

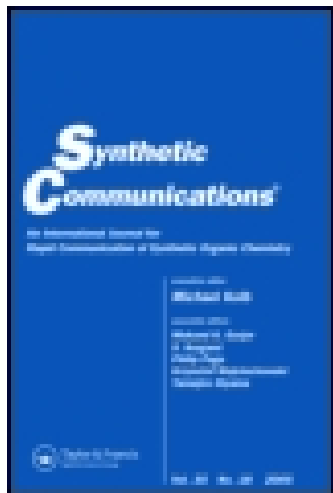
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Publisher: Taylor & Francis

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Synthetic Communications: An International Journal for Rapid Communication of Synthetic Organic Chemistry

Publication details, including instructions for authors and subscription information:

<http://www.tandfonline.com/loi/lcyc20>

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Published online: 24 Sep 2006.

To cite this article: K. Buttke, T. Reiher & H. J. Niclas (1992) A New Modified Electrophilic Cyanation of Aromatics with Activated Aryl Cyanates, *Synthetic Communications: An International Journal for Rapid Communication of Synthetic Organic Chemistry*, 22:15, 2237-2243, DOI: [10.1080/00397919208019077](https://doi.org/10.1080/00397919208019077)

To link to this article: <http://dx.doi.org/10.1080/00397919208019077>

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A NEW MODIFIED ELECTROPHILIC CYANATION OF AROMATICS WITH ACTIVATED ARYL CYANATES

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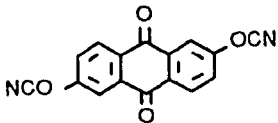
Abstract: The selective cyanation of electron-rich aromatics succeeds in moderate to good yields with the activated aryl cyanates **1a-d** using AlCl_3/HCl . The formation of p-isomeres is preferred.

The electrophilic cyanation of aromatics succeeds with various reagents, e. g. with cyanogen halides ^{1,2,4,5}, cyanogen ⁴, trichloroacetonitrile ³⁻⁵, chlorosulfonyl isocyanate ⁶, aryl cyanates⁷⁻¹⁰ or tosyl cyanide.¹⁰

Thus, the direct cyanation of reactive aromatic hydrocarbons in carbon disulfide using cyanogen bromide/aluminum chloride affords the appropriate nitriles after 18 hours at 48°C in good yields.² The reaction of anilines, trichloroacetonitrile and BCl_3 in the presence of SnCl_4 or AlCl_3 gives 2-aminobenzonitriles.³ Moreover, the treatment of phenols with CH_3SCN and $\text{BCl}_3/\text{AlCl}_3$ leads to 2-hydroxybenzonitriles.³ A further method for introducing the cyano group into

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Dedicated to Prof. D. Martin on the occasion of his 60th birthday

Table 1: Comparative Cyanation of Anisole with Aryl Cyanates

No.	Aryl Cyanate	Yield ^a (%)	Isomer Distribution (%) ^b	
			para	ortho
1a		72	100	0
1b	4-PhCO-C ₆ H ₄ -OCN	84	100	0
1c	4-MeCO-C ₆ H ₄ -OCN	55	100	0
1d	4-OHC-C ₆ H ₄ -OCN	59	100	0
1e	4-MeO-C ₆ H ₄ -OCN	42	81	19
1f	C ₆ H ₅ -OCN	25 ^c	73	27

^a Referred to isolated MeO-C₆H₄-CN; found (bp (°C)/Torr): 133-136/16, reported¹¹: 137/18.

^b Determined by GC and comparison with authentic samples; no meta-isomer was found in all cases.

^c Reported⁸: only 4-methoxybenzocyanide (31 %).

aromatics proceeds via chlorosulfonamides starting from chlorosulfonyl isocyanates.⁶

Finally, electrophilic cyanation is performed with aryl cyanates. Thus, the nitrile group may be introduced into toluene or anisole by means of ArOCN with AlCl₃ + HCl as catalyst. The yields obtained are only moderate.⁸ Despite the usefulness of the reagents and methods mentioned above there are several factors limiting their general application, for example toxic or irritating activities or thermal instability (cf. ref. 6,10).

Table 2: Carbonitriles Prepared ^a

ArH	Ar'-OCN	Ar-CN Yield (%) ^b	Isomer Distribution (%) ^c		
			para	meta	ortho
EtO-C ₆ H ₅	1a	51 ^d	100	0	0
Me-C ₆ H ₅	1a	43	60	5	35
Me-C ₆ H ₅	1b	32	60	10	30
Me-C ₆ H ₅	1f	53 ^e	42	7	51
1,2-(Me) ₂ -C ₆ H ₄	1a	47	90 (3,4)		10 (2,3)
1,4-(Me) ₂ -C ₆ H ₄	1a	28 ^{f,g,h}			
1,3,5-(Me) ₃ -C ₆ H ₃	1a	55 ⁱ			

^a Results for methoxybenzotrile are listed in Table 1.

^b Referred to isolated ArCN.

^c Determined by GC and comparison with authentic samples.

^d Found (bp (°C)/Torr): 140-145/18; reported ¹²: 258.

^e Reported ⁸: ortho/para = 2:1.

