Tetrahedron Vol. 40, No. 10, pp. 1919 to 1925, 1984
Printed in Great Britain.

0040–4020/84 $3.00 + .00

PALLADIUM-CATALYSED CYCLISATION OF 2-SUBSTITUTED HALOGENOARENES BY DEHYDROHALOGENATION

D. E. AMES and A. OPALKO
Chemistry Department, Chelsea College, Manresa Road, London SW3 6LX, England

(*Received in the U.K.* 14 *July* 1983)

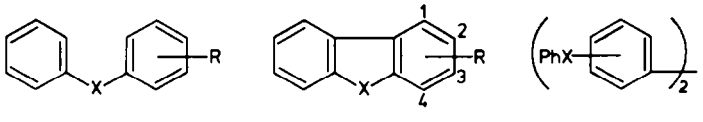
Abstract—Cyclodehydrohalogenation mediated by various palladium catalysts and solvents with different bases (the most generally satisfactory system being palladium(II) acetate in NN-dimethylacetamide (DMA) with sodium carbonate as base) has been examined as a route to some heterocyclic systems. Whereas dehydrogenative cyclisation processes require stoichiometric amounts of palladium(II) reagent, the present procedure involves only catalytic amounts (0.1 molar proportion, or less), of palladium compound. The preparation of dibenzofuran, carbazole, fluorenone, phenanthridone, 6H-dibenzo [c,e][1,2]thiazine-5,5-dioxide, 6H-dibenzo[b,d]pyran and benzofurano[2,3-b]pyridine derivatives is described. The cyclisation of 3-benzamido-2-chloropyridine to 6-hydroxybenzo[c][1,5]naphthyridine illustrates the regiospecificity of the process.

The palladium-promoted cyclisation of diaryl derivatives (**1**; X = 0, NH, NMe, CO, or CONH) occurs by a dehydrogenative coupling process requiring at least stoichiometric amounts of palladium(II) acetate in the presence of acid[1] and gives **2** in varying yields depending on the bridge (X) and substituent (R). This reaction has been applied to the preparation of dibenzofurans,[2] ellipticine,[3] and to the cyclisation of benzoylpyrroles and benzoylindoles.[4] A catalytic method has also been reported[5] in which the diphenyl ether is heated in the presence of catalytic amounts of palladium(II) acetate and acetylacetone under neutral conditions at high pressure in a 1 : 1 mixture of dioxygen and dinitrogen. However, the procedure suffers from a lack of selectivity as coupling products of type **3** from the competing intermolecular dehydrogenative process are formed as well as the required dibenzofuran (**2**).

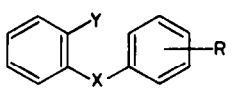
We wish to report investigations into the development of a method for the cyclisation of compounds with the general structure (**4**; Y = halogen) by intramolecular dehydrohalogenative coupling using catalytic amounts of palladium(II) salts under basic conditions.

Palladium-catalysed reactions using organic bases

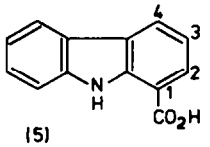
Our initial approach, based on work previously reported,[6] was to use a 2-halogenodiphenylamine-2′-carboxylic acids as models and to attempt to cyclise these to carbazole-1-carboxylic acid (**5**). The original conditions[6] required heating the substrate with ethyl acrylate, triethylamine, and a catalytic amount of palladium(II) acetate in acetonitrile sealed under nitrogen in a stainless steel bomb at 150°. However, we found that ethyl acrylate was not necessary in the present reaction as heating 2 - iododiphenylamine - 2′ - carboxylic acid (**4a**) as described, but without ethyl acrylate, gave carbazole - 1 - carboxylic acid (**5**) in 73% yield. If the mixture was refluxed under dinitrogen for 24 hr with DMF as solvent, the cyclisation product was conveniently obtained though in reduced yield (52%). In each case, 0.027 mole of palladium(II) acetate was used for 1 mole of iodo-compound. The corresponding bromo-



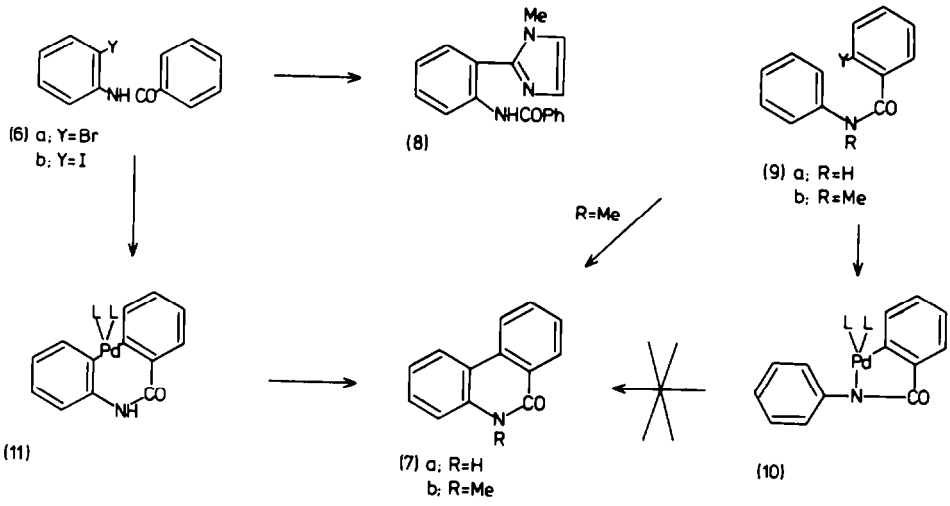
(1) (2) a; X=O R=H
b; X=CO R=H
c, X=O R=2-NO_2
d, X=O R=4-NO_2
e, X=NH·CO R=H
(3)



