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Pyrazine-N,N'-dioxide/tetracyanoethylene electron donor–acceptor bonding and the effect of donor steric demand and symmetry on the cocrystal assembly

Timothy J. Kucharski, Jerry R. Oxsher and Silas C. Blackstock*

Department of Chemistry, The University of Alabama, Tuscaloosa, AL 35487, United States

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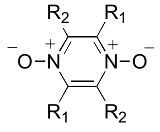
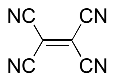
Abstract—The synthesis of a sterically hindered pyrazine dioxide electron donor (2,5-diethyl-3,6-dimethylpyrazine-N,N'-dioxide) and its cocrystallization with tetracyanoethylene (TCNE) are reported. The resulting DA assembly in the cocrystal is compared to that observed for a smaller pyrazine-N-oxide donor. Increased steric demand and lower donor symmetry yield a new, more complex two-dimensional DA assembly with slightly longer DA bonds and higher TCNE content in the cocrystal.

Electron donor–acceptor (DA) attractions (or bonds) can be used to build multi-component networks in crystals.[1–3] We have previously described the cocrystallization of tetramethylpyrazine-N,N'-dioxide, **1**, with tetracyanoethylene (TCNE), which is guided by N-oxide–TCNE DA bonding.[4] The resulting $(\mathbf{1})_2$TCNE cocrystals grow in two isomeric forms: a fast forming (kinetic) polymorph with 1D DA-bonded strands and a more slowly forming (thermodynamic) polymorph having a 2D (layered) DA bonded lattice.



1 R_1,R_2 = Me
2 R_1=Me, R_2=Et



TCNE

In this letter, we consider the effect of altering the steric demand and symmetry of the pyrazinedioxide (PDO) donor on its supramolecular chemistry with TCNE in solution and in the crystalline solid state. Dioxide **2** is prepared by OXONE oxygenation of the corresponding pyrazine,[5] which is generated from 3-aminopentane, as previously reported,[6] via a modified Neber rearrangement[7] and subsequent self-condensation/oxidation.[8]

Ether vapor diffusion into acetonitrile solutions of dioxide **2** affords colorless needle crystals whose structure has been determined by X-ray diffraction analysis.[9] The ethyl groups adopt an *anti* orientation with respect to the pyrazine ring plane in the crystal. Figures 1 and 2 show ORTEP and packing diagrams for crystalline **2**, respectively.

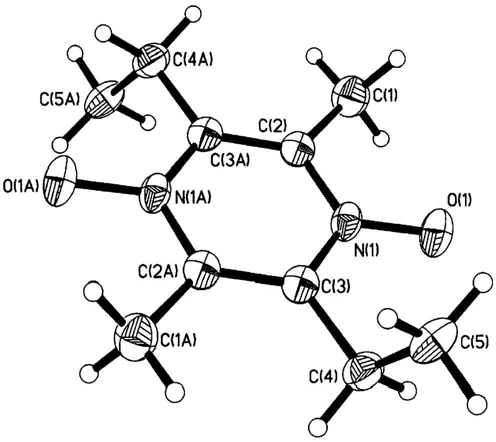


Figure 1. ORTEP diagram (50% ellipsoids) of **2**.

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* Corresponding author. Tel.: +1 205 348 0748; fax: +1 205 348 9104; e-mail: blackstock@ua.edu

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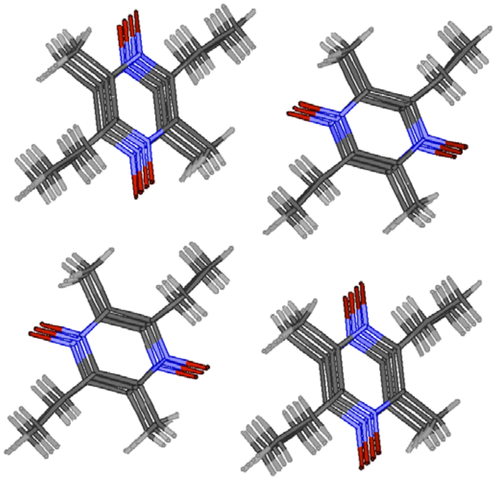

Figure 2. Packing diagram for crystalline **2**.

