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Synthesis of N,N-bispropargylanilines *via* Eglinton coupling—the potential acyclic molecular tweezers

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The synthesis of title compounds **3a-g** from N-cyano- and N-benzenesulfonyl-N-propargyl anilines (**2a-g**) *via* $Cu(OAc)_2$ mediated Eglinton coupling reaction is described.

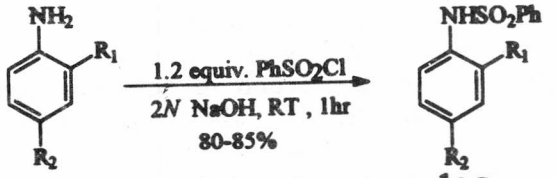
Molecular tweezers are either cyclic or acyclic host molecules that can grasp guest molecules[1] when the guest molecules are enclosed. There are only few types of compounds that have been reported to be efficient molecular tweezers[2]. Suitably substituted cyclophanes, cyclic acetylenes containing aromatic rings and triply bridged macrobicyclic polyamines have been known to function as molecular tweezers[3]. These molecules can preorganise the functional groups so precisely that they are directly opposite to each other when the guest molecules are enclosed. A number of reviews have appeared in the field of host-guest complexation[4]. It is an interesting aspect to note that most of the host molecules contain a linear diyne bridge as their basic structural unit[2].

During the course of some study on aza-Claisen rearrangement, several N-cyano- and N-benzenesulfonyl-N-propargyl anilines[5] were prepared. The possibility of preparing the conjugated diynes by Eglinton coupling[6] was explored. In this paper, we report the synthesis of N-cyano- and N-benzenesulfonyl-N-propargylanilines (**2a-g**) which on treatment with $Cu(OAc)_2$ undergo Eglinton coupling reaction to give N,N-bispropargyl substituted anilines (**3a-g**).

The starting compounds N-cyano substituted anilines **1a-d** were prepared according to the literature procedure[5]. The N-benzenesulfonyl substituted anilines **1e-g** were prepared in good yield by treating substituted anilines with 1.2 equivalent of benzenesulfonyl chloride in the presence of 2*N* NaOH (cf. Scheme I).

Compounds **1a-d** on propargylation with 1 equivalent of propargyl bromide and anhyd. K_2CO_3 in dry acetonitrile gave N-cyano-N-propargyl substituted anilines **2a-d** (Scheme II). Similarly compounds **1e-g** on propargylation in dry acetone yielded N-benzenesulfonyl-N-propargyl substituted anilines **2e-g** (Scheme II).

Oxidative coupling of **2d** with copper(II) acetate, in dry pyridine and dry methanol for 1.5 hr afforded **3d** in quantitative yield (Scheme III). The IR spectrum of **3d** showed no peak at 3300 cm^{-1} confirming the absence of starting material and appearance of a sharp peak at 2220 cm^{-1} confirmed the presence of disubstituted $-C\equiv C-$ bond in the product. Its ^1H NMR spectrum showed a singlet at δ 4.8 for NR_1-CH_2 protons and at δ 7.1a ABq for aromatic protons. The absence of $O\equiv C-H$ proton at δ 2.1 confirmed the formation of **3d**. Its ^{13}C NMR displayed nine peaks (due to symmetry), at δ 73.6 and 68.9 for disubstituted acetylenic carbons confirming its



Compd	R_1	R_2
1e	H	CH_3
1f	H	OCH_3
1g	OCH_3	H

Scheme I

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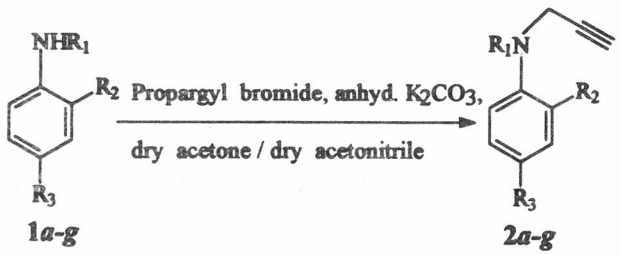
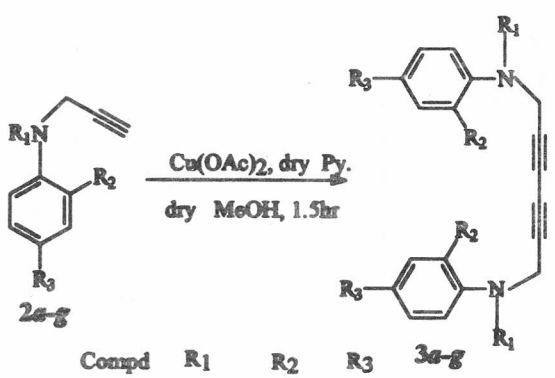


