Pergamon

Tetrahedron Letters, Vol. 38, No. 47, pp. 8199-8202, 1997
© 1997 Elsevier Science Ltd
All rights reserved. Printed in Great Britain
0040-4039/97 $17.00 + 0.00

PII: S0040-4039(97)10194-0

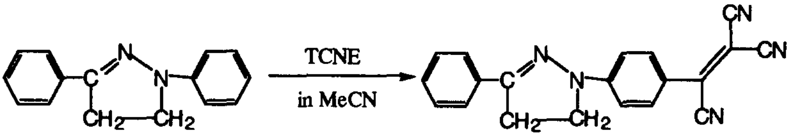
A Novel Synthesis of 1,2-Diazanaphthalenes

Yoshio Matsubara, Akihiro Horikawa and Zen-ichi Yoshida*

Department of Applied Chemistry, Faculty of Science and Engineering
Kinki University, 5-4-1, Kowakae, Higashi-Osaka 577, Japan

Abstract : A novel, one-step synthesis of 1,2-diazanaphthalenes from *p*-substituted acetophenone methylphenylhydrazones and TCNE is described.
© 1997 Elsevier Science Ltd.

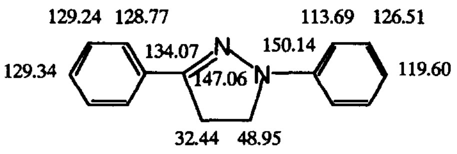
During the course of our investigation on the functionalization of pyrazolines, we found that 1,5-diphenylpyrazoline (**1**) reacted with tetracyanoethylene (TCNE, 1 equiv) in MeCN at room temperature to afford its *p*-tricyanovinyl derivative (**2**) having a beautiful, purple color.[1]



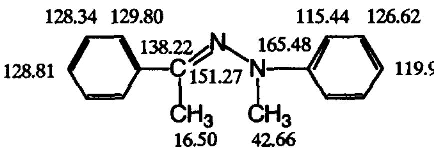
1 **2**

This finding prompted us to examine a similar reaction for acetophenone methylphenylhydrazone (**3a**) which corresponds to the ring-opened compound at the ethylene bridge of **1**, because ^{13}C NMR chemical shifts of the benzene rings for **1** and **3a** are very close to each other as shown in Table 1.

Table 1 ^{13}C NMR chemical shifts for **1** and **3a**



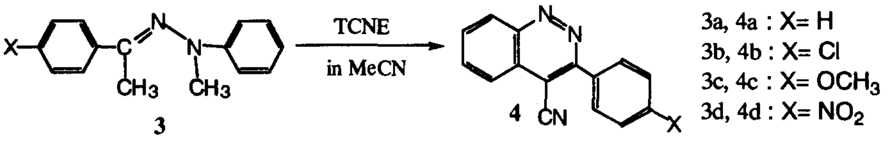
1



3a

Solvent : CD_3COCD_3 for **1** and $CDCl_3$ for **3a**

We tried to react **3a** (0.5 mmol) with TCNE(0.5 mmol) in MeCN(10 mL) at 25 °C for 5 days. Consequently, we found no formation of the expected *p*-tricyanovinyl derivative, but a predominant formation (~70%) of 4-cyano-3-phenyl-1,2-diazanaphthalene (**4a**) as shown in Figure 1.



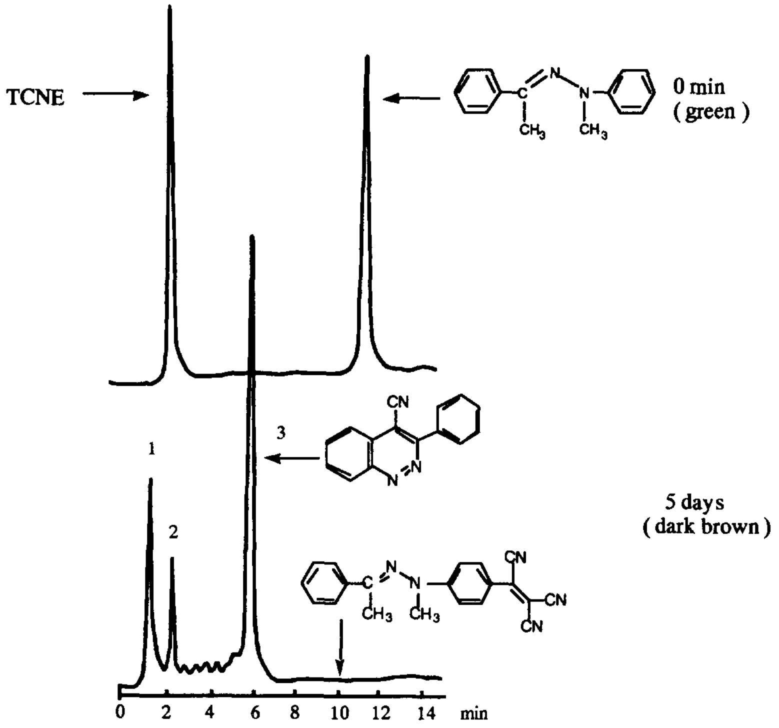


Figure 1 HPLC analysis of the reaction mixtures
(ODS / MeOH : H_2O = 8 : 2)