(4) a; X=NH Y=I R=2-CO_2H
b; X=O Y=I R=H
c; X=CO Y=I R=H
d, X=O Y=Br R=4-NO_2
e; X=O Y=Br R=2-NO_2
f; X=O Y=Br R=4-CHO



(5)



Scheme 1.

and chloro-analogues, however, gave little or no cyclisation product and therefore, in the following reactions, iodo-compounds were used.

The coupling of 2-iododiphenyl ether (**4b**) was examined next. The reactions were effected by heating (i) in dimethylacetamide (DMA) at 140° or (ii) in acetonitrile in a bomb; both experiments gave a mixture of three products containing about 45% of dibenzofuran (GLC). The two reaction mixtures were combined and separated by column chromatography to give diphenyl ether, dibenzofuran (**2a**) and 2,2′-diphenoxybiphenyl.

The preparation of 6-membered rings by this process failed. Iodo-derivatives (**4**), having X = NH·CO, CO·NH, or CO·O, were heated in a bomb with palladium(II) acetate, triethylamine, and acetonitrile, and alternatively with catalyst and base in DMF at 150°. In all cases, the corresponding coupling products (**3**) were obtained and no cyclic product was detected (TLC).

Thus cyclisation, under these conditions, proved to be erratic and only occurred when a one-atom bridge linked the two aryl rings. In the cases with two-atom bridges only intermolecular coupling and reduction occurred and these were also strongly competing processes in the formation of 5-membered rings. Therefore our next objective was to vary the conditions to see if each process could be produced selectively and to attempt to establish a common set of conditions for the formation of both 5- and 6-membered rings. It was felt that a process would be more attractive if simple reaction conditions were employed and so the use of an autoclave was discontinued.

Reactions of 2-iodobenzophenone

2-Iodobenzophenone was heated in the selected solvent with a palladium catalyst and excess of amine at 140° under dinitrogen. After 15 hr, a sample was removed and assayed (GLC) for 9-fluorenone (**2b**), benzophenone, and 2,2′-dibenzoylbiphenyl. The Table shows that varying the conditions has a profound influence on the course of the reaction. The work commenced with the use of triethylamine as base and DMA as solvent. The catalyst was varied but the overall effect did not differ, with formation of the coupling product, as **3**, predominating. Changing the solvent to butan-1-ol reduced the amount of this considerably and favoured formation of reduction product, benzophenone.

When the base was changed to diazabicycloundecene (DBU) with palladium(II) acetate as catalyst, cyclisation was favoured, especially when the amount of base was increased (entries 7, 8, 9 in Table). However, if the catalyst incorporated triphenylphosphine as a ligand, or if triphenylphosphine was added, reduction was the exclusive reaction (entry 13).

Various bases were employed with either butan-1-ol or DMA and the best were found to be 4-dimethylaminopyridine (entry 21) and N-methylimidazole (entry 24). With N-methylimidazole in DMA, the cyclised product was formed exclusively but the reaction did not go to completion. When N-methylimidazole was used as solvent at 190°, only the cyclised product was formed.

Palladium-catalysed reaction in N-methylimidazole

It was hoped that the cyclisation reaction could be applied to the formation of heterocycles: iodophenyl phenyl ether (**4b**) formed dibenzofuran in 8 hr under dinitrogen but required 24 hr in air. Two bromophenyl nitrophenyl ethers **4d** and **4e** were prepared by coupling the sodium salt of 2-bromophenol with the required fluoronitrobenzene. Although 2-nitrodibenzofuran (**2d**) was formed in 24% yield from **4d** using N-methylimidazole as solvent, no 4-nitrodibenzofuran (**2e**) could be isolated after similar treatment of **4e**.

Heating phenyl 2-bromobenzoate at 190° in N-methylimidazole under dinitrogen for 30 hr gave mainly starting material contaminated with phenyl benzoate (10%). Attempts to cyclise N-(2-bromophenyl)benzamide (**6a**) to phenanthridone (**7a**) in N-methylimidazole, or with 4-dimethylaminopyridine added also failed. In each case, two products were formed and were found to be benzanilide and the imidazole (**8**). This structure was indicated by the proton NMR spectrum which displayed doublets at δ 6.9 and 7.15, which can be