1*a-g* 2*a-g*

Compd	R_1	R_2	R_3
1*a*	CN,	H,	H
1*b*	CN,	H,	Cl
1*c*	CN,	H,	OCH_3
1*d*	CN,	H,	CH_3
1*e*	SO_2Ph,	H,	CH_3
1*f*	SO_2Ph,	H,	OCH_3
1*g*	SO_2Ph,	OCH_3,	H

Scheme II



2*a-g* 3*a-g*

Compd	R_1	R_2	R_3
3*a*	CN,	H,	H
3*b*	CN,	H,	Cl
3*c*	CN,	H,	OCH_3
3*d*	CN,	H,	CH_3
3*e*	SO_2Ph,	H,	CH_3
3*f*	SO_2Ph,	H,	OCH_3
3*g*	SO_2Ph,	OCH_3,	H

Scheme III

structure. Its mass spectrum showed a molecular ion peak at m/z 338. All the compounds reported herein gave satisfactory elemental analyses.

Presently, we are engaged in the synthesis and Eglinton coupling reaction of N,N-bispropargyl substituted anilines (**3**) which upon Eglinton coupling reaction will give structurally and biologically important heterocyclic molecular tweezers.

Experimental Section

All melting points and boiling points are uncorrected. IR spectra (ν_{max}, cm^{-1}) were recorded in $CHCl_3$ on a Perkin-Elmer 598 instrument; ^1H NMR (90 MHz) and ^{13}C NMR (22.5 MHz) spectra in $CDCl_3$ (chemical shifts are reported in δ, ppm) on a Varian EM-390 and JEOL FX 90Q instruments respectively with TMS as internal standard; and mass spectra on a JEOL JMS-DX 303 HF instrument. Elemental analysis was performed with a Perkin-Elmer 240B elemental analyser. Column chromatography was carried out with SiO_2 (ACME, 100-200 mesh). TLC was run over glass plates (7.5 cm × 2.5 cm size) coated with silica gel (ACME) of 0.25 mm thickness and visualised using either iodine or UV lamp. The organic extracts of crude products were dried over anhydrous $MgSO_4$. Solvents used were of reagent grade and were purified according to literature procedure[7].

General procedure for Eglinton coupling: Synthesis of 3a-d. A mixture of **2a** (1 g, 6.4 mmoles), copper(II) acetate (2.56 g, 12.8 mmoles) in dry pyridine (8 mL) and dry methanol (8 mL) was stirred for 1.5 hr at room temperature and then kept at 45-50°C for about 5 min. Methanol and pyridine were removed under reduced pressure. The residue was poured into ice water containing 1 *N* HCl to give the diyne **3a** as a solid. It was filtered and purified by passing through silica gel column using chloroform as eluent.

Compounds **3b-d** were prepared similarly from **2b-d**.

3a: Yield 75%; m.p. 150-52°C; TLC: R_f 0.4 ($CHCl_3$: MeOH; 8 : 2) (Found : C, 77.43; H, 4.13; N, 18.10. $C_{20}H_{14}N_4$ requires C, 77.40; H, 4.10; N, 18.07%); IR ($CHCl_3$): 2220 (disubstituted C≡C), 1590 (Aromatic); ^1H NMR ($CDCl_3$): δ 7.3 (m, 10H,, Ar-*H*), 4.5 (s, 4H, N-CH_2); Mass : m/z 310 (M^+).

3b: Yield 68%; m.p. 162-64°C; TLC: R_f 0.4 ($CHCl_3$: MeOH; 8 : 2) (Found : C, 63.32; H, 3.16; N, 14.75. $C_{20}H_{12}N_4Cl_2$ requires C, 63.33; H, 3.18; N, 14.77%); IR ($CHCl_3$): 2220 (disubstituted C≡C), 1590 (Aromatic); ^1H NMR ($CDCl_3$): δ 7.3 (m, 10H, Ar-*H*), 4.5 (s, 4H, N-CH_2); Mass : m/z 379 (M^+).

