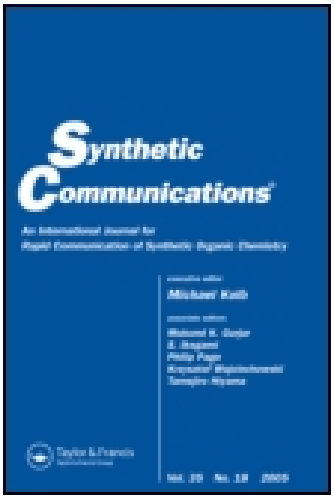

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N-Benzyl DABCO Tribromide-Promoted Oxidative Coupling of Benzyl Cyanides: A Convenient Procedure for the Synthesis of α, α′-Dicyanostilbenes

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N-Benzyl DABCO Tribromide–Promoted Oxidative Coupling of Benzyl Cyanides: A Convenient Procedure for the Synthesis of α, α′-Dicyanostilbenes

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Abstract: A convenient and efficient procedure was developed for preparing α,α′-icyanostilbenes through the oxidative coupling reaction of benzyl cyanide derivatives using N-benzyl DABCO tribromide as the oxidative bromination reagent in the presence of K_2CO_3 as a base.

Keywords: Dicyanostilbene, fumaronitriles, organic ammonium tribromide (OATB), oxidative coupling

INTRODUCTION

Dicyanostilbenes are valuable intermediates that have been used in the pharmacological synthesis[1,2] and preparation of N-methyl-3,4-bis(4-(N-(1-naphthyl)phenylamino)phenyl)-maleimide (NPAMLMe), as an unusual, nondoped, host emitter for red organic light-emitting diods (OLEDs).[3] They are also suitable for the preparation of porphyrazines.[4] Symmetrical and unsymmetrical cyanostillbenes and various substituted cyano- and dihydrocyanostilbenes have been prepared, characterized, and tested for estrogenic activity.[5] The method of preparation of these compounds has been known to chemists and can be traced back to the late 19th century.[4,6]

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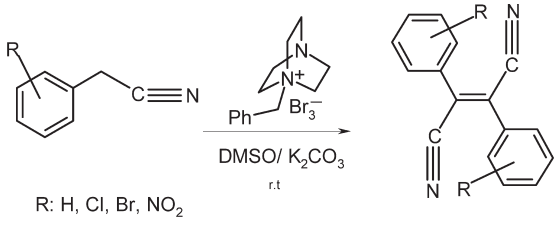
These methods consisted of self-condensation of the respective benzyl cyanides by means of iodine in the presence of sodium methoxide or sodium amide.[7,8] The α,α'-dicyanostilbenes could also result from the dehydrohalogenation of benzyl cyanide derivatives.[9,10] Surveying the literature reveals that the geometrical form of dicyanostillbene in this reaction is the *trans*-form (*E*-isomer).[10]

RESULTS AND DISCUSSION

As an alternative reagent to liquid bromine, organic ammonium tribromide (OATB), such as benzyltrimethyl ammonium tribromide and tetrabutylammonium tri-bromide, which are high-molecular-weight, stable, crystalline solids, are capable of delivering a stoichiometric amount of bromine where small amount of bromine are necessary for microscale reactions.[11] Recently we have developed N-benzyl diaza bicyclo octane (DABCO) tribromide, as one of OATBs for efficient oxidative deprotection of dithioacetals and oxidative cyclysation of benzothiazoles.[12,13] Even though the chemistry of OATBs has been extensively studied, their use as a mild brominating reagent for oxidative coupling reactions has been neglected.

In this article we report our attempt to extend the use of N-benzyl DABCO tribromide as an electrophilic bromine source and one of the OATBs for one-step oxidative coupling procedure of benzyl cyanides into symmetrical α,α'-dicyanostilbenes. To the best of our knowledge this reaction has not been reported previously (Scheme 1).

