Intramolecular Amination of Olefins. Synthesis of 2-Substituted-4-quinolones from 2-Nitrochalcones catalysed by Ruthenium

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2-Substituted-4-quinolones **2** and the corresponding 2,3-dihydro-2-substituted-4-quinolones **3** have been obtained by reduction with CO at 170 °C and 30 atm of 2-nitrochalcones **1**, catalysed by $Ru_3(CO)_{12}$ with DIAN-Me as co-catalyst in ethanol–water.

We have previously reported the synthesis of indoles by carbonylation of *ortho*-nitrostyrenes catalysed by $Ru_3(CO)_{12}$[1,2] and more recently, the same reaction, catalysed by $Pd(O_2CR)_2$ (R = Me; 2,4,6-$Me_3C_6H_2$) in the presence of chelating nitrogen donor ligands, such as 3,4,7,8-tetramethyl-1,10-phenanthroline. Of the two, the palladium system[3] shows greater activity and selectivity even under relatively mild conditions, with superior activity even to previously reported system, $Pd(PPh_3)_2Cl_2$–$SnCl_2$.[4] From these and related studies,[5] there seems to be a marked preference for ring closure to give five membered heterocycles, even when other ring sizes might be formed. This is attributed to a steric effect related to the coordination of the substrate in the key intermediate.[3]

We report here the synthesis of six membered heterocycles, by reduction by CO of 2-nitrochalcones **1**, catalysed by $Ru_3(CO)_{12}$ in ethanol–water in the presence of DIAN-Me (Scheme 1, Table 1).

The conditions described gave conversion of 100% of the starting material; the relative amounts of **2** and **3** were determined by ^1H NMR and the only other product isolated in significant amounts from the reaction mixture was the corresponding 2-aminochalcone **4**.†

Changing the ratio of DIAN-Me to $Ru_3(CO)_{12}$ for **1b** did not markedly affect the product distribution. However at higher DIAN-Me : $Ru_3(CO)_{12}$ ratios, significant amounts of the amine **4b** were also formed. Treatment of **3h** (0.22 mmol) with 2,3-dichloro-5,6-dicyano-p-benzoquinone (0.22 mmol) in toluene (10 ml), for 2 h, at 60 °C gave quantitative (by NMR) conversion to **2h**. Treatment of the reaction mixture **2/3b** or **2/3h** with the same oxidant allowed selective synthesis of the quinolones **2**.

DIAN-Me

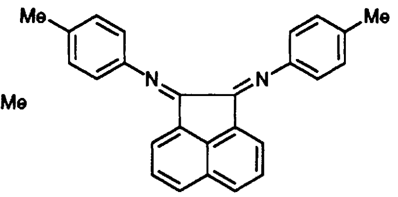


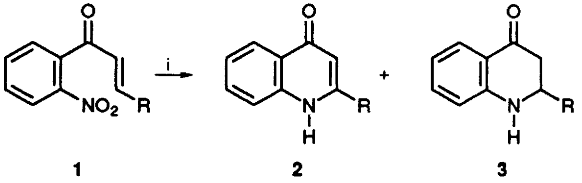
Table 1 Yields of 2-substituted-4-quinolones **2** and 2,3-dihydro-2-substituted-4-quinolones **3** on reduction by CO of the corresponding 2-nitrochalcones **1** catalysed by $Ru_3(CO)_{12}$–DIAN-Me

1	R	2	3
a	C_6H_5	57.3	42.7
b	*p*-$OMeC_6H_4$	60.0	40.0
c	3,4-$(OMe)_2C_6H_3$	21.7	78.3
d	3,4,5-$(OMe)_3C_6H_2$	54.5	25.9[a]
e	2,3,4-$(OMe)_3C_6H_2$	29.3	70.7
f	3-OBn-4-$OMeC_6H_3$	46.3	53.7
g	3-OMe-4-OHC_6H_3	35.0	65.0
h	3,4-OCH_2O–	40.1	59.9
i	3-pyridyl	50.5	49.5
j	2-naphthyl	47.6	52.4
k	2-furyl	35.0	65.0
l	*p*-ClC_6H_4	37.5	62.5

[a] 19.6% of compound **4d** was also observed. Yields determined by NMR.