There are no especially short (less than van der Waals distance) intermolecular contacts in the crystal lattice of **2**. PDO units pack at van der Waals separation in columns with nested ethyl groups, as depicted in Figure 3. Plane-to-plane spacing of the PDO rings is ~3.4 Å; the pyrazine N atom lies directly above the methylene carbon of a neighboring PDO in the stack with an intermolecular C(4)′–N(1)O(1) distance of 3.47 Å and angle of 93°.

When **2** is mixed in solution with TCNE, a violet solution results. The UV–vis spectra of **2**, TCNE, and their mixture are shown in Figure 4. The charge-transfer (CT) absorption band for the DA complex occurs at $\lambda_m = 530$ nm. Benesi–Hildebrand analysis[10] of the CT band (in CH_2Cl_2 with excess TCNE) yields $\varepsilon(530\ \text{nm}) = 4.8(2) \times 10^3\ \text{M}^{-1}\ \text{cm}^{-1}$ and $K_{eq} = 2.1(1)$ for assumed 1:1 DA complexation.

Cooling of concentrated CH_2Cl_2 mixtures affords purple cocrystals whose X-ray diffraction structure has been determined.[11] Interestingly, the cocrystal is composed of 1:1 **2**:TCNE and the asymmetric unit of the (**2**)TCNE lattice contains, two unique half TCNE acceptors and two unique half PDO **2** donors, as illustrated in the ORTEP diagram shown in Figure 5.

A packing diagram of the cocrystal lattice reveals DA-bonded layers (2D networks) composed of closely contacted PDO **2** and TCNE units (Fig. 6), linked by a set of intermolecular NO···C DA bonds. The ethyl substituents of the donor flank the layer faces.

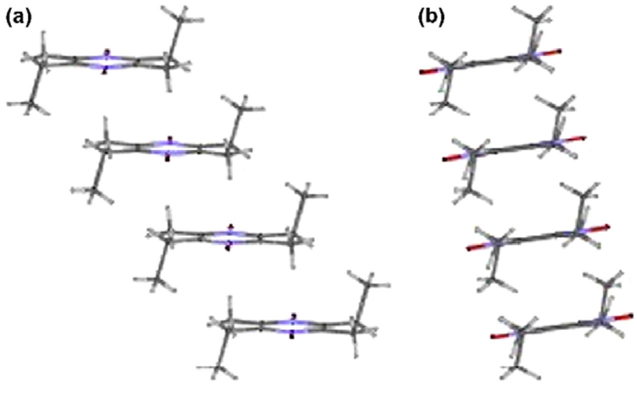

Figure 3. Orthogonal views of molecular stacks in crystalline **2**.

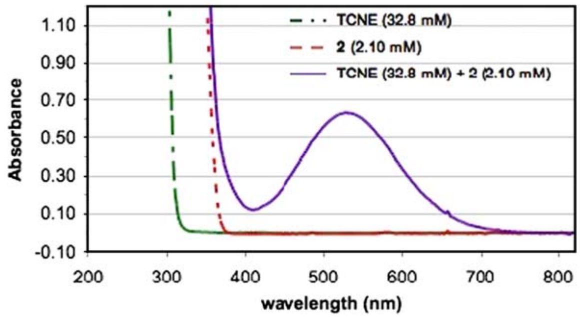

Figure 4. UV–vis spectrum of **2**, TCNE, and mixture in CH_2Cl_2.

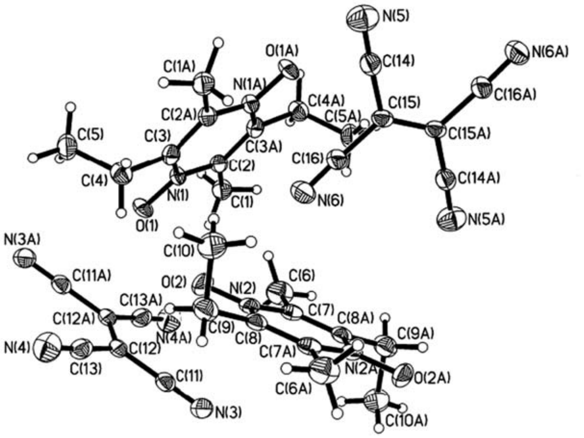

Figure 5. ORTEP (50% ellipsoids) diagram of (**2**)TCNE cocrystal.

