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An Easy Route from Catechols to Phthalonitriles

Ulf Drechsler, Michael Hanack*

Institut für Organische Chemie, Universität Tübingen, Auf der Morgenstelle 18, D-72076 Tübingen, Germany Fax.: +49-7071/29-5244; E-mail: hanack@uni-tuebingen.de

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Abstract: An easy synthetic route from substituted catechols via their corresponding aryl bistriflates to substituted phthalonitriles is described. The displacement of the triflate groups in catechol triflates by cyanide ions proceeded in high yields using zinc cyanide and palladium-1,1'-bis(diphenylphosphino)ferrocene as catalyst. The mild reaction conditions tolerate numerous functional groups and represent a desirable alternative to the generally low-yielding Rosenmund-von Braun reaction.

The common pathway for the preparation of phthalonitriles which are the most important starting materials for the preparation of phthalocyanines¹ is represented by the Rosenmund-von Braun reaction.² Starting from 1,2-dibromobenzenes and reacting them with cuprous cyanide, this reaction often proceeds unsatisfactorily. The harsh reaction conditions and the oxidative workup prohibit the presence of many functional groups. The use of cuprous cyanide generally leads to the formation of the corresponding copper phthalocyanine as an undesired side product. During our ongoing work on phthalocyanines as conducting and non-linear optical materials,³ we needed several functionally substituted phthalonitriles as phthalocyanine precursors. Therefore we sought for a new and easy method to prepare phthalonitriles.

Phenolic hydroxyl groups are easily converted into their corresponding aryl trifluoromethanesulfonates (triflates)⁴ and the transition metalcatalysed replacement of an aromatic triflate group by a cyanide ion has been reported.^{5,6} Nevertheless we found that these procedures are not feasible for the substitution of two ortho-positioned triflate groups by cyanide. In this paper we report the synthesis of several phthalonitriles starting from catechols via the corresponding aryl bistriflates and their replacement by cyanide using a palladium catalyst (Scheme 1). This two-step reaction proceeds under relatively mild conditions and the yields are generally high.



Scheme 1. a) Tf_2O , NEt_3 , CH_2Cl_2 , -20°C; b) $Zn(CN)_2$, $Pd_2(dba)_3$, dppf, DMF.

The transition metal-catalysed substitution reaction can be described by a series of single reactions:⁷ due to the ease of insertion of transition

metals into the carbon-oxygen bond of aryl triflates, the initial step is expected to be the oxidative addition of the aryl triflate to a zero-valent transition metal species to form an arylmetal triflate. In polar solvents, such as DMF, a subsequent dissociation of the triflate anion is predicted to leave a positively charged, coordinatively unsaturated complex.⁸ To the free coordination site a cyanide ion is added and, after reductive elimination of the desired aryl cyanide, the zero-valent metal species is reformed.

This catalytic reaction faces the principal problem that an increased cyanide concentration leads to the formation of stable tetracyano-metal complexes which cannot participate in the catalytic cycle.⁹ For this reason the metal, in our case palladium, should be shielded by a strongly binding chelating ligand. On the other hand, the concentration of free cyanide ions has to be diminished as much as possible.

Due to its strong donor qualities, 1,1'-bis(diphenylphosphino)ferrocene (dppf) is a suitable ligand to stabilise the intermediate cationic species and should also effectively protect the palladium from being complexed with excess cyanide. The concentration of free cyanide could further be lowered by a successive addition of zinc cyanide which also has the advantage of being only slightly soluble in DMF.¹⁰

To produce an active catalyst system tris(dibenzylidene acetone)dipalladium ($Pd_2(dba)_3$) as source of zero-valent palladium and dppf were dissolved in DMF. After complete dissolution, the aryl bistriflates **2a-g**¹¹ were added and, after adjusting the reaction temperature (Table 1), zinc cyanide was added portionwise (compare Table 1, entry 8). Simple extractive and chromatographic workup afforded phthalonitriles¹² in good to excellent yields, as indicated in Table 1.¹³ Due to steric hindrance, substituents in the 3-position of the starting bistriflate require higher reaction temperatures compared to bistriflates containing substituents in the 4-position (Table 1, entries 2 and 4). Reactions on systems carrying electron-withdrawing substituents proceed more rapidly and lead to higher yields (Table 1, entry 3). It should also be noted that, according to the literature,¹⁴ all attempts to catalyse this reaction by nickel proceeded unsatisfactorily.

