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A new method for the synthesis of 4-oxo-4,5-dihydrofuro[3,2-*c*]quinoline is the Pd(0)-catalyzed coupling of *o*-bromonitrobenzene with 3-formyl-2-tributylstannylfuran, followed by reductive ring closure to furo[3,2-*c*]quinoline *N*-oxide and rearrangement.

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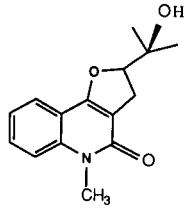
Introduction.

It has been known for some time that *Rutaceae* contain a number of alkaloids which can be classified as methoxylated furo[2,3-*b*]quinolines, thus exhibiting the anthracene annelation pattern [1]. Recently, furoquinoline derivatives with the phenanthrene annelation pattern, such as araliopsine (**1**) and almein (**2**) [3,4] have also been found in



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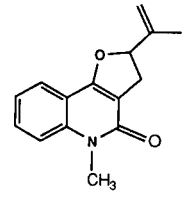

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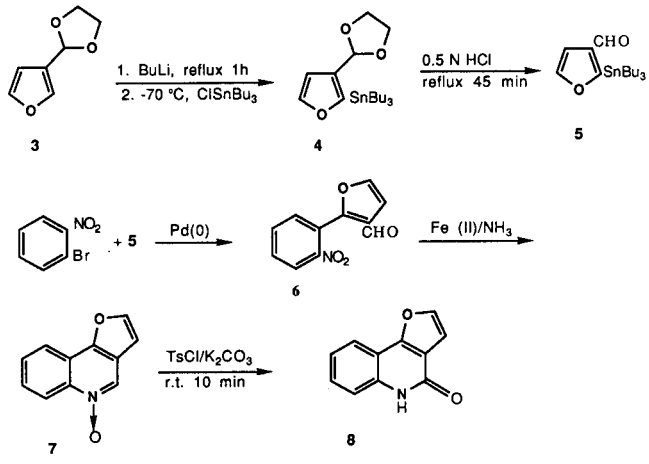
Rutaceae. This type of compound has been prepared by the condensation of diethyl 2-ethoxyethylmalonate with aniline in boiling diphenyl ether to yield a dihydrofuranoquinolone with the phenanthrene annelation pattern [5]. Previous routes to compounds of this type consist of the reaction of halogeno-4-hydroxyquinolin-2-ones with copper(I) isopropenylacetylide in refluxing pyridine [2], or the reaction of 4-hydroxy-*N*-methylquinolin-2-one with dibromoisoprene [4], both of which gave 2-isopropenyl-5-methyl-4-oxofuro[3,2-*c*]quinoline in 17-25% and 28% yields, respectively. Allylation and propargylation of 4-hydroxyquinolin-2-ones followed by Claisen rearrangement led to dihydrofuro[3,2-*c*]quinolinones [6] and furo[3,2-*c*]quinolinones [7], respectively.

Results and Discussion.

We have recently found that *o*-formylthiopheneboronic acids undergo Pd(0)-catalyzed coupling (*e.g.* with *o*-halonitrothiophene) to give *o*-formyl-*o'*-nitrobithienyls in high yields, which, after reduction with ferrous sulfate in aqueous ammonia gave high yields of dithienopyridine *N*-oxides [8]. This method does not work with boronic acids derived from π-excessive heterocyclic ring systems due to facile deboronation under the alkaline conditions employed in the coupling step. However, in such cases heterocyclic tin derivatives can be advantageously used [9]. Thus, the following new approach to 4-oxo-4,5-dihydrofuro[3,2-*c*]quinoline was developed (Scheme 1). Metalation