The two unique donors and two unique acceptors in the crystal are each centered on a center of inversion symmetry. Figure 7 provides more detail of the 2D DA-bonded network. Intermolecular contacts of 2.84–3.02 Å are observed between the PDO oxygen atoms and the olefinic (and some cyano) carbon atoms of

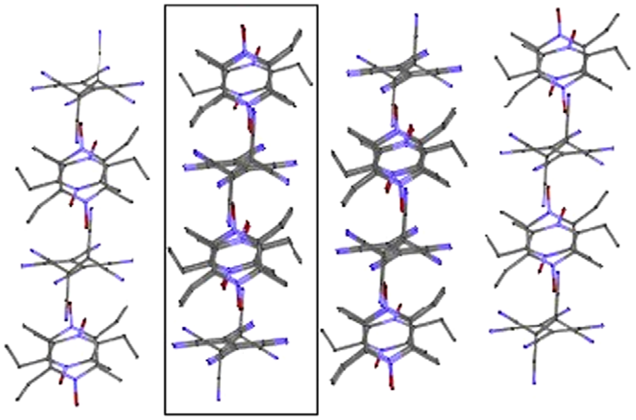

Figure 6. Packing diagram for (**2**)TCNE cocrystal showing DA-bonded layers (vertical).

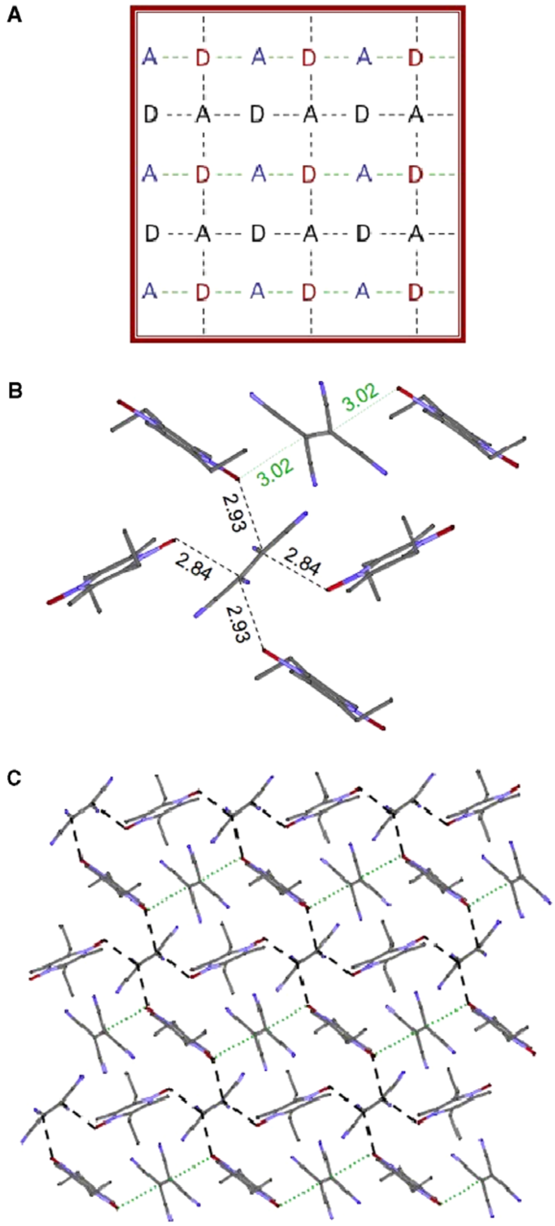

Figure 7. DA-bonded layer network of the (**2**)TCNE cocrystal. (a) DA linkage scheme, (b) DA contacts in Å and (c) layer structure.

