DNA, giving the same monofunctional adduct **3a** as the parent drug MC. However, DMC, unlike the parent drug MC, is apparently not capable of formation of the cross-link adduct **4**. Evidently, expulsion of the C-10″ hydroxyl group of DMC, required for formation of **4**, via intermediate **9** would be much less favorable than expulsion of the C-10″ carbamate from MC (Scheme II). Lack of DNA-cross-linking ability of DMC has been noted by others previously in vitro[31] as well as in vivo.[29-31] It should be interesting to compare the conformational and functional effects of the two drugs on DNA, in light of their differential covalent effects as shown by the present report.

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Communications to the Editor

1,3-Bis(*m*-nitrophenyl)urea: An Exceptionally Good Complexing Agent for Proton Acceptors

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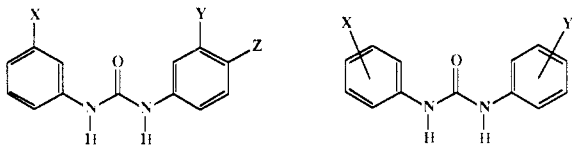
We have shown that intermolecular hydrogen bond patterns and molecular aggregate configurations of organic molecules can be controlled by the number and position of their hydrogen-bonding functional groups[1] since all the proton donors and acceptors are usually incorporated into the hydrogen bond network in the solid state.[2] Guest donors or acceptors are also incorporated if they compete with and displace the "normal" hydrogen bonding groups of the uncomplexed molecule. For example, triphenylphosphine oxide (TPPO), with one good proton acceptor (the phosphoryl group), complexes with amides, sulfonamides, and phenols and replaces the "normal" acceptor group of the host molecule.[3] This complexation process is a model for molecular recognition based on selective hydrogen bond interactions. It is also a useful way to design new solid-state materials since host molecules can be forced into many different solid-state environments by cocrystallizing them with different proton donor molecules.

Diaryl ureas contain one proton acceptor (the carbonyl group) and two N–H proton donors so their "normal" or expected hydrogen bond pattern is a chain of molecules with the urea carbonyl oxygen positioned between and bonding to both urea protons of a neighboring molecule, as found in the crystal structure of *N*,*N*′-diphenylurea.[4] We have found that guest acceptors will cocrystallize with 1,3-bis(*m*-nitrophenyl)urea, **1**, through hydrogen bonding between the N–H urea protons and the acceptor group of the guest which displaces the urea carbonyl groups in the hydrogen bond network. Even though urea carbonyl groups are reported to be reasonably good acceptors,[5] we find that nearly any acceptor is better than the carbonyl group in **1**. Compound **1** is a rare example of an organic molecule that behaves only as an intermolecular proton donor and not as an intermolecular proton acceptor.[6]



X	Y	Z
NO_2	NO_2	H
CF_3	CF_3	H
NO_2	H	H
NO_2	H	NO_2

X	Y
H	H
o-OCH_3	o-OCH_3
o-OCH_3	H
p-OCH_3	p-OCH_3
p-OCH_3	H
m-CH_3	m-CH_3
o-NO_2	o-NO_2
p-NO_2	p-NO_2

Figure 1. Diaryl ureas that form cocrystals with proton acceptors are shown in the left-hand column; those that do not, in the right-hand column.

Urea **1** has been reported previously to exist in three polymorphic forms (all obtained from ethanol solution).[7] When **1** is crystallized from solvents that are only proton acceptors, like acetone, THF, or DMSO, the crystals that form are cocrystal solvates of high quality, although they slowly turn cloudy when removed from the mother liquor. Likewise, when **1** is crystallized from solutions containing a third component which is a proton acceptor, like TPPO, *N*,*N*′-dimethyl-*p*-nitroaniline, or diethylene glycol, good quality cocrystals are also readily obtained.[8]

Through a combination of melting point, IR, NMR, and X-ray crystallographic techniques we have shown that **1** forms 1:1 cocrystals with a wide variety of proton acceptors to give complexes as shown.[9] The carbonyl stretching frequency of **1** varies from

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(4) Dannecker, W.; Kopf, J.; Rust, H. *Cryst. Struct. Commun.* **1979**, *8*, 429–432.