Scheme 1



of furan-3-carboxaldehyde ethylene acetal (**3**) [10,11] with butyllithium, followed by reaction with tributyltin chloride, gave 2-(2-tributylstannyl-3-furyl)-1,3-dioxolane (**4**) in 98% yield, which upon hydrolysis with 0.5 *N* hydrochloric acid in THF gave a 67% yield of 2-tributylstannyl-3-furanaldehyde (**5**). Pd(0)-catalyzed coupling of **5** with *o*-bromonitrobenzene in DMF at 100° gave 3-formyl-2-(2-nitrophenyl)furan (**6**) in 62% yield, which upon reduction with ferrous sulfate in aqueous ammonia gave furo[3,2-*c*]quinoline *N*-oxide (**7**) in 76% yield. Treatment of **7** with tosyl chloride [12] and potassium carbonate solution at room temperature for 10 minutes gave the desired compound **8** in 85% yield. It is obvious that this route leads to a general method for the preparation of various substituted derivatives using the appropriately substituted furan-tin derivatives and substituted bromonitrobenzene.

EXPERIMENTAL

Melting points are uncorrected. The ^{1}H nmr spectra were recorded with a Varian XL-300 spectrometer in deuteriochloroform solution. The mass spectra were recorded on a Finnigan 4021 spectrometer. The gc analyses were carried out on a Varian 3700 gas chromatograph using an OV-17, 3%, 2m column.

2-(2-Tributylstannyl-3-furyl)-1,3-dioxolane (**4**).

To a stirred solution of 5.0 g (0.035 mole) of 2-(3-furyl)-1,3-dioxolane [10,11] in 35 ml of anhydrous ether, 26 ml of 1.5 *N* *n*-butyl-

lithium in hexane was added dropwise under nitrogen at room temperature. After being refluxed for one hour, the reaction mixture was cooled to −70° and 12 g (0.037 mole) of tri-*n*-butyltin chloride (purchased from Merck) in 40 ml of dry ether was added dropwise. After the addition was complete, the mixture was warmed to room temperature and was extracted twice with water. The organic layer was dried over magnesium sulfate and evaporated. The oily residue was chromatographed on silica gel 60 using toluene as eluent; 14.8 g (98%) of a colorless liquid was obained; ^{1}H nmr (deuteriochloroform): δ 7.62 ppm (d, 1H, H_5, $J_{4,5}$ = 1.9 Hz), 6.53 (d, 1H, H_4), 5.71 (s, 1H, CH), 4.03 (m, 4H, CH_2CH_2), 0.8-1.8 (m, 27H, (*n*-Bu)$_3$).

2-Tributylstannylfuran-3-carboxaldehyde (**5**).

A reaction mixture consisting of 14.0 g (0.0326 mole) of 2-(2-tributylstannyl-3-furyl)-1,3-dioxolane, 35 ml of 0.5 *N* hydrochloric acid and 60 ml of tetrahydrofuran was refluxed for 40 minutes. After cooling to room temperature, 50 ml of ether was added and the organic phase was separated. The water was extracted with ether and the combined organic phases were washed with saturated sodium bicarbonate solution and water, and dried over magnesium sulfate. After removal of the solvent, the remaining oil was chromatographed on silica gel 60, using toluene as eluent to give 8.5 g (67%) of a colourless liquid; ^{1}H nmr (deuteriochloroform): δ 9.92 (s, 1H, CHO), 7.72 (d, 1H, H_5, J = 2.0 Hz), 6.83 (d, 1H, H_4), 0.9-1.8 (m, 27H, (*n*-Bu)$_3$).

2-(2'-nitrophenyl)furan-3-carboxaldehyde (**6**).