Table 1. Palladium-catalysed reactions of 2-iodobenzophenone

Entry	Solvent[b]	Catalyst[c]	Base	(molar prop.[n])	Starting material(% after 15hr)	Yield of Product (%)[a] Benzophenone	Fluorenone	2,2'-Dibenzoylbiphenyl
1	DMA	A	Et_3N	1	Trace	25	15	60
2	DMA	A	Et_3N	4	Trace	15	10	75
3	DMA	B	Et_3N	4	5	15	10	70
4	DMA	C	Et_3N	4	5	15	5	75
5	Butan-1-ol	A	Et_3N	4	-	85	5	10
6	Butan-1-ol	C	Et_3N	4	-	75	-	25
7	Butan-1-ol	A	DBU	1	-	55	35	10
8	Butan-1-ol	A	DBU	2	-	30	70	-
9	Butan-1-ol	A	DBU	3	-	25	75	-
10	Butan-1-ol	D	DBU	2	-	35	65	-
11	Butan-1-ol	E	DBU	2	-	35	65	-
12	Butan-1-ol	B	DBU	2	-	95	5	-
13	Butan-1-ol	C	DBU	2	-	100	-	-
14	DMF	A	DBU	2	70	20	10	-
15	DMA	A	DBU	2	60	30	5	5
16	Butan-1-ol	A	DABCO	2	33	33	33	-
17	Butan-1-ol	A	DBN	2	55	10	35	-
18	Butan-1-ol	A	2,6-L	2	60	15	Trace	25
19	Butan-1-ol	A	2,6-L	2	-	50	-	50
20	Butan-1-ol	A	Pr^i_2NH	2	-	75	-	25
21	Butan-1-ol	A	4-DMAP	2	Trace	Trace	95	-
22	Butan-1-ol	A	DMAB	2	90	10	Trace	Trace
23	DMA	A	Pyridine	2	60	15	25	-
24	DMA	A	NMI	2	85	Trace	15	-
25	DMA	A	4-DMAP	2	45	-	55	-
26	4-Picoline	A	-	-	80	-	20	-
27	Pyridine	A	-	-	65	Trace	35	-
28	NMI[f]	A	-	-	-	Trace	100	-

The reaction was monitored by GLC on a Pye 104 instrument using a 2m×3mm (i.d.) glass column ntaining 10% MS 200 on Chromasorb W (HP, 80-100 mesh) with a dinitrogen flow rate of 40 ml/min and a lumn temperature programme of 200°C for 7 min, 10°C/min to 240°C, then isothermal. Approximate retention mes: benzophenone 2 min, 2-iodobenzophenone 3 min, fluorenone 9 min, and 2,2'-dibenzoylbiphenyl 30 min.

NMI is N-methylimidazole.

A is $Pd(OAc)_2$, 40mg; B is $(Ph_3P)_2PdCl_2$, 120mg; C is $Pd(OAc)_2$, 40mg,with Ph_3P, 90mg; D is $PdCl_2$, mg; and E is $(MeCN)_2PdCl_2$, 40mg.

DBU is1,8-diazabicyclo[5,4,0]undec-7-ene; DABCO is 1,4-diazabicyclo[2,2,2]octane; DBN is 1,5-azabicyclo[4,3,0]non-5-ene; 2,6-L is 2,6-dimethylpyridine; 4-DMAP is 4-dimethylaminopyridine.

Mixture heated at reflux temperature.

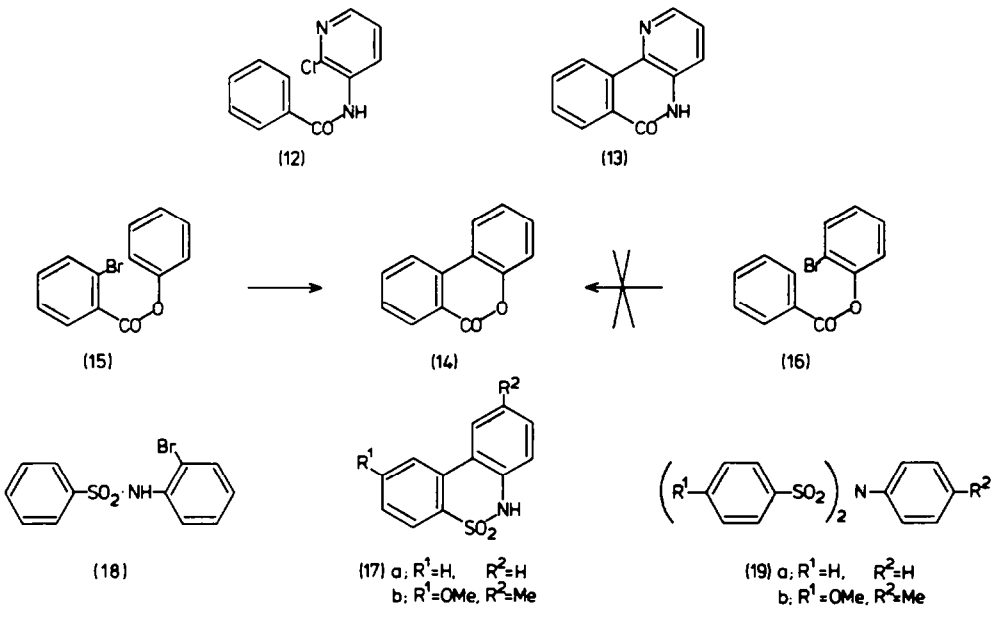
Mixture heated at 190°C.

assigned to the 4- and 5-positions of imidazole ring. A double doublet at 8.65 is attributed to the aromatic 6-proton, possibly due to a deshielding effect of the carbonyl group.