The pharmacological activities of substituted 4-quinolones have been reported.[6] They are usually obtained by condensation of anilines with ketoesters, followed by cyclisation.[7,8] 2,2,5-Trimethyl thiobenzylidene-1,3-dioxan-4,6-dione proved to be more convenient than the ketoester for the synthesis of 2-phenyl-4-quinolone.[9] To our knowledge, there has been only one report on a metal assisted cyclisation reaction of this type, which required stoichiometric quantities of $PdCl_2(PPh_3)_2$.[10] Very recently, it has been reported that *ortho*-iodoanilines undergo intramolecular heterocyclisation with terminal arylacetylenes, at 20 atm of CO, 120 °C, in the presence of Et_2NH and $PdCl_2(dppf)$ [dppf = 1,1′-bis-(diphenylphosphino)ferrocene] as catalyst to yield 2-aryl-4-quinolones in high yields.[6] Our reaction would seem more synthetically useful as the starting materials **1a–l** are readily accessible. Reduction of the reaction time to 1 h, with otherwise similar conditions for either **1b** or **h** also gave the corresponding 2-aminochalcones **4b** and **h** and when the catalytic reaction for **1b** was conducted in toluene, the major product was the 2-aminochalcone **4b** (75–80% by flash chromatography), the remaining material being **3b** together with trace amounts of **2b**. This change in outcome with solvent might be due to the adventitous introduction of moisture to the reaction.

We have recently reported that $Ru_3(CO)_{12}$ in the presence of DIAN-Me is an active catalyst for the reduction of nitrobenzene to aniline by CO–H_2O.[11] The ruthenium catalyst is highly selective, since products derived from the reduction of the olefinic or the ketonic groups were not observed. Experiments conducted under the catalytic conditions on **2b** or **3b** have shown that there is no significant interconversion. Even when compound **3b** was treated with **1b** (a potential oxidant) under the catalytic conditions (but in the absence of the catalytic system) no compound **2b** was formed. This suggests that these compounds are primary products of the catalytic reactions. An intermediate nitrene complex may be responsible for the direct formation of the quinolones **2**. The performed 2-aminochalcone **4b**, under the usual catalytic conditions was partially converted (66.7%) into **3b** even in the absence of the catalyst; addition of the ligand, or $Ru_3(CO)_{12}$, alone did not modify the reaction. However, when the reaction was conducted in the presence of both $Ru_3(CO)_{12}$ and DIAN-Me, the amine **4b** was completely converted into **3b**. It can be concluded that compounds **3** are formed *via* the intermediate reduction of **1** to the corresponding amines **4**, followed by cyclization, the latter reaction being also favoured by the presence of the $Ru_3(CO)_{12}$–DIAN-Me catalytic system. Compounds **2** may be formed by a different route, similar to the one observed in the synthesis of indoles from 2-nitrostyrenes.[1–3] When the analogous reaction was conducted for



Scheme 1 *Reaction conditions*: i 170 °C, 30 atm of CO, **1** (2.47×10^{-1} mmol), $Ru_3(CO)_{12}$ (2.47×10^{-3} mmol), DIAN-Me (7.41×10^{-3} mmol), in EtOH (23.5 ml)–H_2O (1.5 ml) for 3 h.

1b by using Pd(O_2CMe)$_2$–3,4,7,8-tetramethyl-1,10-phenanthroline as catalyst in dry toluene quinolone **2b** was the major product, with traces of the amine **4b**. Work is in progress in order to investigate the activity and selectivity of the palladium catalyst in this reaction with the other substrates.

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Footnote

† All compounds exhibited satisfactory analytical and spectral data. All reported can be isolated in pure form by flash chromatography (SiO_2 eluent CH_2Cl_2–MeOH 95 : 5).

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