Upon mixing **3a** (in MeCN) and TCNE (in MeCN), the solution turned green because of the formation of a 1 : 1 charge transfer complex of **3a** (donor, IP 8.49 eV) with TCNE (acceptor, EA 2.3 eV).[2] After standing for five days, **3a** and TCNE were totally consumed, and **4a** was formed as the major product (peak 3). The compound of peak 2 was an intermediate convertible into **4a** by TCNE. The compound of peak 1 is a byproduct which is not identified at present.

When DMF was used instead of MeCN, the solution turned red. The red species was identified as the **3a** radical cation (λmax 419 and 553 nm) based on the UV-vis spectra of the **3a** radical cation generated by electrooxidation. Upon standing this red solution at 25°C for 1 day (or more), the tricyanovinyl derivative of **3a** was exclusively formed as reported.[3] However, no appreciable amount of **4a** was obtained even after 5 days.

The crucial factor for **4a** formation was the selection of solvents. Among the tested solvents (values in parentheses are the yields of **4a**) [MeCN(60%), EtCN(40%), benzene(15%), chloroform(5%), MeOH(0%), DMF(0%)], acetonitrile was best for **4a** formation.

Regarding reaction temperature, around 80°C was optimal. Higher temperature gave low yields due to side reactions. At lower temperatures, prolonged reaction times were required to achieve full conversion of the reactants.

Other important factors for **4a** formation were (1) molar ratio of **3a** to TCNE, and (2) concentration of the reactants: HPLC yield of **4a** was highest at the molar ratio of **3a** to TCNE = 1 : 1.5 and at the concentration of 0.5 mmol of **3a** in 5 - 10 mL of MeCN.

A typical example of the reaction conditions is as follows: A solution of **3a**(0,5 mmol) and TCNE(0.75 mmol) in 5 mL of MeCN was refluxed under an argon atmosphere for 8 h. After the solvent was evaporated under reduced pressure, the crude product was purified by column chromatography (silica gel / hexane) and subsequent recrystallization from methanol to give **4a** (pale yellow crystals, mp 169-170°C) in 60% isolated yield. The chemical structure of **4a** was elucidated as 4-cyano-3-phenyl-1,2-diazanaphthalene by IR and UV-vis spectra, elemental analysis, HRMS, and ^{1}H and ^{13}C resonance assignment from ^{1}H-^{1}H COSY and ^{1}H-^{13}C COSY.[4,5]

Other 1,2-diazanaphthalenes, for example, **4b** (mp 157-158°C)[6], **4c** (mp 200-203°C)[7] and **4d** (mp 240-241°C)[8] can be prepared using the above procedure in 30-50% yield.

TCNE is essential for this reaction. Tetracyanoquinodimethane (TCNQ, EA 2.8 eV) did not afford **4a** at all. Other cyano compounds like fumaronitrile, malononitrile and trimethylsilyl cyanide also did not serve as substitutes for TCNE. ^{1}H NMR analysis of the products arising from TCNE in the reaction at 25°C demonstrated the formation of a considerable amount of 2,2,3,3-tetracyanobutane[9] and no formation of 1,1,2,2-tetracyanoethane.[10] In the reaction at higher temperature (>50°C), 2,2,3,3-tetracyanobutane was not detected, presumably because of its decomposition to a methyldicyanomethyl radical ($\cdot$ $C(CN)_2CH_3$). Such sort of captodative radical is well known to be generated very easily.[11] The mechanism of the mysterious formation of **4** will be reported in due course.

In conclusion, a versatile and single-step synthesis of 1,2-diazanaphthalenes from readily available starting materials was discovered. Since the chemistry of 1,2-diazanaphthalenes has hitherto remained almost unexplored because of the lack of versatile synthetic methods, our finding will contribute to the study of 1,2-diazanaphthalenes, especially, of biologically active ones which are of current interest as immunomodulators and anxiolytics.

Acknowledgments: This work was supported in part by Research for Future Program (JSPS-RFTF 96R 11601) from JSPS. Z. Y. thanks Professor D. H. R. Barton for suggesting a possible mechanism for the present reaction.