3c: Yield 72%; m.p. 151-53°C; TLC: R_f 0.4 ($CHCl_3$: MeOH; 8 : 2) (Found : C, 71.32; H, 4.86; N, 15.21. $C_{22}H_{18}N_4O_2$ requires C, 71.33; H, 4.89; N, 15.12%); IR ($CHCl_3$): 2220 (disubstituted C≡C), 1590 (Aromatic); ^1H NMR ($CDCl_3$): δ 6.9 (ABq, 8H, Ar-*H*), 4.3 (s, 4H, N-CH_2), 3.7 (s, 6H, dimethoxy); Mass : m/z 370 (M^+).

3d: Yield 82%; m.p. 156-58°C; TLC: R_f 0.4 ($CHCl_3$: MeOH; 8 : 2) (Found : C, 78.10; H,5.32; N, 16.56. $C_{22}H_{18}N_4$ requires C, 78.08; H, 5.36; N, 16.55%); IR ($CHCl_3$): 2220 (disubstituted C≡C), 1590 (Aromatic); ^1H NMR ($CDCl_3$): δ 7.1 (ABq, 8H, Ar-*H*), 4.8 (s, 4H, N-CH_2), 2.3 (s, 6H, dime-

thyl); ^{13}C NMR ($CDCl_3$): δ 136.1, 133.2, 129.9, 115.9, 112.5, 73.6, 68.9, 40.1, 19.8; Mass: m/z 338 (M^+).

General procedure for Eglinton coupling: Synthesis of 3e-g. A mixture of **2e** (1 g, 3.5 mmoles), copper(II) acetate (1.40, 7.0 mmoles) in dry pyridine (8 mL) and dry methanol (8 mL) was stirred for 1.5 hr at room temperature and then refluxed for about 2.5 hr. Methanol and pyridine were removed under reduced pressure. The residue was poured into ice water containing 1 *N* HCl to give the dyne **3e** as a solid. It was filtered and purified by passing through silica gel column using chloroform as eluent.

Compounds **3f-g** were prepared similarly from **2f-g**.

3e: Yield 75%; m.p. 136-38°C; TLC: R_f 0.4 ($CHCl_3$: MeOH; 8 : 2) (Found : C, 67.65; H, 4.86; N, 4.90. $C_{32}H_{28}N_2S_2O_4$ requires C, 67.58; H, 4.96; N, 4.92%); IR (KBr): 2220 (disubstituted C≡C), 1590 (Aromatic), 1340, 1150; ^1H NMR ($CDCl_3$): δ 7.4 (m, 10H, Ar-*H*), 7.0 (ABq, 8H, Ar-*H*), 4.4 (s, 4H, N-CH_2), 2.2 (s, 6H, dimethyl); ^{13}C NMR ($CDCl_3$): δ 138.5, 138.3, 130.1, 126.6, 73.4, 69.5, 41.9, 21.5; Mass: m/z 568 (M^+).

3f: Yield 80%; m.p. 137-39°C; TLC: R_f 0.4 ($CHCl_3$: MeOH, 8 : 2) (Found : C, 63.88; H, 4.79; N, 4.70. $C_{32}H_{28}N_2S_2O_6$ requires C, 63.98; H, 4.69; N, 4.66%); IR ($CHCl_3$): 2220 (disubstituted C≡C), 1610 (Aromatic), 1340, 1150; ^1H NMR ($CDCl_3$): δ 7.5 (m, 10H, Ar-*H*), 7.1 (ABq, 8H, Ar-*H*), 4.4 (s, 4H, N-CH_2), 3.8 (s, 6H, dimethoxy); Mass: m/z 600 (M^+).

3g: Yield 72%; m.p. 150-52°C; TLC: R_f 0.4 ($CHCl_3$: MeOH; 8 : 2) (Found : C, 63.79; H, 4.82; N, 4.75. $C_{32}H_{28}N_2S_2O_6$ requires C, 63.98; H, 4.69; N, 4.66%); IR (KBr): 2220 (disubstituted C≡C), 1590 (Aromatic), 1340, 1150; ^1H NMR ($CDCl_3$): δ 7.6 (m, 10H, Ar-*H*), 6.91 (m, 8H, Ar-*H*), 4.4 (s, 4H, N-CH_2), 3.36 (s, 6H, dimethoxy); Mass: m/z 600 (M^+).

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