Palladium-catalysed reactions using inorganic bases

In attempting to form 6-membered rings using inorganic bases, it was decided to prepare phenanthridone (**7a**) which could be easily isolated, owing to its high melting point and low solubility. It could be prepared from either of two amides, depending on which ring was halogen-substituted, and work commenced with N-(2-iodophenyl)benzamide (**6b**). This was heated with a catalytic amount of palladium(II) acetate (0.1 molar equivalent with respect to the halide in all the following examples) at 170° in DMA with sodium carbonate under dinitrogen for 2.5 hr to give phenanthridone in 44% yield. Replacing iodine by bromine (**6a**) gave the product in 53% yield also after 2.5 hr heating. The chloro-derivative required 36 hr heating before it was all consumed and the product was isolated in only 15% yield.

When the bromine was present in the benzoyl ring, as in **9a**, treatment under the standard conditions did not give any of the expected product (**7a**). Failure of **9a** to cyclise was attributed to the formation of palladium complex (**10**) as an intermediate rather than the diaryl complex (**11**) which would be expected

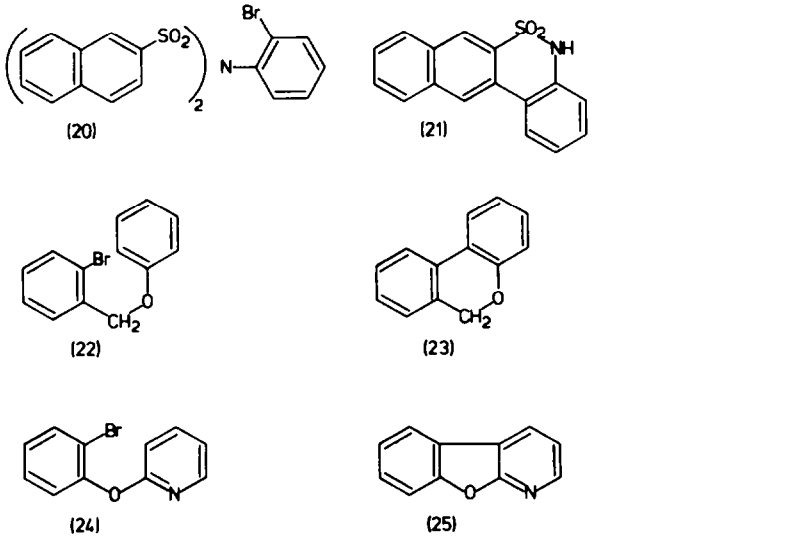


to lead to the formation of **7a**. To test this hypothesis, it was necessary to block the N–H function and this was achieved by preparing the N-methylderivative (**9b**) which gave N-methylphenanthridone (**7b**) in 50% yield.

Cyclisation of 3-benzamido-2-chloropyridine (**12**) to the naphthyridone (**13**) was achieved in 42% yield. In this particular example, a chloro-substituent was synthetically viable due to the activation of the α-position in the pyridine ring.

The preparation of benzocoumarin (**14**) from **15** or **16** was next examined. Phenyl 2-bromobenzoate (**15**) in DMA with palladium(II) acetate and sodium carbonate at 170° gave only a small amount of biphenyl-2,2′-dicarboxylic acid as extensive hydrolysis occurred. Replacement of sodium carbonate by lithium carbonate gave product (**14**) in 7% yield. Use of sodium acetate with bis(triphenylphosphine)palladium(II) chloride furnished **14** in 40% yield. Even under these conditions, if the bromine was in the phenol ring (**16**) extensive hydrolysis occurred and no cyclised product was isolated.

Turning to the preparation of 6H - dibenzo[*c*,*e*][1,2]thiazine - 5,5 - dioxide (**17a**) monosulphonamide (**18a**) was heated under the standard conditions for 24 hr but only starting material was isolated. However, the bis-sulphonamide (**19**) cyclised to give cyclic product (**17**) in 56% yield. The bis-sulphonamide (**19b**) was cyclised by heating in DMA with bis(triphenylphosphine)palladium(II) chcloride and sodium acetate, product (**17b**) being isolated in 25% yield. Preparation of a tetracyclic system from the bis-2-naphthylsulphonamide (**20**) similarly gave cyclic product in 25% yield. Two possible products might be formed by cyclisation at positions 1 or 3 of the naphthyl unit, but only one product was isolated. The proton NMR spectrum displayed two singlets at δ 8.4 and 8.5 which would be expected for the 1- and



4-protons of the naphthalene system. This indicates that the product had structure (**21**), formed by attack at the less-hindered 3-position.

Cyclisation of 2-bromobenzyl phenyl ether (**22**) using bis(triphenylphosphine)palladium(II) chloride gave two products which were separated by column chromatography and were identified as 6H-dibenzo[*b*,*d*]pyran (**23**) and benzyl phenyl ether. Cyclisation of 2-bromoazobenzene to benzo[*c*] cinnoline could not be achieved.