To find the optimum conditions for this reaction, we examined the stoichiometry, temperature, and the effects of different OATBs and various solvents. During these examinations we encountered better results by performing the reaction at room temperature and applying 1 stoichiometric equiv. of N-benzyl DABCO tribromide and 3 stoichiometric equiv. of K_2CO_3. For investigating the effect of solvent the model compound **1** was selected. Compound **1** was reacted with 1 molar equivalent of N-benzyl DABCO tribromide (Table 1, entry 1) in dimethylsulfoxide at room temperature for 1 h to

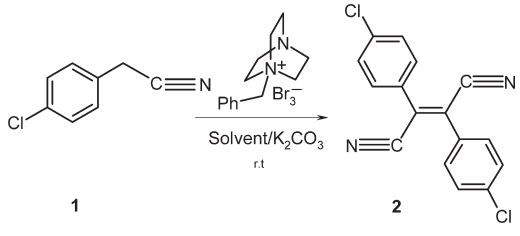


Scheme 1. Oxidative coupling of benzyl cyanide derivatives using N-benzyl DABCO tribromide.

Table 1. Variation of solvent in the oxidative coupling of benzylcyanide with N-benzyl DABCO tribromide

Entry	Solvent	Reaction conditions	Yield (%)
1	DMSO	rt/1 h	88
2	MeOH	rt/3 h	63
3	CH_2Cl_2	rt/3 h	45
4	CH_2Cl_2-CCl_4	rt/5 h	<10
5	CCl_4	rt/5 h	<10

give the desired product **2** in 88% yield. Dichloromethane and methanol were also found effective, but the yields were low (Table 1, entries 2, 3). Other nonpolar solvents such as CCl_4 and its mixture with CH_2Cl_2 gave little product (<10%) (Table 1, entries 4, 5)



1 2

By examining the effect of two different OATBs in the reaction course, it was found that N-benzyl DABCO tribromide gave higher yield and the reaction proceeded in a shorter time (88%, 1 h versus 80%, 1.5 h) (Table 2).

The generality of the method was confirmed by the successful conversion of various substrates to the corresponding α,α'-dicyanostilbene compounds, and the results are summarized in Table 3. The best yield (90%) was obtained for 4-nitro benzyl cyanide (Table 3, entry 1), and the least yield (57%) is reported for α-naphthyl acetonitrile (Table 3, entry 6). The reaction proceeds easily and cleanly and no bromination takes place on the aromatic ring.

Table 2. Variation of OATBs in the oxidative coupling of benzylcyanides

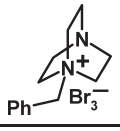
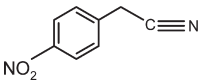
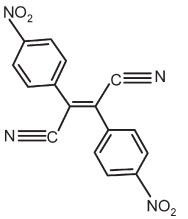
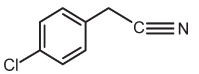
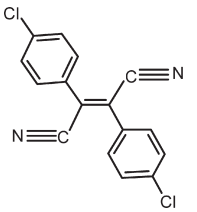
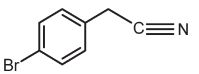
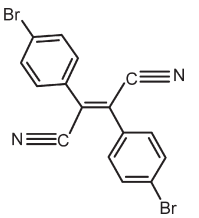
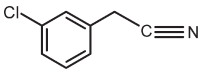
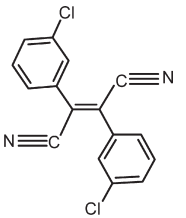
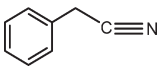
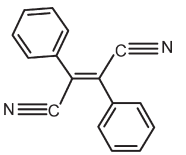
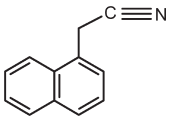
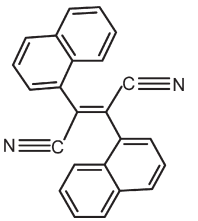
Entry	OATB	Reaction conditions	Yield (%)
1	$PhCH_2NEt_3Br_3$	rt/1.5 h	80
2		rt/1 h	80

Table 3. Result of oxidative coupling reaction of benzyl cyanide leading to derivatives of α,α'-dicyanostilbenes

Entry	Arycyanide	Time (h)	Dicyanostilbene[a]	Mp found (°C) (mp lit.)	Yield (%)[b]
1		1		188–190 (190)[15, 16]	90
2		1		166–168 (168)[14]	88
3		1.5		212–214 (212–214)[7a]	82

(*continued*)

Table 3. Continued

Entry	Arycyanide	Time (h)	Dicyanostilbene[a]	Mp found (°C) (mp lit.)	Yield (%)[b]
4		1.5		174–176	73
5		2.5		161–163(161–163)[17]	60
6		3		167–169	57

[a]^{1}H-NMR reveals that only the E-isomer is produced in the reaction course.
[b]All yields refer to the isolated products.