TCNE. These contacts are 0.20–0.37 Å shorter than the sum of van der Waals radii and provide clear structural evidence of attractive *N*-oxide/TCNE DA bonding in the cocrystal. (Note: O···C van der Waals distance is 3.22 Å using Bondi's radii.)[12]

The complex nature of the **2**/TCNE DA array is consistent with its relative reluctance to form, compared to the case of the **1**/TCNE network, whose DA cocrystals grow rapidly and in high yield from cooled CH_2Cl_2 mixtures of moderate concentration. For **2**/TCNE CH_2Cl_2 mixtures, higher concentrations and much longer crystallization times are required to produce cocrystals which leave behind a still vividly colored solution, suggesting a higher solubility in CH_2Cl_2 of (**2**)TCNE than of (**1**)$_2$TCNE.

Comparison of the (**1**)$_2$TCNE and (**2**)TCNE lattice structures is noteworthy. There is a stoichiometric difference in the two cases and a difference in the asymmetric unit of the lattices. The red polymorph of (**1**)$_2$TCNE contains a 2D DA-bonded network (Fig. 8) similar to that observed for (**2**)TCNE, except that the latter lattice has 'opened up' enough to include a second TCNE moiety in the assembly at the 'starred' positions marked in Figure 8c. In both cocrystals, supramolecular 'rings' of 8 molecules (4D, 4A) fuse together within the layers, but in the ethyl-substituted PDO structure, the steric requirements of the ethyl group seem to open up the supramolecular D_4A_4 cycle enough for another TCNE to be incorporated in the network. The 'extra' TCNE in the network results in two distinct D and A units in this more complex DD′AA′ array. One donor and one acceptor are eta-4 linkers while the others are eta-2 linkers with respect to their complexation geometries within the lattice. While we can only speculate on the growth

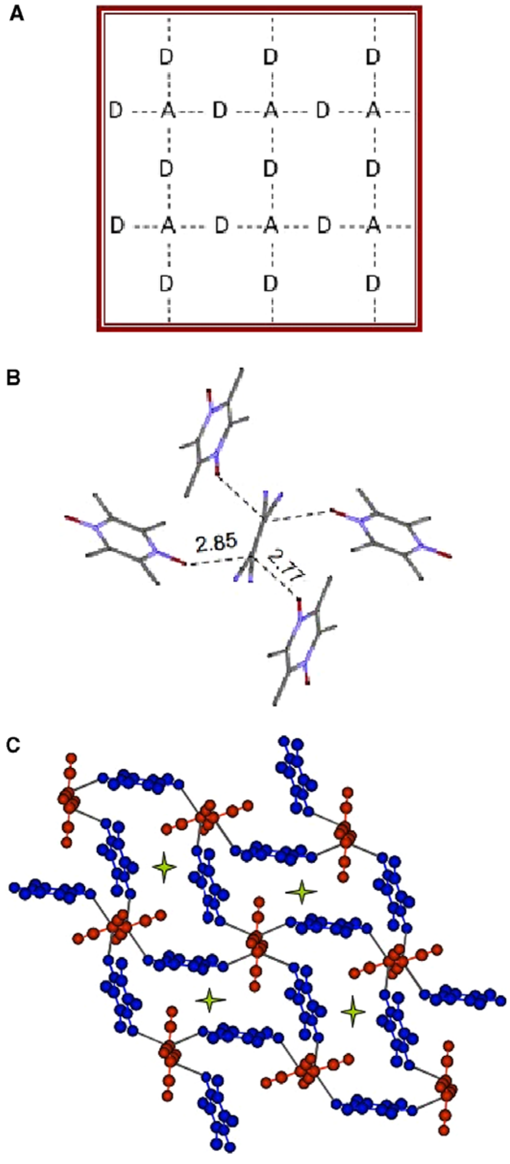

Figure 8. DA-bonded layer network of (**1**)$_2$TCNE cocrystal. (a) DA linkage scheme, (b) DA contacts in Å and (c) layer structure.

mechanism and the relative energetics of the DA assembly in (**2**)TCNE, we note that the intermolecular D–A contacts of the 'interstitial' eta-2 TCNE units are longer (and fewer) than those at the eta-4 TCNE groups, consistent with the interpretation that the ethyl group pocket in the array is promoting the incorporation of an 'extra' acceptor in what might otherwise prefer to be a D_2A network.

