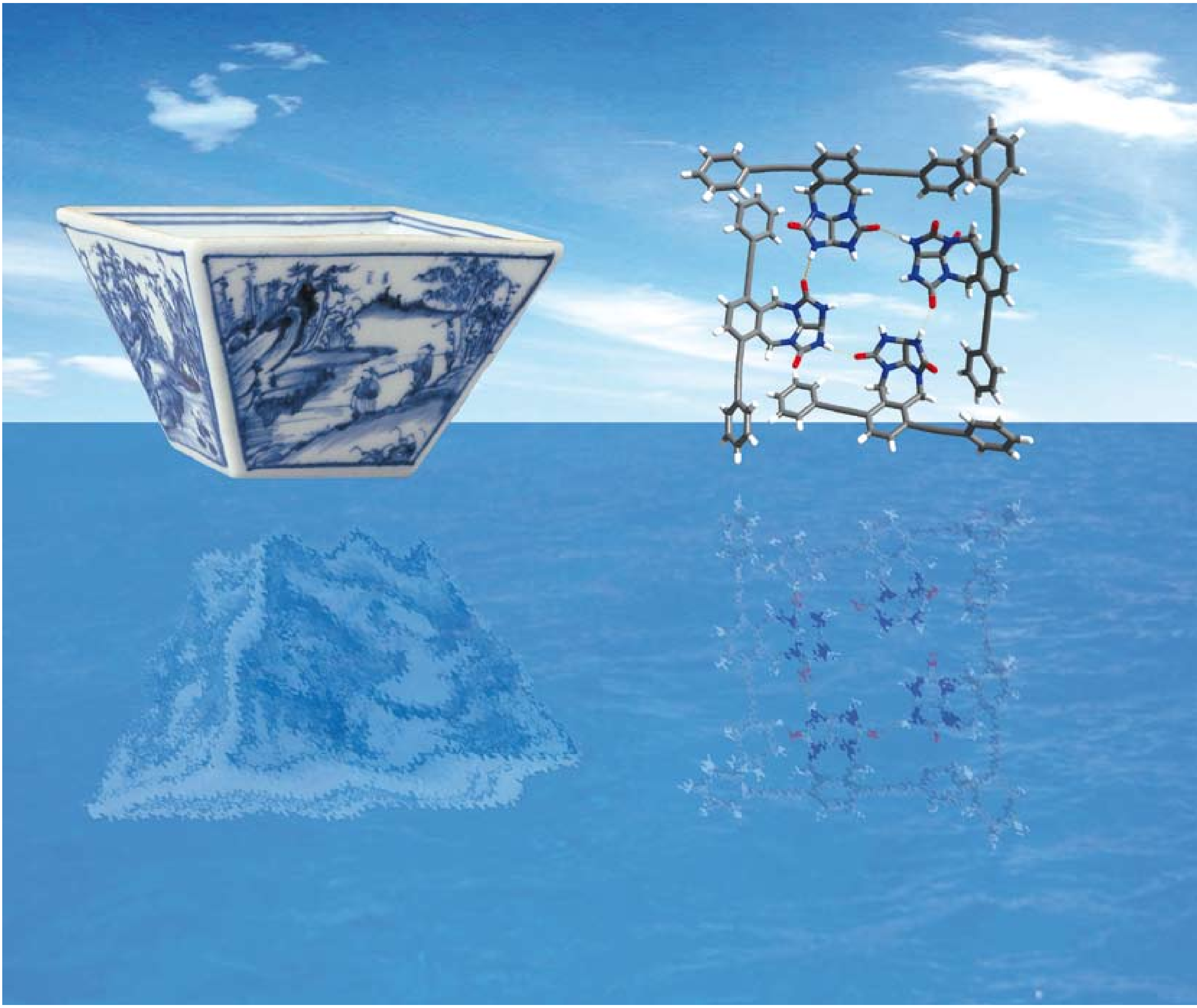
ChemComm

Chemical Communications

www.rsc.org/chemcomm

Number 27 | 21 July 2008 | Pages 3073–3204



ISSN 1359-7345

RSC Publishing

COMMUNICATION
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FEATURE ARTICLE
Matthias Tamm
Synthesis and reactivity of functionalized cycloheptatrienyl–cyclopentadienyl sandwich complexes

1359-7345(2008)27;1-#

Tetrameric molecular bowl assembled from glycoluril building blocks†

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Received (in Austin, TX, USA) 15th January 2008, Accepted 3rd March 2008
First published as an Advance Article on the web 4th April 2008
DOI: 10.1039/b800785c

Glycoluril derivative 1—whose bulky Ph–C$\equiv$C– substituents prevent formation of H-bonded tapes—undergoes solvent dependent assembly in the crystal; a tetrameric molecular bowl is formed by $R_4^4(24)$ H-bonding interactions from CH_2Cl_2 whereas DMF results in H-bond dimerization followed by oligomerization *via* C–H···π interactions.