(5) Taft reports a value of 0.71 for β (the solvatochromic parameter for proton-accepting strength) compared to 0.55 for THF and 0.94 for triphenylphosphine oxide (Kamlet, M. J.; Abboud, J.-L. M.; Abraham, M. H.; Taft, R. W. *J. Org. Chem.* **1983**, *48*, 2877–2887).

(6) The nitro groups in **1** are potential proton acceptors (ref 1c), but they are not used as hydrogen bond acceptors in complexes we have studied. Other examples of compounds that are proton donors but not acceptors include the *m*-CF_3 and mono *m*-NO_2 analogues of **1**, 1,8-biphenylenediol (Hine, J.; Hahn, S.; Miles, D. E. *J. Org. Chem.* **1986**, *51*, 577–584), and fluorinated alcohols (ref 5).

(7) Groth, P. *An Introduction to Chemical Crystallography*; Wiley: New York, 1906; pp 29–30.

(8) The observation that crystal quality is better for cocrystals than for the pure substrate has been observed frequently in our lab (see, for example, ref 3b).

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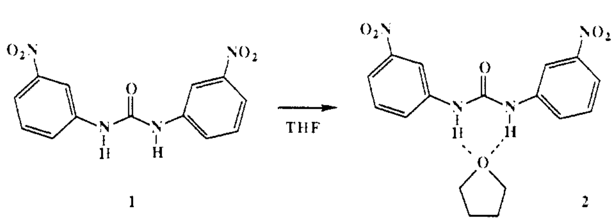

1 2

1660 cm^{-1} for one of its homogeneous polymorphs (where there is no guest molecule) to 1720 cm^{-1} for a 1:1 solid-state complex of **1** with THF. Single-crystal X-ray structures done on the THF cocrystal **2** and related cocrystals where the acceptor component is *N,N*-dimethyl-*p*-nitroaniline (**3**), diethyleneglycol (**4**), or triphenylphosphine oxide (**5**)[10] show that both urea protons chelate the guest acceptor group leaving the urea carbonyl free (except in **4** where one of the diethyleneglycol protons forms a hydrogen bond to the carbonyl group of **1**).

Surprisingly, *N,N'*-diphenylurea and other diaryl ureas with ortho- or para-substituted electron-withdrawing groups (EWG) or *m*-methyl groups do not form cocrystals even with the strong acceptors like triphenylphosphine oxide.[11] However, ureas substituted with *m*-CF_3 groups or with at least one *m*-NO_2 group will complex like **1**, Figure 1. The complexation properties of these compounds correlates with the presence of a strong EWG in the meta position.[12] The effect is not steric, since $-CF_3$ substituents work but $-CH_3$ groups do not, and it is not a resonance effect since ortho- and para-substituted EWGs do not induce cocrystal formation but meta-substituted EWGs do. There is evidence from the crystal structures of **2–5** that complexation occurs when the weakly acidic ortho-C-H protons lie near the carbonyl oxygen. In the four cocrystal structures of **1** reported here, the diaryl urea molecules are more nearly planar than in *N,N'*-diphenylurea (torsion angles of phenyl rings range from 2.3 to 9.1° in **2–4**, and are −19.1 and 23.5° in **5**, while the torsion angles of phenyl rings in *N,N'*-diphenylurea are ±43.0°[4]). The H---O distances in the C-H---O contacts on meta EWG rings is 2.23 to 2.29 Å (which are less than the 2.4 Å limit set by Taylor and Kennard for C-H---O hydrogen bonds),[13] compared to H···O of 2.49 and 2.66 Å in *N,N'*-diphenylurea. The C-H---O angles in **2–5** are 118 to 125°, and the protons are nearly in the same planes as the lone pairs of electrons in these structures.

Thus, in structures with meta EWGs the molecules become nearly planar, and the ortho- C-H protons lie as close as possible to the carbonyl group. The urea carbonyl group forms no intermolecular hydrogen bonds in these structures, so the N-H protons are free to bind to guest molecules. A possible explanation for the highly specific complexation behavior of **1** is that a weak C-H---O interaction takes place which drastically reduces the effective β-value of the carbonyl group.[5] Further studies are underway to clarify the nature of this interaction and its role in determining the complexation behavior of **1** and related compounds.