In conclusion, we have found that the steric change of ethyl for methyl substitution on pyrazinedioxide affects its aggregation with TCNE, such that a second unique TCNE unit is incorporated in the resulting DD′AA′ network layer of the more hindered donor. Otherwise, the basic DA networking pattern as previously observed in $(\mathbf{1})_2$TCNE crystals[4] is essentially preserved in (**2**)TCNE. The 2D networks observed in both cocrystals demonstrate the efficacy of *N*-oxide/TCNE bonding as a tool for guiding molecular assembly in the solid state.

Acknowledgments

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Supplementary data

Supplementary data associated with this article can be found, in the online version, at doi:10.1016/j.tetlet.2006.04.155.

References and notes

1. Some reviews of electron donor–acceptor complexation include: (a) Bent, H. A. *Chem. Rev.* **1968**, *68*, 587; (b) Mulliken, R. S.; Person, W. B. *Molecular Complexes: A Lecture and Reprint Volume*; Wiley-Interscience: New York, 1969; (c) Foster, R. *Organic Charge-Transfer Complexes*; Academic Press: New York, 1969; (d) Andrews, L. J.; Keefer, R. M. *Molecular Complexes in Organic Chemistry*; Holden-Day: San Francisco, 1964.
2. Some reviews of crystal engineering include: (a) *Crystal Design: Structure and Function (Perspectives in Supramolecular Chemistry)*; Desiraju, G. R., Ed.; Wiley: New York, 2003; (b) Desiraju, G. R. *Crystal Engineering, The Design of Organic Solids*; Elsevier: Amsterdam, 1989; (c) Gavezzotti, A. *Acc. Chem. Res.* **1994**, *27*, 309; (d) *The Crystal as a Supramolecular Entity. Perspectives in Supramolecular Chemistry*; Desiraju, G. R., Ed.; Wiley: New York, 1996; (e) Weber, E. *Top. Curr. Chem.* **1998**, *198*, 1.
3. For some examples of crystal engineering via electron donor–acceptor bonding, see: (a) Bertolasi, V.; Gilli, P.; Ferrara, V.; Gilli, G. *New J. Chem.* **2001**, *25*, 408; (b) Bosch, E.; Radford, R.; Barnes, C. L. *Org. Lett.* **2001**, *3*, 881; (c) Cardillo, P.; Corradi, E.; Lunghi, A.; Aldo Meille, S.; Messina, T. M.; Metrangolo, P.; Resnati, G. *Tetrahedron* **2000**, *56*, 5535; (d) McGee, B. J.; Sherwood, Lindsay J.; Greer, M. L.; Blackstock, S. C. *Org. Lett.* **2000**, *2*, 1181; (e) Bodige, S. G.; Selby, T. D.; McKay, S. E.; Blackstock, S. C. *Trans. Am. Cryst. Assoc.* **1998**, *33*, 135; (f) Greer, M. L.; Blackstock, S. C. *Mol. Cryst. Liq. Cryst.* **1998**, *313*, 55; (g) Greer, M. L.; Duncan, J. R.; Duff, J. L.; Blackstock, S. C. *Tetrahedron Lett.* **1997**, *38*, 7665; (h) Greer, M. L.; Blackstock, S. C. *J. Am. Chem. Soc.* **1997**, *119*, 11343; (i) Blackstock, S. C.; Poehling, K.; Greer, M. L. *J. Am. Chem. Soc.* **1995**, *117*, 6617.
4. Greer, M. L.; McGee, B. J.; Rogers, R. D.; Blackstock, S. C. *Angew. Chem., Int. Ed.* **1997**, *36*, 1864.