The surge in interest in glycoluril as a covalent building block for supramolecular chemistry is fueled by the remarkable recognition properties of the cucurbit[*n*]uril family[1] of molecular containers and their application in areas as diverse as molecular machines, drug delivery, and fluorescent sensors.[2] This line of inquiry can be traced to the pioneering work of Mock, Nolte, and Rebek who used the glycoluril framework as a concave building block to construct non-covalent assemblies in homogeneous solution and other organized media.[3] As a result of its curved but rigid skeleton and its multiplicity of hydrogen bond donating (NH) and accepting (C═O) groups, glycoluril and its derivatives have recently emerged as a versatile building block for studies of crystal engineering.[4,5] For example, Wu and co-workers have described how substituents control the hierarchical organization of (chiral) molecular clips in the crystalline state.[6] In this paper, we describe how the confluence of rigidity and steric effects can be used to steer the amide supramolecular synthon away from its common 8-membered NH···O═C H-bonded interaction motif (known as an $R_2^2(8)$ motif) and toward a chiral tetrameric molecular bowl based on an H-bonded 24-membered ring (known as an $R_4^4(24)$ interaction motif).

An examination of the extended hydrogen bonding pattern displayed within the crystal structure of glycoluril (Fig. 1(a), R = H, Me)[7] reveals the existence of two different H-bonded tape motifs[4,8] (highlighted in blue and red) based on amide NH···O═C hydrogen bonding interactions. Accordingly, it occurred to us, and others, that glycoluril derivatives that contain two alkyl groups covalently attached to their (*cis* or *trans*) N-atoms would predictably form H-bonded tapes in the solid state.[4,5] For example, Fig. 1(b) shows the linear H-bonded tape that is formed from *cis*-dialkylated glycolurils *via* formation of 8-membered NH···O═C H-bonded rings. Given the robust nature of this supramolecular synthon we wondered whether it would be possible to steer the assembly toward less common interaction motifs. For this purpose, we designed compound **1** which contains two H-bonding ureidyl groups, an *o*-xylylene *cis*-capping unit, and most importantly two Ph–C$\equiv$C– substituents that were expected to sterically preclude tape formation (Fig. 1(b)). We prepared compound **1** by the reaction of diethoxycarbonyl glycoluril[9] and 2,3-bis(bromomethyl)-1,4-dibromobenzene[10] using *t*-BuOK as base in anhydrous DMSO, followed by the Sonogashira reaction[11] with ethynylbenzene (73% yield).[12]

We were fortunate to obtain single crystals of **1** as needles from a solution in CH_2Cl_2 and as plates from a solution in DMF.‡ Single-crystal data sets were recorded on a Smart Apex CCD area detector at 292(2) K. The crystal structure from CH_2Cl_2 was solved in the tetragonal $P4/n$ space group whereas the structure of the crystals obtained from DMF was solved in the triclinic $P\bar{1}$ space group. The molecular structure of **1** within both crystals is quite similar (Fig. 2) and no unusual structural features were observed.

We first examined the crystals obtained from DMF. Fig. 3 illustrates the important aspects of the packing of **1** within the crystal. Initially two molecules of **1** undergo dimerization due to the formation of two self-complementary N–H···O═C interactions (d = 2.09 Å and θ = 167.5°) to yield the $R_2^2(8)$ hydrogen bonding motif commonly observed in the crystal structures of amides. Rather than undergo further oligomerization by $R_2^2(8)$