A 100 ml three-necked flask, equipped with condenser, magnetic stirrer, thermometer and nitrogen inlet, was charged with 4.0 g (0.0103 mole) of 2-tributylstannylfuran-3-carboxaldehyde, 2.02 g (0.01 mole) of 2-bromonitrobenzene, 0.35 g (0.0003 mole) of tetrakis(triphenylphosphine)palladium(0) and 60 ml of anhydrous DMF. The mixture was stirred under nitrogen at 100° for 24 hours. After cooling the mixture to room temperature, it was evaporated and the residue diluted with water. The water was extracted three times with ether and the combined organic phases were dried over magnesium sulfate. After removal of the solvent, the residue was recrystallized from ethanol to give 1.34 g (62%) of the title compound, mp 93-94°; ^{1}H nmr (deuteriochloroform): δ 9.88 ppm (d, 1H, CHO), 8.11 (m, 1H, $H_{3'}$), 7.73 (m, 2H, $H_{4'}H_{5'}$), 7.63 (m, 1H, $H_{6'}$), 7.52 (dd, 1H, H_5), 6.93 (d, 1H, H_4), $J_{H4\text{-}H5}$ = 2.0 Hz, $J_{CHO\text{-}H5}$ = 0.5, $J_{H3'\text{-}H4'}$ = 7.2, $J_{H4'\text{-}H5'}$ = 7.6, $J_{H5'\text{-}H6'}$ = 7.09 Hz.

Anal. Calcd. for $C_{11}H_7NO_4$: C, 60.8; H, 3.25; N, 6.45. Found: C, 60.6; H, 3.42; N, 6.34.

Furo[3,2-*c*]quinoline *N*-Oxide (**7**).

The title compound was prepared according to the procedure described in ref [8], from 0.26 g (0.0012 mole) of 2-(2-nitrophenyl)-furan-3-carboxaldehyde, 2.8 g (0.01 mole) of ferrous sulfate in 10 ml of water, two drops of 2 *M* hydrochloric acid and 3 ml of aqueous ammonia. Upon workup, the residue was recrystallized from ethanol to give 0.16 g (76%) of the title compound as white needles, mp 152-153°; ir (potassium bromide): 1191 cm^{-1} (N-O); ^{1}H nmr (deuteriochloroform): δ 8.98 (s, 1H, H_4), 8.87 (m, 1H, H_6), 8.3 (m, 1H, H_9), 7.86 (d, 1H, H_2), 7.81 (m, 2H, H_7, H_8), 6.96 (d, 1H, H_3), J_{H2H3} = 2.1 Hz, J_{H6H7} = 7.7, J_{H8H9} = 7.0 Hz; ^{13}C nmr (deuteriochloroform): δ 146.7 ppm (dd, C2, $^1J_{C2H2}$ = 206.4 Hz, $^2J_{C2H3}$ = 10.8 Hz), 130.8 (d, C4, ^{1}J = 187.4), 129.0 (dd, C7, C8, ^{1}J = 163), 121 (dd, C6, ^{1}J = 170), 120.3 (dd, C9, ^{1}J = 166), 105.1 (dd, C3, ^{1}J = 181, $^2J_{C3H2}$ = 13.6 Hz).

Anal. Calcd. for $C_{11}H_7NO_2 \cdot H_2O$: C, 65.00; H, 4.43; N, 6.89. Found: C, 64.84; H, 4.42; N, 6.86.

4-Oxo-4,5-dihydrofuro[2,3-*c*]quinoline (**8**).

A heterogeneous reaction mixture consisting of 0.08 g (0.00043 mole) of furo[2,3-*c*]quinoline *N*-oxide, 0.1 g (0.0005 mole) of tosyl chloride in 3 ml of chloroform and 3 ml of 10% potassium carbonate solution was shaken at room temperature for 10 minutes, until the starting *N*-oxide disappeared. The resulting precipitate was filtered off and washed thoroughly with ether. The crude product was recrystallized from ethanol to give 0.07 g (85%) of the title compound as pale yellow needles, mp 232-233° (lit [5] 234-237°); ir (potassium bromide): 3100-2900, 1680, 1650 cm^{-1}; ^{1}H nmr (deuteriochloroform): δ 8.0 ppm (m, 1H, H_6), 7.69 (d, 1H, H_2), 7.3-7.5 (m, 2H, H_7, H_8), 7.52 (m, 1H, H_9), 7.14 (d, 1H, H_3), J_{H2H3} = 2.1 Hz.

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‡ On leave of absence from the Central Research Institute for Chemistry, Hungarian Academy of Sciences, Budapest, Hungary.

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