Formation of five-membered rings

Cyclisation of 2-bromobenzophenone with palladium(II) acetate and sodium carbonate gave 9-fluorenone in almost quantitative yield but it was contaminated with 1% of benzophenone (GLC). The cyclisation of 2-bromophenyl substituted-phenyl ethers to substituted dibenzofurans using palladium(II) acetate and sodium carbonate in DMA has been reported earlier.[7] When this procedure was applied to 4-(2-bromophenoxy)benzaldehyde (**4f**) cyclisation did not give the expected dibenzofuran aldehyde but formed a 4 : 1 mixture of dibenzofuran (**2a**) and diphenyl ether. However, decarbonylation of aromatic aldehydes over palladium is a known process.[8]

2.(2-Bromophenoxy)pyridine (**24**) reacted slowly under the standard conditions yielding product (**25**) in 10% yield. An example of intermolecular dehydrohalogenative coupling occurring with cyclisation is the conversion of 2-iodobiphenyl into tetraphenylene (1,2;3,4;5,6;7,8 - tetrabenzocyclo- octa -1,3,5,7 - tetrene.

CONCLUSIONS

The present method offers advantages over the earlier process[1] in that it is a catalytic procedure requiring much less catalyst. It has also been used to form a variety of heterocycles, as it tolerates a wider range of bridging groups. The presence of a halogen atom can make the reaction regioselective as demonstrated in the preparation of **13**. Standard reaction conditions for cyclisation require heating the aryl halide with palladium(II) acetate (0.1 molar proportion) in the presence of sodium carbonate in DMA under dinitrogen at 150–170°. If milder conditions are required, then sodium carbonate can be replaced by sodium acetate.

The two competing processes can be selected by modifying the reaction conditions. If *reduction* is required, the aryl halide can be heated in a protic solvent, particularly an alcohol, with either triethylamine or DBU in the presence of catalytic mounts of bis(triphenylphosphine)palladium(II) chloride. Reduction of aryl halides with palladium salts is well-known.[9] If *dehalogenative coupling* is required, the reaction is performed in the presence of triethylamine and a palladium salt in an aprotic solvent such as DMA.[10]

EXPERIMENTAL

M.ps (capillary) are uncorrected. IR spectra (Nujol) were determined with a Perkin–Elmer 521 spectrophotometer. UV spectra were obtained on a Pye Unicam SP 700C or Perkin–Elmer 554 spectrophotometer in 95% ethanol. NMR spectra were determined at 60 MHz on a Varian EM 360 spectrometer with TMS as internal standard.

9H-*Carbazole-1-carboxylic acid* (**5**)

2′-Iododiphenylamine-2-carboxylic acid (1.7 g), acetonitrile (3 ml), triethylamine (1.1 g), and palladium(II) acetate (30 mg) were placed in a 45 ml stainless steel bomb. This was flushed with dinitrogen, sealed, and heated in an oil-bath at 150° for 7 hr. After cooling, the contents were removed with chloroform, evaporated to dryness, and treated with water, followed by dilute hydrochloric acid. The precipitated solid was collected, and recrystallised from acetonitrile to give 9H-carbazole-1-carboxylic acid (0.78; 73%), m.p. 276–278° (lit.[11] 271–273°).

Palladium-catalysed reaction of 2-iododiphenyl ether

(a) The iodide (2.75 g), triethylamine (1.8 g), and palladium(II) acetate (60 mg) in DMA (20 ml) were heated under dinitrogen at 140° for 16 hr. Water was added to the cooled solution and the aqueous phase was decanted from the oil which separated. GLC showed that the oil consisted of a mixture of diphenyl ether (30%), dibenzofuran (45%), and 2,2′-diphenoxybiphenyl (25%).

(b) 2-Iododiphenyl ether (2.75 g), triethylamine (1.8 g), and palladium acetate (60 mg) in acetonitrile (10 ml) were heated in a 45 ml stainless steel bomb under dinitrogen at 140° for 15 hr. After cooling, the contents were dissolved in chloroform. GLC showed that the mixture consisted of diphenyl ether (50%), dibenzofuran (45%), and 2,2′-diphenoxybiphenyl (5%).

The products from (a) and (b) were combined and separated by chromatography on silica with cyclohexane to give diphenyl ether (0.6 g), dibenzofuran (0.7 g), and 2,2′-diphenoxybiphenyl (0.29 g).

Palladium-catalysed reactions of 2-iodobenzophenone

2-Iodobenzophenone (0.5 g), palladium salt or complex, and base were heated at 150° in solvent or base (10 ml) under dinitrogen for 15 hr (see Table for details). A sample was removed for assay by GLC or TLC.

2,2′-*Dibenzoylbiphenyl*

2-Iodobenzophenone (1.54 g), triethylamine (1 g), and palladium(II) acetate (30 mg) in DMA were heated at 150° for 6 hr under dinitrogen. The cooled mixture was poured into water and the precipitated solid was collected and recrystallised from ethanol to give 2,2′-dibenzoylbiphenyl (0.44 g; 44%), m.p. 167–170° (lit.[12] 165.5–168°).

Palladium-catalysed reactions in N-methylimidazole

Aryl halide (10 mmol), and palladium(II) acetate (0.22 g) in N-methylimidazole (10 ml) were heated under dinitrogen at 190° (bath) for the time specified below and then poured into water. The precipitate was either recrystallised or extracted with toluene, the solution being washed with 2M-hydrochloric acid, and water, dried ($MgSO_4$) and evaporated to give product.