MECHANISM OF THE REACTION

The condensation of two molecules of α-halobenzylcyanides with bases and related reactions were studied by numerous investigators, and several mechanisms were postulated.[3,6,7b,18–22] On the basis of the scattered evidence found in the literature, the proposed mechanism involves α-proton abstraction from benzyl cyanide, followed by a rapid halogenation and subsequent nucleophilic attack of the formed carbanion on α-bromobenzyl cyanide to form 2-bromo-2,3-diaryl stillbene, and finally elimination of hydrogen bromide to give the desired compound.[3,6] On the basis of these studies, we propose a mechanism that indicates a logical explanation for the reaction pathway (Scheme 2).

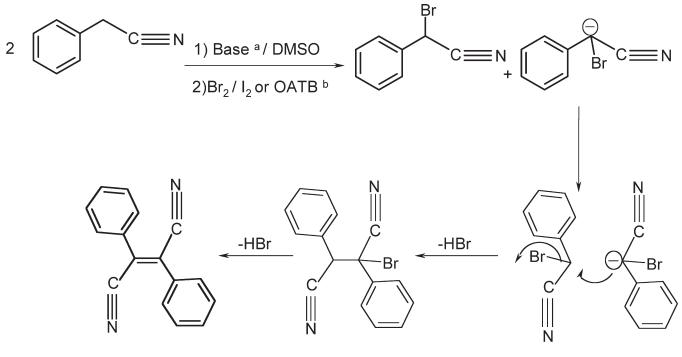
In conclusion, an efficient method has been developed for the preparation of α,α'-dicyanostilbenes. The reagent used in this methodology is safe, easily available, and nontoxic as compared to the reported procedures.

EXPERIMENTAL SECTION

The compounds were characterized by their spectroscopic data (^{1}H NMR and ^{13}C NMR spectra and compared with authentic samples.[4,7a,9a,17] A Bruker (DRX-500 Avance) NMR instrument was used to record the spectra, and all of spectra were determined in $CDCl_3$ at ambient temperature. N-Benzyl-DABCO-tribromide was prepared as reported in reference [12].

General Procedure for the Preparation of Dicyanostillbnes

N-Benzyl-DABCO-tribromide (1 mmol) in one portion was added to a stirred mixture of benzylcyanide (1 mmol) and K_2CO_3 (3 mmol) in DMSO (10 ml). The stirring was continued for the time noted in Table 3, at room temperature. By adding a portion of water (10 ml) the α,α'-dicyanostillbene was slowly



Scheme 2. Mechanism proposed for oxidative coupling of benzylcyanide by oxidative brominative reagents:[3,6] a) base: K_2CO_3, and b) OATB: N-benzyl-DABCO-tribromide.

precipitated from the solution. The solid was separated by filtration and washed with portions of water. Pure compound (*E*-isomer) was easily obtained by recrystallization of the solid from dilute methanol and/or by column chromatography for some derivatives.

Data

Bis-(3-chlorophenyl)fumaronitrile (**Table 3, Entry 4**). Lemon-yellow solid. Yield 73%. Mp: 174–176 °C. ^{1}H NMR (500 MHz, $CDCl_3$): δ (ppm) 7.85 (s, 2H), 7.77 (d, 2H, $J = 7.71$ Hz), 7.54–7.61 (m, 4H). ^{13}C NMR (125 MHz, $CDCl_3$): δ (ppm) 135.9, 133.5, 132.5, 131, 129.1, 127.2, 125.5, 116.2.

Dinaphtylfumaronitril (**Table 3, Entry 6**). White solid. Yield 57%. Mp: 167–169 °C. ^{1}H NMR (500 MHz, $CDCl_3$): δ (ppm) 9.30 (d, 2H, $J = 8.5$ Hz), 8.13 (d, 2H, $J = 8.2$ Hz), 8.03 (d, 2H, $J = 7.5$ Hz), 7.95 (d, 2H, $J = 7.5$ Hz), 7.74 (t, 2H, $J = 7.3$ Hz), 7.62–7.69 (m, 4H). ^{13}C NMR (125 MHz, $CDCl_3$): δ (ppm) 133.2, 132.5, 130.1, 127.9, 127.4, 125.4, 125.1, 124.9, 123.2, 122.2, 121, 116.8.