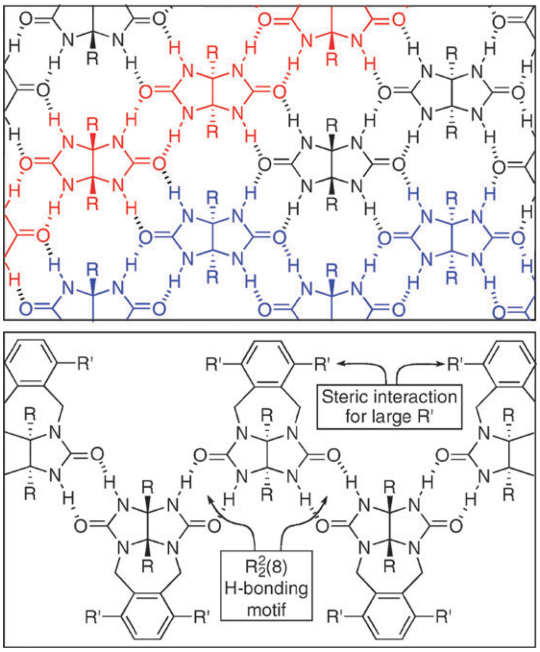

Fig. 1 (a) H-bonding pattern observed in the structures of glycolurils (R = H, Me). The red and blue highlighted regions corresponds to $R_2^2(8)$ H-bonded tapes; (b) H-bonded tape formed from *cis*-dialkylated glycolurils.

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† Electronic supplementary information (ESI) available: Synthesis and fluorescence emission for compound **1**. CCDC reference numbers 671165 and 671166. For ESI and crystallographic data in CIF or other electronic format see DOI: 10.1039/b800785c

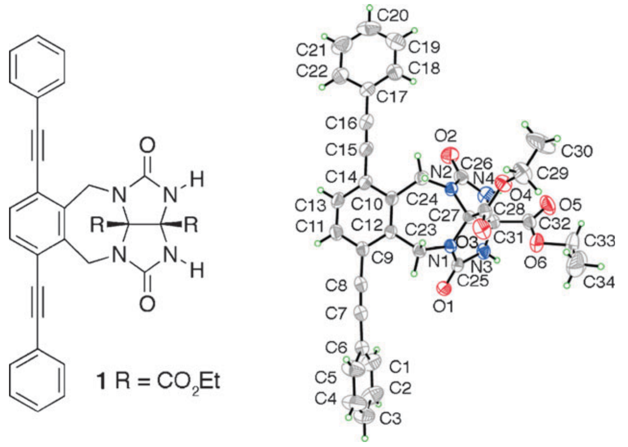

Fig. 2 Chemical structure (left) and ORTEP drawing and atom numbering (right) for **1**. Thermal ellipsoids are drawn at the 30% probability level. Solvent molecules have been omitted for clarity.

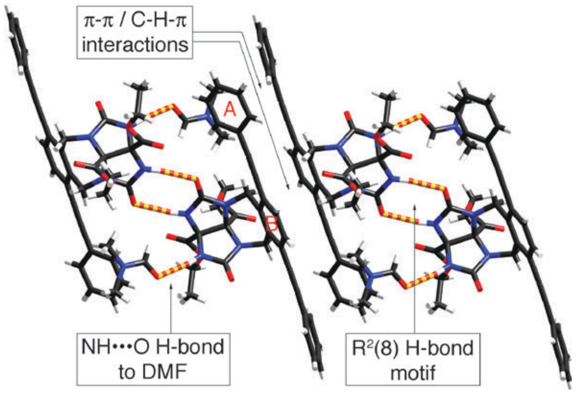

Fig. 3 View of the packing of **1** in the crystals obtained from DMF highlighting H-bonds, π–π and CH–π interactions. Color code: C, grey; H, white; N, blue; O, red; H-bonds, red-yellow striped. Centroids of aromatic rings A and B are labelled in red.

H-bonds—which is sterically precluded by the bulky Ph–C≡C– substituents—the remaining ureidyl NH H-bond donating groups are satisfied by H-bonding to the amide C=O of the DMF solvent (d = 1.98 Å and θ = 171.6°). These dimeric building blocks—with their extended π-surfaces—pack in a tape-like fashion due to favorable intermolecular interactions between these aromatic rings. For example, clear C–H···π interactions exist between the pairs of terminal aromatic rings (C1–H1···centroidA, d = 2.95 Å, θ = 128°) as well as between the bridging CH$_2$-groups of the capping *o*-xylylene ring and its neighbor (C23–H23B···centroidB, d = 2.81 Å, θ = 135°) aromatic ring. Compound **1** displays its commonly observed 8-membered ring H-bonding motif due to the presence of DMF as H-bond acceptor which caps the assembly at the stage of dimers which do not suffer extreme steric interactions.