References and Notes

1. Matsubara, Y.; Horikawa, A.; Tateishi, K.; Yoshida, Z. to be submitted.
2. Origin of the green color was proved to be due to the 1 : 1 charge transfer complex (λmax 802 nm, log ε 1.02) formation between **3a** and TCNE by continuous variation method using UV-vis spectroscopy for **3a** - TCNE system in benzene.
3. Tosi, G.; Bruni, P.; Cardellini, L.; Bocelli, G. *Gazz. Chim. Ital.* **1984**, *114*, 111.
4. Characteristic data for **4a** : IR (KBr pellet, cm^{-1}) 2225(ν_{CN}), UV-vis (MeOH, nm) λ max (log ε) 256(4.51), 357(3.45). HRMS(FAB) *m/z* 231.0812, Calcd for $C_{15}H_9N_3$ 231.0800. Anal. Calcd for $C_{15}H_9N_3$: C, 77.91; H, 3.92; N, 18.17 Found : C, 78.04; H, 4.02; N, 18.21. ^1H and ^{13}C resonance assignments from ^1H-^1H COSY and ^1H-^{13}C COSY: ^1H NMR($CDCl_3$) δ 7.63 d (2H, H_{ortho}), 7.65 d (1H, H_{para}), 8.18 m (2H, H_{meta}), 8.01 m (2H, H^5 and H^8), 8.27 m (1H, H^6), 8.90 m (1H, H^7); ^{13}C NMR($CDCl_3$) δ 124.62(phenyl without hydrogen), 129.01(C_{ortho}), 129.79(C_{meta}), 130.72(C_{para}), 104.76(C-4), 114.72(CN), 124.31(C-6), 130.88(C-7), 131.60(C-5), 134.17(C-8), 134.84(C-4a), 148.61(C-8a), 154.66(C-3).
5. The X-ray structure of **4a** determined by Prof. Kai (Osaka University) accords with this structure. Details will be published elsewhere.
6. Selected spectral data for **4b** : IR(KBr cm^{-1}) 2227(CN); ^1H NMR($CDCl_3$) δ 8.16 d (2H, H_{ortho}), 7.62 d (2H, H_{meta}), 8.03 m (2H, H^5 and H^8), 8.27 m (1H, H^6), 8.73 m(1H, H^7); ^{13}C NMR($CDCl_3$) δ 133.25(C_{ortho}), 124.33(phenyl without hydrogen), 129.38(C_{meta}), 137.33(C_{para}), 104.69(C-4), 114.54(CN), 130.92(C-5), 130.98(C-8), 131.84(C-6), 134.36(C-7), 134.36(C-4a), 148.69(C-8a), 153.38(C-3); HRMS: Found: *m/z* 265.0385, Calcd. for $C_{15}H_8N_3Cl$ 265.0408.
7. Selected spectral data for **4c** : IR(KBr cm^{-1}) 2222(CN); ^1H NMR($CDCl_3$) δ 3.93 s (3H, CH_3), 7.15 d (2H, H_{meta}), 8.21 d (2H, H_{ortho}), 7.97 m (2H, H^5 and H^8), 8.24 m (1H, H^6), 8.69 m(1H, H^7); ^{13}C NMR($CDCl_3$) δ 161.80(C_{para}), 115.10(C_{meta}), 127.21(C_{ortho}), 124.20(phenyl without hydrogen) 55.47(OCH_3), 103.41(C-4), 114.57(CN), 124.72(C-6), 130.40(C-4a), 130.86(C-7), 131.18(C-5), 134.06(C-8), 148.27(C-8a), 154.15(C-3); HRMS: Found: *m/z* 261.0893, Calcd. for $C_{16}H_{11}ON_3$ 261.0900.
8. Selected spectral data for **4d** : IR(KBr cm^{-1}) 2230(CN); ^1H NMR($CDCl_3$) δ 8.39 d (2H, H_{ortho}), 8.51 d (2H, H_{meta}), 8.10 m (2H, H^5 and H^8), 8.33 m (1H, H^6), 8.79 m(1H, H^7); ^{13}C NMR($CDCl_3$) δ 140.70(C_{para}), 124.17(C_{meta}), 130.88(C_{ortho}), 124.49(phenyl without hydrogen) 105.93(C-4), 114.16(CN), 124.49(C-6), 130.88(C-4a), 131.06(C-7), 132.64(C-5), 134.81(C-8), 149.11(C-8a), 152.28(C-3); HRMS: Found: *m/z* 276.0648, Calcd. for $C_{15}H_8O_2N_4$ 276.0650.
9. Hori, M.; Kataoka, T.; Shimizu, H.; Ohono, S. *J. Org. Chem.* **1980**, *45*, 2468.
10. Bagby, M.O.; Smith, Jr.,C. R.; Wolf, I. A. *J. Org. Chem.* **1969**, *34*, 2732.
11. For example, Vries, L. *J. Am. Chem. Soc.* **1978**, *100* , 926.

(*Received in Japan* 28 *June* 1997; *revised* 16 *September* 1997; *accepted* 17 *September* 1997)