2-Iodobenzophenone (4.5 hr; toluene isolation) and 2-bromobenzophenone (4.5 hr; similarly) gave 9-fluorenone in almost quantitative yield but GLC showed a trace of benzophenone to be present.

2-Iododiphenyl ether (8 hr, toluene isolation) gave dibenzofuran in almost quantitative yield but contaminated with 5% of diphenyl ether (GLC).

2-Bromo-4′-nitrodiphenyl ether (23 hr; crystallisation from ethanol) gave 2-nitrodibenzofuran (24%), m.p. 153–155° (lit.[13] 150.5–151.5°).

N-[2-(1-*Methylimidazol-2-yl*)*phenyl*]*benzamide* (**8**)

N-(-Bromophenyl)benzamide (2.75 g), 4-dimethylaminopyridine (1.46 g), and palladium(II) acetate (0.22 g) in N-methylimidazole (10 ml) were heated at 190° for 24 hr. The solvent was removed under reduced pressure and water was added to the residue. The solid was filtered off and dissolved in chloroform. This solution was extracted with 2M-hydrochloric acid, evaporated, and the residue was crystallised from ethanol to give benzanilide (0.8 g; 40%). The acid

extract was basified and the precipitate collected and crystallised from isopropanol to give N-(2-(1-methylimidazol-2-yl)phenyl]benzamide (**8**) (0.4 g; 14%) m.p. 118–120°. Found: C, 73.2; H, 5.8; N, 15.4. $C_{17}H_{15}N_3O$ requires C, 73.6; H, 5.5; N, 15.3%. IR ν_{max} 3300–3000 (NH) and 1665 s cm^{-1} (C=O); NMR δ ($CDCl_3$), 3.7 (3H, s, Me), 6.9 (1H, d, imidazole H), 7.15 (1H, d, imidazole H), 7.0–7.5 (6H, m, ArH), 7.8–8.0 (2H, m, benzoyl H-2 and H-6), 8.65 (1H, dd, aniline H-6) and 11.9 (1H, s, NH); and UV λ_{max} 229 (ϵ 14,700), 255 (ϵ 18,200), and 280 nm (ϵ 10,900).

Palladium-catalysed cyclisation using sodium carbonate

The aryl halide (10 mmol), palladium(II) acetate (0.22 g), and anhydrous sodium carbonate (1.3 g) in DMA (20 ml) were heated at 160–170° under nitrogen for the time specified. The mixture was poured into water to give a precipitate which was purified by crystallisations or by chromatography.

N-(2-Iodophenyl)benzamide (2 hr), N-(2-bromophenyl)benzamide (2.5 hr), and N-(2-chlorophenyl) benzamide (36 hr) gave phenanthridone, m.p. 291–293° (lit.[14] 293°) in 44, 53, and 15% yields respectively.

2-Bromo-N-phenylbenzamide failed to give any phenanthridone (TLC).

2-Bromo-N-methyl-N-phenylbenzamide (**9b**)

2-Bromobenzoyl chloride (13.3 g) was added dropwise to a stirred mixture of N-methylaniline (5.98 g) and 10% sodium hydroxide solution (45 ml). The mixture was stirred for 2 hr more and the product was isolated with ether. 2-Bromo-N-methyl-N-phenylbenzamide was obtained as an oil (16 g; 98%). Found: C, 58.0; H, 4.1; N, 4.7. $C_{14}H_{12}BrNO$ requires C, 58.0; H, 4.2; N, 4.8%. IR ν_{max} (liquid film) 1650 cm^{-1} (C=O); NMR δ ($CDCl_3$) 3.5 (3H, s, Me) and 6.8–7.6 (9H, m, ArH).

N-Methylphenanthridone (**7b**)

The foregoing bromo-compound was cyclised under the general conditions at 160° for 24 hr. Addition of water and isolation with toluene gave N-methylphenanthridone (1.04 g; 50%), m.p. 105–108° (lit.[15] 108.5°) after crystallisation from ethanol.

3-Benzamido-2-chloropyridine (**12**)

3-Amino-2-chloropyridine (12.8 g) and triethylamine (11 g) in dichloromethane (200 ml) were treated with a solution of benzoyl chloride (14 g) in dichloromethane (50 ml) over 45 min. The mixture was stirred at ambient temperature overnight, washed with water, dried ($MgSO_4$), and evaporated to give a gum. Crystallisation from cyclohexane with a little ethanol gave 3-benzamido-2-chloropyridine (**12**) as crystals, m.p. 87–89° (9.9 g; 43%). Found: C, 62.0; H, 3.8; N, 12.1. $C_{12}H_9ClN_2O$ requires C, 62.0; H, 3.9; N, 12.0%. IR ν_{max} 3300–3100 (NH) and 1700 cm^{-1} (C=O); NMR δ ($CDCl_3$) 7.15 (1H, dd, pyridine 5-H), 7.4–7.8 (5H, m, phenyl), 8.05–8.25 (1H, dd, pyridine 4-H), 8.5 (1H, br s, NH), and 8.75–8.9 (1H, dd, pyridine 6-H).

