 min) of 2-acetyl-4-bromo-3-methylisoxazol-5(2H)-one (100 mg) gave the title compound as a colorless oil (47 mg, 59%). FT-IR spectrum (a film), ν, cm^{-1}: 1635, 1537, 1487, 752, 680. ^{1}H NMR spectrum, δ, ppm: 1.98 (3H, s, CH_3); 2.09 (3H, s, CH_3). MS (EI, 70 ev), *m/z* (I_{rel}, %): 177 $[M+2]^+$ (18), 175 $[M]^+$ (18), 140 (52), 138 (53), 134 (36), 132 (34), 129 (36), 96 (73), 94 (80), 82 (42), 80 (7), 71 (42), 57 (62), 55 (54), 43 (100), 41 (72). Found: *m/z* 176.9622 $[M+2]^+$, 174.9639 $[M]^+$. C_5H_6BrNO. Calculated: M = 176.9614, 174.9633.

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