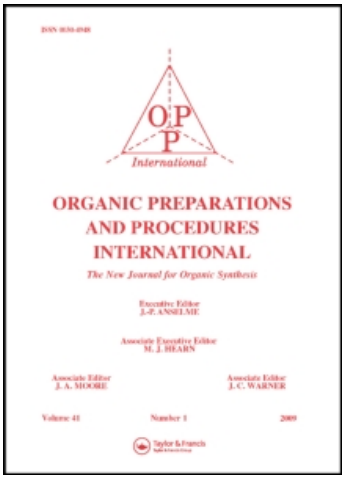

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METHYL 2-(5-ISOPROPYL-3-ISOXAZOLYL) BENZOATE

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OPPI BRIEFS

METHYL 2-(5-ISOPROPYL-3-ISOXAZOLYL)BENZOATE

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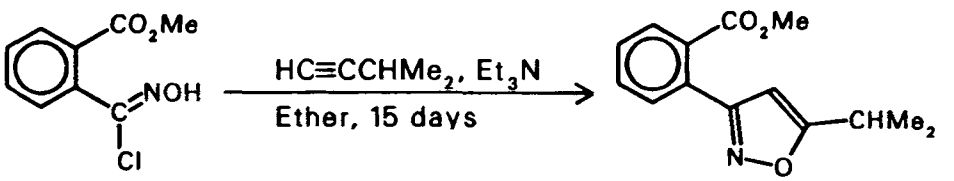
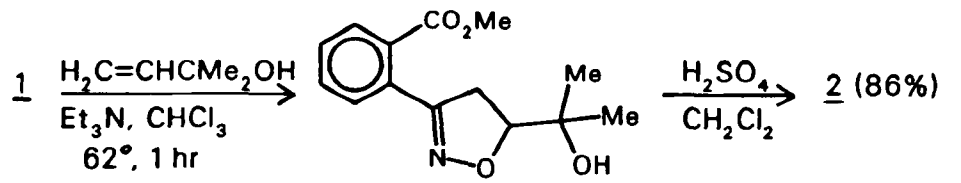
2-(5-Aryl-3-isoxazolyl)benzoates possess good herbicidal and plant growth regulant activity.[1] In the course of analog synthesis, methyl 2-(5-isopropyl-3-isoxazolyl)benzoate (2) was prepared in 60% yield by 1,3-dipolar cycloaddition of o-methoxycarbonylbenzonitrile oxide [generated by dehydrochlorination of o-methoxycarbonylbenzohydroximinoyl chloride (1)[2]] to 3-methyl-1-butyne. This route employed a large excess of the expensive, low boiling (29°) 3-methyl-1-butyne and required several days for completion of the reaction. Subsequent multi-site field tests of the plant growth regulant activity of 2 required several pounds of 2, and thus the novel, two-step route to 2 starting from the very inexpensive 2-methyl-3-buten-2-ol was developed to provide a rapid, cost-effective method suitable for large scale preparations. The greater reactivity of olefins than of acetylenes toward nitrile oxides[3] allowed use of fewer equivalents of dipolarophile (dimerization of the nitrile oxide competes with the cycloaddition), and the high boiling point of 2-methyl-3-buten-2-ol allowed use of a higher reaction temperature, resulting in rapid, high yield formation of the adduct 3. Acid-catalyzed dehydration of 3 and double bond migration within the dehydration product(s) resulted in the thermodynamically most stable product, the isoxazole 2. We anticipate that use of allylic alcohols as synthon equivalents of alkylacetylenes can find wide applications in synthesis of 5-alkylisoxazoles.



1 2 (60%)



3 (71%)

EXPERIMENTAL SECTION

NMR spectra were determined with a Varian EM-360L 60 MHz spectrometer; IR spectra were obtained on a Perkin-Elmer 727B spectrometer.

Methyl 2-(5-isopropyl-3-isoxazolyl)benzoate (2).- To a solution of 10.7 g (0.050 mol) of 1 and 38.8 g (0.57 mol) of 3-methyl-1-butyne in 200 mL of ether stirred at 0-5° was added dropwise during 30 min a solution of 5.05 g (0.050 mol) of triethylamine in 30 ml of ether. The mixture was stirred at 0-5° for 2 hrs and at 20° for 15 days, it was washed three times with water, dried ($CaSO_4$), and concentrated under vacuum. The residue was held at 90° at 16 mm for 10-15 min to give 9.79 g of product. The product was distilled in a Kugelrohr apparatus. The center cut, 7.66 g, was collected at 85° (0.05 mm) and was filtered to remove traces of a solid. The filtered oil, 7.42 g (60%), was the desired ester.