Benzo[c][1,5]naphthyridine-6(5H)-one (**13**)

The benzamidopyridine (2.32 g), palladium acetate (0.22 g) and anhydrous sodium carbonate (1.3 g) in DMA (20 ml) were heated at 170° under dinitrogen for 20 hr. Addition of water, isolation with ether, column chromatography (silica-gel-chloroform), and crystallisation from cyclohexane gave benzo[*c*][1,5]naphthyridin-6(5H)-one (**13**) (0.87 g; 42%), m.p. 95–97°. Found: C, 73.5; H, 4.1; N, 14.5. $C_{12}H_8N_2O$ requires C, 73.5; H, 4.1; N, 14.3%. IR ν_{max} 3060 w (OH, NH), 1615 s and 1545 s (aromatic, pyridine) cm^{-1}; NMR δ ($CDCl_3$) 7.1–7.65 (4H, m, 3, 7, 8 and 10-H) and 7.9–8.5 (4H, m, 2, 4 and 7-H and OH/NH); mass spectrum *m/z* 196 (100%, M^+).

3,4-Benzocoumarin

Phenyl 2-bromobenzoate (2.77 g), palladium(II) acetate (0.22 g), triphenylphosphine (0.53 g), and sodium acetate (2.0 g) in DMA (20 ml) were heated and stirred at 170° for 2 hr under dinitrogen. The cooled mixture was poured into water and acidified with 2M-hydrochloric acid. Isolation with ether and crystallisation from ethanol gave 3,4-benzocoumarin (0.8 g; 41%), m.p. 91–93° (lit.[16] 92.5°).

N,N-Dibenzenesulphonyl-2-bromoaniline (**19a**)

Benzenesulphonyl chloride (11 g) in dichloromethane (20 ml) was added gradually to 2-bromoaniline (11 g) and triethylamine (8 g) in dichloromethane (50 ml). The mixture was washed with water, dried ($MgSO_4$) and evaporated. Crystallisation from cyclohexane-ethyl acetate gave N,N-dibenzenesulphonyl-2-bromoaniline (8.22 g; 29%), m.p. 147–149° Found: C, 47.8; H, 3.1; N, 3.25. $C_{18}H_{14}BrNO_4S_2$ requires C, 47.8; H, 3.1; N, 3.1%.

6H-Dibenzo[c,e][1,2]thiazine-5,5-dioxide (**17a**)

The sulphonamide (**19a**) (3.12 g), palladium(II) acetate (0.22 g), and sodium carbonate (2.1 g) in DMA (20 ml) were heated and stirred under dinitrogen for 2 hr at 150°. After addition of water, the solution was washed with toluene and then acidified. Isolation with ether and crystallisation from cyclohexane–ethanol gave 6H-dibenzo[c,e][1,2]thiazine-5,5-dioxide (0.9 g; 56%), m.p. 196–198 (lit.[17] 197–198°).

2 - Bromo - N,N - di(4 - methoxybenzenesulphonyl) - 4 - methylaniline (**19b**)

4-Methoxybenzenesulphonyl chloride (20.6 g) was added dropwise to a stirred mixture of 2-bromo-4-methylaniline (9.3 g) and 10% sodium hydroxide solution (150 ml). After 15 min, the solid was collected and crystallised from ethanol to give 2 - bromo - N,N - di(4 - methoxybenzenesulphonyl)-4 - methylaniline (19.44 g; 74%), m.p. 167–170°. Found: C, 48.2; H, 4.0; N, 2.9. $C_{21}H_{20}BrO_6NS_2$ requires C, 47.9; H, 3.8; N, 2.7%.

2 - Bromo - N,N - di(naphthalene - 2 - sulphonyl)aniline (79%), prepared similarly, had m.p. 152–153°. Found: C, 56.6; H, 3.5; N, 2.4. $C_{26}H_{18}BrNO_4S_2$ requires C, 56.6; H, 3.3; N, 2.5%.

2 - Methoxy - 9 - methyldibenzo[c,e][1,2]thiazine - 5,5 - dioxide

2 - Bromo - N,N - di(4 - methoxybenzenesulphonyl) - 4-methylaniline (**19b**) (5.26), sodium acetate (2.0 g) and bis(-triphenylphosphine)palladium(II) dichloride (0.5 g) in DMA (40 ml) were heated and stirred under dinitrogen at 150° for 6 hr. The cooled mixture was diluted with water and washed with toluene. Acidification and isolation with chloroform, followed by crystallisation from cyclohexane-isopropanol gave 2 - methoxy - 9 - methyldibenzo[c,e][1,2]thiazine - 5,5 - dioxide (0.7 g; 25%), m.p. 202–204°. Found: C, 61.0; H, 5.0; N, 4.9. $C_{14}H_{13}NO_3S$ requires C, 61.1; H, 4.8; N, 5.1%. IR ν_{max} 3050–3200 (NH), 1590 s (aromatic), 1290 s and 1160 s (SO_2) cm^{-1}; NMR δ ($CDCl_3$ + DMSO) 2.4 (3H, s, Me), 3.9 (3H, s, OMe), 6.9 (1H, dd, 3-H), 7.1 (2H, s, 7-H and 8-H), 7.35 (1H, d, 1-H), 7.65 (1H, s, 10-H), 7.7–8 (1H, d, 4-H), and 10.15 (1H, br s, NH); MS *m/z* 275 (100% M^+).