Bis-(4-bromophenyl)fumaronitrile (**Table 3, Entry 3**). Off-white solid. Yield 82%. Mp: 212–214 °C. ^{1}H NMR (500 MHz, $CDCl_3$): δ (ppm) 7.72 (d, 4H, $J = 8.8$ Hz), 7.76 (d, 4H, $J = 8.8$ Hz). ^{13}C NMR (125 MHz, $CDCl_3$): δ (ppm) 133.1, 131, 130.5, 127.2, 125, 116.5.

Diphenylfumaronitrile (**Table 3 Entry 5**). White solid. Yield 60%. Mp: 161–163 °C. ^{1}HNMR (500 MHz, $CDCl_3$): δ (ppm) 7.89–7.91 (m, 4H), 7.48–7.52 (m, 6H). ^{13}CNMR (125 MHz, $CDCl_3$): δ (ppm) 131, 129.5, 128.1, 126.2, 124.1, 116.9.

Bis-(4-chlorophenyl)fumaronitrile (**Table 3, Entry 4**). White solid. Yield 88%. Mp:166–168 °C. ^{1}H NMR (500 MHz, $CDCl_3$): δ (ppm) 7.81 (d, 4H, $J = 8.6$ Hz), 7.56 (d, 4H, $J = 8.6$ Hz). ^{13}C NMR (125 MHz, $CDCl_3$): δ (ppm) 133.5, 131.2, 130.7, 127.3, 125.6, 116.5.

Bis-(4-nitrophenyl)fumaronitrile (**Table 3, Entry 1**). Off-yellow solid. Yield 90%. Mp: 188–190 °C. ^{1}H NMR (500 MHz, DMSO d-6): δ (ppm) 8.16 (d, 4H, $J = 8.4$ Hz), 8.48 (d, 4H, $J = 8.4$ Hz). ^{13}C NMR (125 MHz, DMSO d-6): δ (ppm) 142.1, 132, 131.4, 125.2, 121, 116.9.