NMR ($CDCl_3$): δ 7.95 (m, 1, ArH), 7.63 (m, 3, ArH), 6.15 (d, 1, J ≅ 1 Hz, 4-H), 3.83 (s, 3, OCH_3), 3.17 (m, 1, $CHMe_2$), 1.33 (d, 6, J = 7 Hz, CH_3).

IR (film): 1720 cm^{-1}.

Anal. Calcd for $C_{14}H_{15}NO_3$: C, 68.56; H, 6.16

Found: C, 68.49; H, 6.20.

Methyl 2-[4,5-dihydro-5-(1-hydroxy-1-methylethyl)-3-isoxazolyl]benzoate (3).- To a solution of 15.00 g (0.0702 mol) of 1 and 12.09 g (0.1404 mol) of 2-methyl-3-butene-2-ol in 250 ml of $CHCl_3$ stirred in an ice bath under N_2 was added 7.10 g (0.0702 mol) of triethylamine portionwise. The mixture than was stirred at reflux for 1.5 hr, washed with three 250 ml portions of water, dried ($CaSO_4$), and concentrated under vacuum to 18.0 g (97.4%) of light orange oil. This oil was distilled in a Kugelrohr apparatus to yield 1.03 g of forerun at 20-130° (0.15 mm). The product (13.1 g., 71% yield) was collected at 145-150° (0.18 mm) as a light yellow oil, n_D^{25} 1.5453.

NMR ($CDCl_3$): δ 8.0-7.83 (m, 1), 7.63-7.4 (m, 3), 4.65 (dd, 1, J+J' = 20 Hz), 3.87 (s, 3, OCH_3), 3.28 (d, 2, separation = 10 Hz), 2.20 (s, 1, OH), 1.38 (s, 3), 1.23 (s, 3). IR (film): 3430 cm^{-1} (broad), 1720 cm^{-1}.

Anal. Calcd for $C_{14}H_{17}O_4$: C, 63.86; H, 6.51

Found: C, 63.83; H, 6.53

Methyl 2-(5-isopropyl-3-isoxazolyl)benzoate (2).- A 5.00 g (0.0189 mol) sample of methyl 2-[4,5-dihydro-5-(1-hydroxyl-1-methylethyl)-3-isoxazolyl] benzoate (3) was dissolved in 15 ml of CH_2Cl_2, and this solution was added in 2 ml portions to 12.5 ml of rapidly stirred concd H_2SO_4. A slight exotherm occurred; some CH_2Cl_2 boiled off. NMR analysis of both layers showed that the reaction was complete within 15 min and that the product was in the H_2SO_4 layer. The H_2SO_4 portion was added dropwise at a fairly rapid rate to 60 ml of ice water with stirring. Then the water was extracted with 100 ml of CH_2Cl_2 and again with 50 ml of CH_2Cl_2. The CH_2Cl_2 layers were combined, washed with three 100 ml portions of H_2O, dried ($CaSO_4$), and concentrated under vacuum to 3.99 g (86%) of an orange

oil, n_D^{25} 1.5343. GC analysis showed the product to be >98% pure 2. The IR and NMR spectra of this material and of authentic 2 (see above) were identical.

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CHLORINATION OF 5,13-DI-t-BUTYL-8,16-DIMETHYL[2.2]METACYCLOPHANE†

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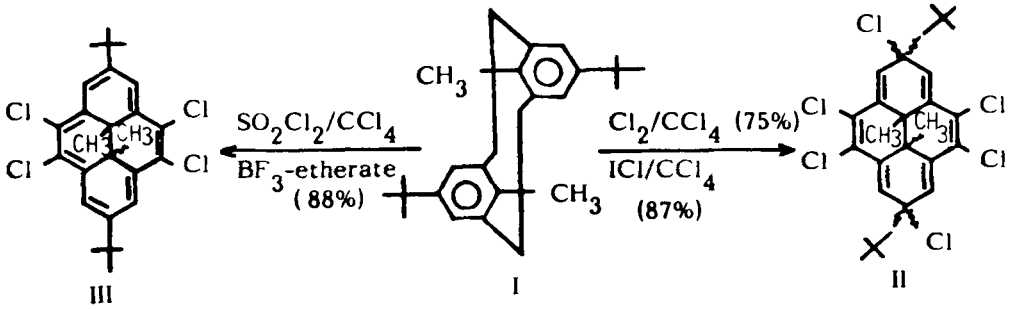
It was previously reported that bromination of 5,13-di-t-butyl-8,16-dimethyl[2.2]metacyclophane (I) afforded a novel product, 2,7-di-t-butyl-4,5,9,10-tetrabromo-10b,10c-dimethyl-10b,10c-dihydropyrene.[1] We now describe the chlorination of I with chlorine, iodine monochloride, and sulfuryl chloride (Scheme I).



Scheme I