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(9) Acceptors that give cocrystals are as follows: tetrahydrofuran, diethyl ether, 1,4-dioxane, acetone, butanone, cyclohexanone, cyclopentanol, dimethyl sulfoxide, triphenylphosphineoxide, acetonitrile, diethyleneglycol, *p*-nitroaniline, *N,N*-dimethyl-*p*-nitroaniline, polyethyleneoxide.

(10) Unit cell parameters: **2** (THF), a = 9.586 (3) Å, b = 11.636 (4) Å, c = 8.289 (3), Å, α = 107.24 (3)°, β = 93.94 (3)°, γ = 86.73 (3)°, $P\bar{1}$, Z = 2; **3** (DMPNA), a = 20.002 (5) Å, b = 15.414 (5) Å, c = 7.165 (4) Å, β = 107.61 (4)°, C_2/c, Z = 4; **4** (DEG), a = 11.247 (6) Å, b = 12.029 (6) Å, c = 7.54 (1) Å, α = 103.98 (7)°, β = 102.30 (9)°, γ = 98.94 (4)°, $P\bar{1}$, Z = 2; **5** (TPPO), a = 12.37 (1) Å, b = 15.136 (6) Å, c = 8.311 (6) Å, α = 101.93 (4)°, β = 91.22 (6)°, γ = 110.94 (4)°, $P\bar{1}$, Z = 2. Complete crystallographic details will be presented elsewhere.

(11) An exception is 1,3-bis(*p*-nitro)phenyl urea which forms a cocrystal with DMSO. We think that the DMSO is not hydrogen-bonded to the urea protons, however, since the IR carbonyl frequency of the complex is only 5 cm^{-1} higher than in the uncomplexed crystals. Urea itself is also a good proton donor and will complex with many acceptor molecules. In these cocrystals, all four hydrogen bonds of urea are used as donors and the carbonyl oxygen is an acceptor site for one or two hydrogen bonds (see, for example: Gartland, G. L.; Craven, B. M. *Acta Crystallogr., Sect. B: Struct. Crystallogr. Cryst. Chem.* **1974**, *B30*, 980–987).

(12) Studies by Hart et al. have shown that dialkylureas that are substituted with trityl groups will form clathrates with various small organic molecules. Sometimes these guests form hydrogen bonds to the urea protons. It is presumed that the steric bulk of the trityl groups inhibits close packing of the urea hosts and promotes clathrate formation. Hart, H.; Lin, L.-T.; Goldberg, I. *Mol. Cryst. Liq. Cryst.* **1986**, *137*, 227–286, and references cited therein.

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Depth Sensitivity of Wetting: Monolayers of ω-Mercapto Ethers on Gold

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Wettability is a property of surfaces that is both theoretically and practically important.[2] We[3] and others[4] have shown qualitatively that the wettability of a solid is determined by the structure of its outermost few angstroms. A more quantitative knowledge of the influence on wetting of the depth of functional groups beneath the surface would be invaluable in understanding the intermolecular forces acting at interfaces.[5] Here we correlate the wettability of ordered monolayers of ω-mercapto ethers ($HS(CH_2)_{16}O(CH_2)_nCH_3$; n = 0–5)[6] adsorbed on gold with the depth of the polar ether functional group below the solid-liquid interface. Long-chain alkanethiols adsorb from solution onto gold surfaces and form monolayer films in which the hydrocarbon chains are densely packed, all-trans, and tilted about 30° from the normal to the surface.[7,9] Assuming a similar structure for monolayers formed from mercapto ethers (Figure 1), variation in the chain length, n, of the terminal alkyl group provides angstrom-scale control over the position of the polar ether group beneath the surface.

X-ray photoelectron spectroscopy (XPS) and external reflection infrared spectroscopy of these monolayers confirmed their composition. The C-H stretching modes in the infrared indicated crystalline packing in both the polymethylene backbones and the terminal O-alkyl chains.[8] Progressive attenuation of the O(1s)

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