5. 2,5-diethyl-3,6-dimethylpyrazine-*N*,*N*′-dioxide **2**: To a solution of 2,5-diethyl-3,6-dimethylpyrazine (1.651 g, 10.00 mmol) in 10 mL dichloromethane was added a saturated solution of Oxone® (61.48 g, 100.0 mmol) in water (250 mL). The biphasic mixture was heated to 45 °C with vigorous stirring for 40 h. The mixture was cooled to room temperature and extracted with dichloromethane (10×50 mL). The organic phases were combined and dried over anhydrous K_2CO_3. The solvent was removed under reduced pressure to yield 1.730 g of a crude mixture of 1.8:1 *N*-oxide:di-*N*-oxide (64% conversion for **2**). The mono and dioxides are separated by recrystallization from CH_3CN/ether to afford colorless white needles of **2** (0.694 g, 35.4%); mp 163–165 °C; ^1H NMR (500 MHz, $CDCl_3$): δ 3.03 (q, 2H, $J = 7.5$ Hz), 2.55 (s, 3H), 1.25 (t, 3H, $J = 7.5$ Hz); ^{13}C NMR (125 MHz, $CDCl_3$): δ 146.54, 141.97, 21.18, 13.64, 10.12; HRMS (*m*/*z*): calcd for $C_{10}H_{16}N_2O_2$: 196.1212. Found: 196.1205 (−3.5 ppm).
6. Coffen, D. L.; Hengartner, U.; Katonak, D. A.; Mulligan, M. E.; Burdick, D. C.; Olson, G. L.; Todaro, L. J. *J. Org. Chem.* **1984**, *49*, 5109.
7. (a) Neber, P. W.; Burghard, A. *Justus Liebigs Ann. Chem.* **1932**, *493*, 281; (b) Vertappen, M. M. H.; Ariaans, G. J. A.; Zwanenburg, B. *J. Am. Chem. Soc.* **1996**, *118*, 8491.
8. Chiba, T.; Sakagami, H.; Murata, M.; Okimoto, M. *J. Org. Chem.* **1995**, *60*, 6764.
9. Crystal data for 2,5-diethyl-3,6-dimethylpyrazine-*N*,*N*′-dioxide **2**: The asymmetric unit is one-half molecule. Empirical formula, $C_{10}H_{16}N_2O_2$: formula weight, 196.25; colorless flat needles, crystal dimensions $0.30 \times 0.16 \times 0.08$ mm; monoclinic, $P2(1)/n$ (International Table No. 14); $a = 4.2965(9)$ Å, $b = 10.581(2)$ Å, $c = 11.040(2)$ Å; $\alpha = 90°$, $\beta = 96.589(4)°$, $\gamma = 90°$; $V = 498.59(18)$ Å^3; $Z = 2$; $D_{calcd} = 1.307$ g/cm^3; $F_{000} = 212$; λ (Mo K_α) = 0.71073 Å; $T = 173$ (2) K; data/restraints/parameters = 717/0/97; R_1 $[I > 2\sigma(I)] = 0.0372$, $wR^2 = 0.0877$, GOOF = 1.095. Detailed X-ray crystallographic data is available from the Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge CB2 1EZ UK (CCDC No. 602834).
10. (a) Benesi, H. A.; Hildebrand, J. H. *J. Am. Chem. Soc.* **1949**, *71*, 2703; (b) Andrews, L. J.; Keefer, R. M. *Molecular Complexes on Organic Chemistry*; Holden-Day: San Francisco, 1964; Chapter 4.
11. Crystal data for 2,5-diethyl-3,6-dimethylpyrazine-*N*,*N*′-dioxide **2**/TCNE cocrystal: The asymmetric unit is two half-molecules of **2** and two half-molecules of TCNE. Empirical formula, $C_{16}H_{16}N_6O_2$: formula weight, 324.35; dark purple rhomboids, crystal dimensions $0.90 \times 0.60 \times 0.15$ mm; triclinic, P-1 (International Table No. 2); $a = 9.602(2)$ Å, $b = 10.033(2)$ Å, $c = 10.457(2)$ Å; $\alpha = 111.194(3)°$, $\beta = 98.245(4)°$, $\gamma = 112.850(4)°$; $V = 816.969$ Å^3; $Z = 2$; $D_{calcd} = 1.319$ g/cm^3; $F_{000} = 340$; λ (Mo Kα) = 0.71073 Å; $T = 173$ (2) K; data/restraints/parameters = 2339/0/271; R_1 $[I > 2\sigma(I)] = 0.0583$, $wR^2 = 0.1065$, GOOF = 1.022. Detailed X-ray crystallographic data is available from the Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge CB2 1EZ UK (CCDC No. 602833).
12. (a) Bondi, A. *J. Phys. Chem.* **1964**, *68*, 441; (b) Rowland, R. S.; Taylor, R. *J. Phys. Chem.* **1996**, *100*, 7384.