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Palladium-catalysed Heteroannulation with Acetylenic Carbinols: Synthesis of 3-Acylmethylisoindolin-1-ones

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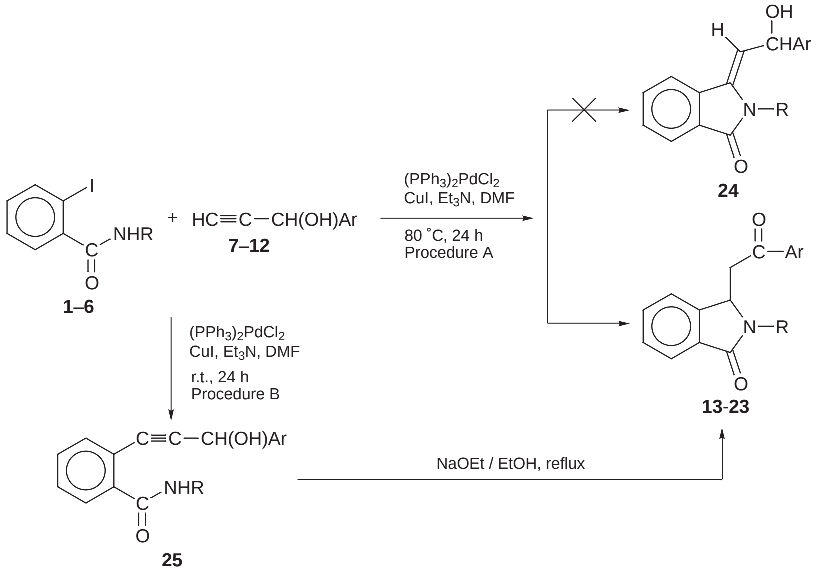
Palladium-catalysed reactions of 2-iodobenzamides **1–6** with acetylenic carbinols **7–12** having a terminal acetylenic group and an adjacent carbinol functionality result in the formation of the 3-acylmethylisoindolin-1-ones **13–23** in one step.

In continuation of our studies of palladium-catalysed reactions,[9,10] we have investigated the palladium-catalysed reactions of 2-iodobenzamide **1** and *N*-substituted 2-iodobenzamides **2–6** with acetylenic carbinols containing a terminal acetylenic group with an adjacent carbinol group and found that instead of the expected 3-alkylidene isoindolin-1-ones **24**, 3-acylmethylisoindolin-1-ones **13–23** were obtained in satisfactory yields as shown in Scheme 1.



Scheme 1

The reactions were usually carried out by heating a mixture of 2-iodobenzamide or its *N*-substituted derivatives and an acetylenic carbinol in the presence of bis(triphenylphosphine)palladium(II) dichloride as catalyst and copper(I) iodide as a cocatalyst at 80 °C for 24 h (Procedure A). After usual work-up, the isoindolin-1-ones were obtained in good to excellent yields (Table 1).

When the palladium-catalysed reactions were carried out at room temperature only the disubstituted alkynols **25** were obtained. These could be cyclised with sodium ethoxide in ethanol under reflux to the 3-acylmethylisoindolin-1-ones **14, 16, 18** (Procedure B). The overall yields, however, were poorer than those obtained by carrying out the reaction in one step at a higher temperature (80 °C). The structures of the compounds were derived from analytical and spectroscopic data. The infrared absorption at 1690–1700 $\mathrm{cm^{-1}}$ was indicative of a five membered γ-lactam ring. The isoindolin-1-ones obtained by the catalytic hydrogenation of 3-alkylidene isoindolin-1-ones[10] also showed infrared absorption at 1680–1690 $\mathrm{cm^{-1}}$ for the carbonyl group. The isoquinolinones usually showed absorption at 1640–1660 $\mathrm{cm^{-1}}$ for the NCO carbonyl group.[9a,13] The ^{1}H and ^{13}C NMR data agreed with the assigned structures. Finally the compounds **14,20** were found to be identical with the 3-benzoylmethyl-*N*-methylsoindolin-1-one and 3-*p*-toluoylmethyl-*N*-anisylisoindolin-1-one, respectively, obtained from the catalytic hydrogenation of the corresponding 3-alkylidene isoindolin-1-ones.[14,15]

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Table 1 Yields of isoindolin-1-ones

Entry	2-Iodobenzamides **1–6** (R)	Acetylenic carbinol HC≡C–CH(OH)Ar **7–12** (Ar)	3-Acylmethyl isoindolin-1-one **13–23** (Yield%)[a]
1	**1** (H)	**8** (C_6H_4F-*p*)	**13** (55)
2	**2** (Me)	**7** (Ph)	**14** (74)
3	**2** (Me)	**10** (C_6H_4OMe-*p*)	**15** (51)
4	**2** (Me)	**12** (piperonyl)	**16** (72)
5	**3** (CH_2Ph)	**8** (C_6H_4F-*p*)	**17** (69)
6	**4** (C_6H_4Me-*p*)	**10** (C_6H_4OMe-*p*)	**18** (56)
7	**5** (C_6H_4OMe-*p*)	**7** (Ph)	**19** (59)
8	**5** (C_6H_4OMe-*p*)	**9** (C_6H_4Me-*p*)	**20** (60)
9	**5** (C_6H_4OMe-*p*)	**8** (C_6H_4F-*p*)	**21** (75)
10	**5** (C_6H_4OMe-*p*)	**12** (piperonyl)	**22** (58)
11	**6** (C_6H_4Cl-*m*)	**11** (C_6H_4OMe-*m*)	**23** (50)

[a] Isolated yields of chromatographically pure compounds based on 2-iodobenzamides.

Techniques used: IR, ^1H and ^{13}C NMR

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