The toluene solution was treated with 2M-sodium hydroxide; the separated aqueous layer was acidified with 2M-HCl. Extraction with chloroform, and chromatography on silica gel in chloroform, gave 2 - bromo - N - (4 - methoxybenzenesulphonyl) - 4 - methylaniline (0.7 g; 25%), m.p. 116–118°, from cyclohexane. Found: C, 47.6; H, 4.1; N, 4.0. $C_{14}H_{14}BrNO_3S$ requires C, 47.2; H, 4.0; N, 3.9%. NMR δ ($CDCl_3$) 2.2 (3H, s, Ar–Me), 3.8 (3H, s, OMe), and 6.65–7.7 (8H, m, ArH and NH).

Similarly 2 - bromo - N,N - di(naphth - 2 - ylsulphonyl)aniline (**20**) gave 2 - bromo - N - (napthth - 2 - ylsulphonyl)aniline (8%), m.p. 109–110°, from cyclohexane-propan-2-ol. Found: C, 53.3; H, 3.2; N, 3.9. $C_{16}H_{12}BrNO_2S$ requires C, 53.0; H, 3.3; N, 3.9%; and 5H - benzo[c]naphtho[2,3-e][1,2]thiazine - 6,6 - dioxide (**21**) (25%), m.p. 241–243°, from ethyl acetate. Found: C, 68.2; H, 4.3;

N, 5.0. $C_{16}H_{11}NO_2S$ requires C, 68.3; H, 3.9; N, 5.0%. IR ν_{max} 3200–3100 br m (NH), 1280 s and 1150 s (SO_2) cm^{-1}; NMR ($CDCl_3$ + DMSO) δ 7.0–7.8 (6H, m, ArH), 7.8–8.3 (3H, m, ArH), 8.4 (1H, s, 7-H or 12-H) and 8.5 (1H, s, 7-H or 12-H); MS *m/z* 281 (85%, M^+).

Cyclisation of 2-*bromobenzyl phenyl ether* (22)

The bromo-ether (2.63 g), sodium acetate (2 g), and bis(triphenylphosphine)palladium(II) dichloride (0.5 g) in DMA (20 ml) were heated and stirred under dinitrogen for 2 hr at 160°. The cooled soln was poured into water and worked up with toluene. Chromatography on a silica column in 4 : 1 hexane–chloroform gave diphenyl ether (0.61 g; 35%), m.p. 38–40° (lit.[18] 40°) and 6H-dibenzo [b,d]pyran (0.69 g; 40%) as an oil (90% pure, GLC) b.p., and (lit.[19] b.p. 108–110°/2mmHg).

Cyclisation of 2-*bromobenzophenone*

2-Bromobenzophenone (2.61 g), sodium carbonate (1.3 g) and palladium(II) acetate (0.22 g) in DMA (20 ml) were stirred in dinitrogen at 170° for 4 hr. Isolation with toluene gave 9-fluorenone (1.8 g; quantitative, but GLC showed that 1% of benzophenone was present as a contaminant).

Cyclisation of 4-(2-*bromophenoxy*)*benzaldehyde*

The aldehyde (2.77 g), sodium carbonate (1.3 g), and palladium(II) acetate (0.22 g) were stirred in DMA (20 ml) under dinitrogen at 170° for 22 hr. Addition of water and working up with toluene gave an oil which was shown by NMR and GLC to be a 4 : 1 mixture of dibenzofuran and diphenyl ether.

2-(2-*Bromophenoxy*)*pyridine*

Sodium hydride (4.8 g; 50% dispersion in oil) was washed with toluene and suspended in DMSO (90 ml). 2-Bromophenol (17.3 g) in DMSO (10 ml) was added over 1 hr. After evolution of hydrogen had ceased, 2-fluoropyridine (9.71 g) was added and the mixture was heated at 120° for 36 hr. Addition of water and isolation with ether gave 2-(2-bromophenoxy)pyridine (7 g; 28%), m.p. 80–82°. Found: C, 53.0; H, 3.4; N, 5.8. $C_{11}H_8BrNO$ requires C, 52.8; H, 3.2; N, 5.6%.

Cyclisation of 2-(2-*bromophenoxy*)*pyridine*

Bromo-compound (2.5 g), sodium carbonate (1.3 g) and palladium acetate (0.22 g) in DMA (20 ml) were heated as before (48 hr). After addition of water and working up with ether, separation on a column of silica using chloroform as solvent gave starting material (0.63 g; 25%) and benzofurano2,3-*b*]pyridine (0.2 g; 10%), m.p. 60–62° (lit.[20] 62–63°).

Palladium-catalysed reaction of 2-*iodobiphenyl*

2-Iodobiphenyl (2.8 g), sodium carbonate (1.3 g), and palladium(II) acetate (0.22 g) were heated under the standard conditions for 24 hr. Addition of water, filtration, and crystallisation from ethanol gave tetraphenylene (0.43 g, 28%) as crystals, m.p. 233–235 (lit.[21] 233°).

Acknowledgements—We thank Dr. K. Heatherington and his staff for spectra and analyses and Wyeth Laboratories for financial support and facilities.

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