A New Method of Synthesis of Arylmalononitriles catalysed by a Palladium Complex

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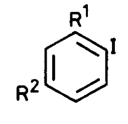
Arylmalononitriles are prepared in good yields using a palladium-catalysed coupling reaction between aryl halides and malononitrile.

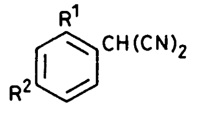
Malononitrile derivatives are important intermediates in the synthesis of heterocyclic compounds.[1] Alkylmalononitriles are obtained easily from the direct reaction of malononitrile anion with alkyl halides, whereas aryl halides do not react with the anion under the same conditions. Several synthetic routes[2] to arylmalononitriles have appeared but these involve complicated procedures with multiple steps, produce low yields, or are not of general applicability. Recently, palladium-catalysed C–C bond formation has been widely used in organic syntheses[3] and we have reported on a coupling reaction of aryl halides with ethynyl compounds catalysed by a palladium complex.[4] We have now used this method to synthesise arylmalononitriles and have found that the malononitrile anion reacted smoothly with various aryl halides in the presence of the palladium catalyst [equation (1)].

$$\text{Ar–X} + \text{NaCH(CN)}_2 \xrightarrow{\text{Pd catalyst}} \text{Ar–CH(CN)}_2 + \text{NaX} \quad (1)$$

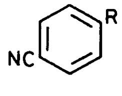
In (**1a**—**g**), (**3**), and (**5a,b**) the halogen atom on the aromatic ring was formally replaced by a dicyanomethyl group, and the corresponding arylmalononitriles were produced in 56—95% yields (Table 1). The reactivity of the halides was in the order I ≫ Br > Cl, and functional groups



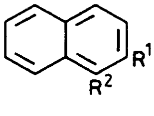
(1) **a**; $R^1 = R^2 = H$
b; $R^1 = H$, $R^2 = Me$
c; $R^1 = Me$, $R^2 = H$
d; $R^1 = H$, $R^2 = OMe$
e; $R^1 = OMe$, $R^2 = H$
f; $R^1 = H$, $R^2 = Cl$
g; $R^1 = H$, $R^2 = Ph$



(2) **a**; $R^1 = R^2 = H$
b; $R^1 = H$, $R^2 = Me$
c; $R^1 = Me$, $R^2 = H$
d; $R^1 = H$, $R^2 = OMe$
e; $R^1 = OMe$, $R^2 = H$
f; $R^1 = H$, $R^2 = Cl$
g; $R^1 = H$, $R^2 = Ph$



(3) R = Br
(4) R = CH(CN)$_2$



(5) **a**; $R^1 = H$, $R^2 = I$
b; $R^1 = I$, $R^2 = H$
(6) **a**; $R^1 = H$, $R^2 = CH(CN)_2$
b; $R^1 = CH(CN)_2$, $R^2 = H$

Table 1. Palladium-catalysed synthesis of arylmalononitriles [equation (1)].[a]

Ar–X	Product (yield/%)[b]
(1a)	**(2a)** (85)
(1b)	**(2b)** (92)
(1c)	**(2c)** (95)
(1d)	**(2d)** (88)
(1e)	**(2e)** (72)
(1f)	**(2f)** (86)
(1g)	**(2g)** (86)
(3)[c]	**(4)** (56)
(5a)	**(6a)** (86)
(5b)	**(6b)** (86)

[a] The aryl halide (10 mmol) and the malonitrile anion [11 mmol, generated *in situ* from $CH_2(CN)_2$ and NaH] reacted in the presence of $(PPh_3)PdCl_2$ (0.14 mmol) in THF (40 ml) under reflux for 4 h. [b] Satisfactory elemental analyses and spectral data were obtained for all the new compounds. [c] 0.50 mmol of the palladium catalyst and 25 mmol of the anion were used in the reaction of (**3**).

such as OR and CN on the aromatic ring did not seem to affect the reaction. The active catalysts are palladium complexes such as $(PPh_3)_2PdCl_2$ and $Pd(PPh_3)_4$, while the nickel and platinum analogues are relatively ineffective.

The synthetic procedure is quite simple: thus a mixture of the aryl halide (1.0 mol) and *in situ* generated malononitrile anion (1.1 mol) was heated in tetrahydrofuran (THF) in the presence of the catalyst (0.01 mol) with stirring under nitrogen for several hours. After quenching with dilute hydrochloric acid, the product was extracted with diethyl ether. Purification by silica gel column chromatography, followed by recrystallization from EtOH or sublimation afforded pure arylmalononitriles.

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References

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