 Table 1. Conversion of catechols into phthalonitriles via their corresponding bistriflates.

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Entry	Catechol	Bistriflate (2) Yield (%)	Reaction temp. (°C)	Phthalonitrile (3) Yield (%)
1	1a	82	70	92
2	1b	85	90	88
3	1c	86	60	98
4	1 d	89	90	81
5	le	72	60	95
6	1f	75	60	75
7	1g	78	70	85
8 ^a	1a	82	70	_

^{*a*} zinc cyanide was added at once

In conclusion, this synthetic route represents a desirable alternative to the Rosenmund-von Braun reaction². The relatively mild reaction conditions in this two-step reaction tolerate numerous functional groups which makes this route very useful for the preparation of substituted

phthalonitriles. Contrary to the Rosenmund-von Braun reaction, formation of phthalocyanines as side products is avoided.

References and Notes

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- (11) Typical Procedure for Aryl Bistriflates (2a-g). To a solution of trifluoromethanesulfonic anhydride (23 mmol) in dry dichloromethane (15 ml) was added dropwise at -20°C under a nitrogen atmosphere a solution of the catechol 1a-g (10 mmol)

and triethylamine (23 mmol) in dichloromethane (10 ml). After complete addition the mixture was allowed to warm to room temperature and stirred overnight. Extractive workup and chromatographic purification on silica gel using hexane-ethyl acetate (2:1) gave the bistriflates in 72 to 89% yield. Representative data for **2d**: ¹H-NMR (250 MHz, CDCl₃) δ (ppm): 7.30 (m, 3H), 3.60 (s, 3H), 2.76 (t, 2H), 2.30 (t, 2H), 1.65 (m, 4H); ¹³C-NMR (62.9 MHz, CDCl₃) δ (ppm): 173.5, 141.0, 138.8, 138.1, 130.3, 129.1, 120.7, 118.4 (q, J_{CF}=314.5 Hz), 51.3, 33.3, 29.8, 28.9, 24.3; MS (EI) 489.0 (M⁺+1); Anal. Calcd. for C₁₄H₁₄F₆S₂O₈ (488.37): C, 34.43; H, 2.89; F, 23.34; S, 13.13; Found: C, 34.66; H, 2.82; F, 24.04; S, 13.11.

- (12) Typical Procedure for Phthalonitriles (3a-g). To a solution of Pd₂(dba)₃ (0.4 mmol) and dppf (1.6 mmol) in DMF (20 ml) was added at room temperature the aryl bistriflate 2a-g (10 mmol) in DMF (5 ml) under a nitrogen atmosphere. After adjusting the final reaction temperature (see Table 1), zinc(II) cyanide (in total 12 mmol) was added in 15 to 20 equal portions over a 2 h period. Extractive workup and chromatographic purification on normal grade silica gel using hexane-ethyl acetate (2:1) as eluent afforded the corresponding phthalonitriles in 75 to 98% yield. Representative data for **3d**: ¹H-NMR (250 MHz, CDCl₃) δ (ppm): 7.60 (m, 3H), 3.64 (s, 3H), 2.89 (t, 2H), 2.34 (t, 2H), 1.68 (m, 4H); ¹³C-NMR (62.9 MHz, CDCl₃) δ (ppm): 173.6, 148.2, 133.7, 132.9, 131.2, 116.4, 115.7, 115.6, 114.6, 51.6, 34.4, 33.5, 29.9, 24.3; MS (EI) 242.2 (M⁺); Anal. Calcd. for C₁₄H₁₄N₂O₂ (242.28): C, 69.41; H, 5.82; N, 11.56; Found: C, 69.73; H, 5.69; N, 11.67.
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