^f Moreover, 18 % of the corresponding benzamide could be isolated.

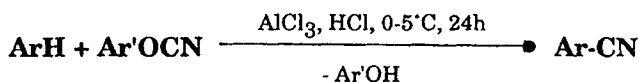
^g The product contains small amounts of trimethylbenzene and tetramethylbenzene as determined by GC/MS coupling (cf. ref. ¹³).

^h Found (bp (°C)/Torr): 104/16; reported ¹⁴: 223-226/730

ⁱ Found (bp (°C)/Torr): 116-125/18; reported ¹⁵: 235-238

Within the framework of our studies on reactions of activated aromatic compounds we have studied the cyanating ability of aryl cyanates **1a-f**, especially cyanates **1a-d** activated by carbonyl groups.

Now we have found that the electrophilic cyanation of electron-rich aromatics (ArH) succeeds with improved para-selectivity when the aryl cyanates **1a-d** are used. The reaction is carried out with AlCl₃ + HCl as catalyst. Moderate to good yields of isolated carbonitriles are obtained by treating the aromatic compounds with Ar'-OCN at 0 to 5 °C for 24 h (Tables 1, 2).



Comparative studies of the cyanation of anisole show that yields are best with **1b** (84 %) or **1a** (72 %), leading exclusively to 4-methoxybenzotrile (Table 1).

However, the aryl cyanates **1e,f** furnish considerable amounts of 2-methoxybenzotrile in addition to 4-methoxybenzotrile. The results in Table 2 show that phenetole is cyanated by **1a** in para-position. Furthermore, in the cases of toluene and o-xylene the formation of para-isomers is preferred when **1a** or **1b** are used as cyanating reagents. On the other hand, **1f** affords 51 % of o-tolunitrile.

Experimental

All aromatic compounds used as starting material or as authentic samples are commercially available. GC was performed using the gas chromatograph HP 5890 A (Hewlett Packard, USA) and the data system Auswert 2 (Central Institute of Organic Chemistry, Berlin, FRG). A capillary column HP5 of 0.2 mm and a length of 25 m was used. A temperature programme of 8K/min from 50°C to 280°C was applied. ¹³C-NMR spectra were recorded on a Varian GEMA 300 spectrometer in DMSO-d₆/TMS (internal standard: HMDS), IR spectra on a specord 75 IR (Carl Zeiss, Jena). Mass spectra were obtained on a Hewlett-Packard 5985-B spectrometer.

The aryl cyanates **1a**^{7,16} and **1b-f**¹⁷ were prepared according to known procedures. New aryl cyanates:

1a; yield: 84 %, m.p. not detectable; anal. calcd. for C₁₆H₆N₂O₄

(290.24); % C 66.21, %H 2.08, % N 9.65; found: %C 65.92, % H 2.09, % N 9.28; mass spectrum, m/e (relative intensity) M^+ 290 (100), 262 (35); IR, ν_{CN} : 2230, 2260 cm^{-1} .

1b; yield: 86 %, m.p. 98-101°C; anal. calcd. for $\text{C}_{14}\text{H}_9\text{NO}_2$ (223.22); % C 75.32, % H 4.06, % N 6.28; found: % C 75.42, % H 4.06, % N 6.27; ^{13}C -NMR, δ : 194.14, 154.75, 136.46, 135.64, 132.95, 132.47, 129.57, 128.61, 115.74, 107.96; mass spectrum, m/e (relative intensity) M^+ 223 (37), 146(43), 105 (100); IR, ν_{CN} : 2220, 2250, 2280 cm^{-1} .

4-Methoxybenzotrile

(Typical Procedure for Cyanations with **1a**)

AlCl_3 (32.0 g, 0.24 mol) is added under ice-cooling and vigorous stirring to 100 ml of anisole. Then this mixture is added under stirring at -70°C to a suspension of **1a** (14.5 g, 0.05 mol) in 100 ml of carbon disulfide. The mixture is allowed to warm to 0°C and a stream of dry HCl is passed through until saturation is achieved. After standing overnight, the reaction mixture is diluted with 200 ml of diethyl ether, poured onto ice, filtered by suction, and the precipitate is washed with diethyl ether several times. The ether phase is then successively washed with 2N NaOH and water, dried over Na_2SO_4 , and distilled. Yield: 9.64 g (72 %) b.p. $133\text{-}136^\circ\text{C} / 16$ Torr.

Preparation of Carbonitriles with **1b**

(General Procedure)

AlCl_3 (32.0 g, 0.24 mol) is added under ice-cooling and stirring to 50 ml of aromatic. To this stirred mixture, a solution of **1b** (22.3 g, 0.1 mol) in

50 ml of aromatic is added dropwise at 0-5 °C. Then a stream of dry HCl is passed through the reaction mixture at 0-5 °C until saturation is achieved. After standing overnight at 5 °C, the reaction mixture is diluted with 200 ml of absolute diethyl ether and a stream of dried NH₃ is passed through to render the mixture basic. The precipitate is isolated by suction and thoroughly washed with diethyl ether. The ether phase is then successively washed with 2N NaOH and water, dried over Na₂SO₄, and distilled.

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(Accepted in The Netherlands 6 April, 1992)