REFERENCES

1. Cheng Fu, S.; Sah, P. P. T. Synthesis of 4,4′-dicyanostilbene. *J. Amer. Chem. Soc.* **1942**, *64*, 1482.

2. Irie, M.; Mohri, M. Thermally irreversible photochromic system: Reversible photocyclization of diarylethene derivatives. *J. Org. Chem.* **1988**, *53*, 803–808.
3. (a) Yeh, H. C.; Wu, W. C.; Wen, Y.-S.; Dai, D. C.; Wang, J. K.; Chen, C. T. Derivatives of α,β-dicyanostilbene: Convenient precursor for the synthesis of diphenylmaleimide compounds, *E-Z* isomerization, crystal structure, and solid-state florescence. *J. Org. Chem.* **2004**, *69*, 6455–6462; (b) Yeh, H. C.; Chan, L. H.; Wu, W. C.; Chen, C. T. Non-doped red organic light-emitting diodes. *J. Mater. Chem.* **2004**, *14*, 1293–1298.
4. Cook, A. H.; Listead, R. P. Phthalocyanines, part XI: The prepararion of octaphenylporphyrazines from diphenylmaleinitrile. *J. Chem. Soc.* **1937**, 929–933.
5. Niederl, J. B.; Ziering, A. Symmetrical cyanostilbens. *J. Amer. Chem. Soc.* **1942**, 2486–2487.
6. Ogata, Y.; Nagura, K. Kinetics of the oxidative coupling of benzyl cyanides by halogen or hypohalite. *J. Org. Chem.* **1974**, *39*, 394–340.
7. (a) Weizmann, M.; Patai, S. 4,4′-Dibromo-α,α'-dicyanostilbene. *J. Amer. Chem. Soc.* **1949**, 2587; (b) Boyer, J. H.; Selvarajan, R. α,β-Dicyanostilbene from phenylethynyl azide and from phenylethynyl isocyanate. *J. Am. Chem. Soc.* **1969**, 6122–6126.
8. Davies, W.; Maclaren, J. A. The reaction of α-bromobaenzyl cyanide with ethyl xanthamidate (thioncarbamate). *J. Chem. Soc.* **1951**, 1434–1437.
9. (a) Taylor, E. C.; Berchtols, G. A.; Goeckner, N. A.; Stroehmann, F. G. Some further reaction of α-cyanobenzyl benzenesulfonate. *J. Org. Chem.* **1961**, *26*, 2715–2718; (b) Minami, T.; Takimoto, F.; Agawa, T. Reaction of N-sulfinylarylamines with carbonyl compounds and a nitrile in the presence of copper. *J. Org. Chem.* **1976**, *41*, 3811–3813.
10. Williams, A. J.; Le Fever, J. W. The configuration of the so-called "diphenylmaleinitrile". *J. Chem. Soc.* **1957**, 2425–2426.
11. Jordan, A. D.; Luo, C.; Reitz, A. B. Efficient conversion of substituted aryl thioureas to 2-aminobenzothiazoles using benzyltrimethylammonium tribromide. *J. Org. Chem.* **2003**, *68*, 8693–8696.
12. Matloubi Moghaddam, F.; Zali Boeini, H. Oxidative cyclization of thiobenzanilides to benzothiazoles using N-benzyl-DABCO tribromide under mild conditions. *Synlett.* **2005**, 1612–1614.
13. Matloubi Moghaddam, F.; Zali Boeini, H.; Zargarani, D.; Rezanejad Bardjee, G. N-Benzyl-DABCO tribromide as an efficient and mild reagent for deprotection of dithioacetals. *Synth. Commun.* **2005**, *36*, 1093–1096.
14. Anbar, M.; Dostrovsky, I.; Samuel, D.; Yoffe, A. D. Esters of inorganic oxyacids, part I: The mechanism of hydrolysis of alkyl esters, ^{18}O being used as tracer, and its relation to other reactions in alkalin media. *J. Chem. Soc.* **1954**, 3603–3611.
15. Hanna, S. B.; Iskander, Y.; Raid, Y. The influence of the nitro-group upon side-chain reactivity, part I: The reaction between 4-nitrobenzyl cyanide and alkali. *J. Chem. Soc.* **1961**, 217–220.
16. Torston, J. T.; Shriner, R. L. Salts of nitro compounds, I: Preparation, alkylation and acylation of salt of phenylnitro acetonitrile. *J. Org. Chem.* **1937**, *2*, 183–194.
17. Dodson, T.; Turner. α-Cyanoalkyl sulfonates, I: The reactions of α-cyanobenzyl benzenesulfonate. *J. Am. Chem. Soc.* **1951**, *73*, 4517–4519.
18. Hassner, A.; Isbister, R. J. Stereochemistry, XLV: Additions to bromophenylethyne. *J. Amer. Chem Soc.* **1969**, 6126–6128.
19. Swain, C. G.; Thornton, E. R. Mechanism of α-elimination by hydroxide ion on *p*-nitrobenzylsulfonium ion in aqueous solution. *J. Amer. Chem. Soc* **1961**, *83*, 4033–4034.

20. Coe, D. G.; Gale, M. M.; Linstead, R. P.; Timmons, C. J. The cis and trans-α,β-dicyanostilbenes, part I: The geometrical configuration and cyclisation of the trans-isomer, the previously alleged diphenylmaleidinitrile. *J. Chem. Soc.* **1957**, 123–130.
21. Haueser, C. R.; Brasen, W. R.; Skell, P. S.; Kantor, S. W.; Brodhag, A. E. Dimeric olefins *versus* amines from α-aryl alkyl halides with alkali amides in liquid ammonia. Intermediate dimeric halides and their dehydrohalogenation: Imines from amines. *J. Am. Chem. Soc.* **1956**, *78*, 1653–1658.
22. Shipp, K. G.; Kaplan, L. A. Reaction of α-substituted polynitrotoluenes, II: The generation and reactions of 2, 4, 6-trinitrobenzyl anion. *J. Org. Chem.* **1966**, *31*, 857–861.