Two further aspects of the structure of **1** from DMF deserve comment. First, although **1** is achiral its two ureidyl groups are enantiotopic and self-association can, therefore, lead to homochiral or heterochiral dimeric pairs. As observed previously for related structures,[4] heterochiral recognition is preferred which leads to the display of the CO$_2$Et groups on alternating faces of the dimeric pairs. Second, compound **1** is fluorescent in homogeneous solution and shows an emission band that ranges from 325 to 475 nm which exhibits two well-resolved maxima at 349 and 366 nm (Fig. S1, ESI†). In contrast, the supramolecular organization imposed by the powdered crystal results in a much broader emission band with a maximum at 441 nm (Fig. S2, ESI†). The substantial red shift (75–92 nm) observed and the loss of the vibronic structure of the emission band suggest that the emission of **1** is governed by excimers.

To attempt to access different H-bonding motifs we crystallized **1** from anhydrous CH$_2$Cl$_2$ that does not possess any good H-bond acceptor sites. Gratifyingly, we observed the formation of discrete tetramers by four NH···O=C H-bonds (d = 1.99 Å and θ = 154.5°) which defines a 24-membered H-bonding ring motif ($R^4_4(24)$) that is rarely observed in the crystal structures of amides (Fig. 4(a)).[8,13] These four NH···O=C hydrogen bonds seam together the lower rim of a molecular bowl. At the same time, reciprocal C–H···π interactions (C21–H21···centroidC, d = 2.98 Å, θ = 131°) between the eight C≡C–Ph groups define the upper rim of the tetrameric molecular bowl.[14,15] Additional N–H···O H-bonds (N4–H4A···O9) to water also play an important roles in connecting the four molecules of **1** to form a 3-D bowl-shaped structure. This square molecular bowl has dimensions of 12.2 × 12.2 × 5.0 Å for a bowl volume of 744 Å^3 which contains solvating H$_2$O molecules.

The organization of (**1**)$_4$ in the crystal is intriguing (Fig. 4(b)). For example, although **1** is achiral the tetrameric bowl (**1**)$_4$ is chiral due to the twisting of the Ph–C≡C– substituents with respect to one another during the formation of C–H···π interactions. In the crystal, these chiral bowls (**1**)$_4$ segregate themselves into homochiral stacks; the bowls of one handedness all point in the one direction and resemble a stack of badminton shuttlecocks (Fig. 4(c)). Stacks of (**1**)$_4$ of opposite chirality are oriented anti-parallel to one another. These stacks of bowls are held together by C–H···π interactions (C23–H23A···centroidD, d = 2.94 Å, θ = 132°) between the *o*-xylylene sidewalls of (**1**)$_4$ and bridging CH$_2$-group on the sidewall of adjacent bowls.

In summary, we reported the synthesis of **1**—which contains two large Ph–C≡C– substituents which sterically preclude H-bonded tape formation—and report the X-ray crystal structure of **1** as its DMF and H$_2$O solvates. DMF promotes dimerization of **1** by an 8-membered H-bonding ring motif ($R^2_2(8)$) and caps the dimer with additional NH···O=C H-bonds. In contrast, crystallization of **1** obtained from CH$_2$Cl$_2$ results in the formation of discrete chiral tetrameric molecular bowl (**1**)$_4$ by formation of a 24-membered H-bonded ring ($R^4_4(24)$) stabilized by CH···π interactions. The sizable cavity (12.2 × 12.2 × 5.0 Å) of (**1**)$_4$ is partially filled by solvating H$_2$O molecules. The study reinforces the importance of solvent choice in studies of crystal engineering particularly when rational design of less commonly observed interaction motifs are contemplated. Ongoing work aims to deepen and widen these chiral tetrameric molecular bowls by the use of larger aromatic walls, to enhance their stability in homogenous solution, and ultimately to use them as a controlled release or sensing component for advanced applications.

We gratefully acknowledge the financial support of this work by the National Natural Science Foundation of China (Grant Number 20672042) and the National Science Foundation (CHE-0615049).

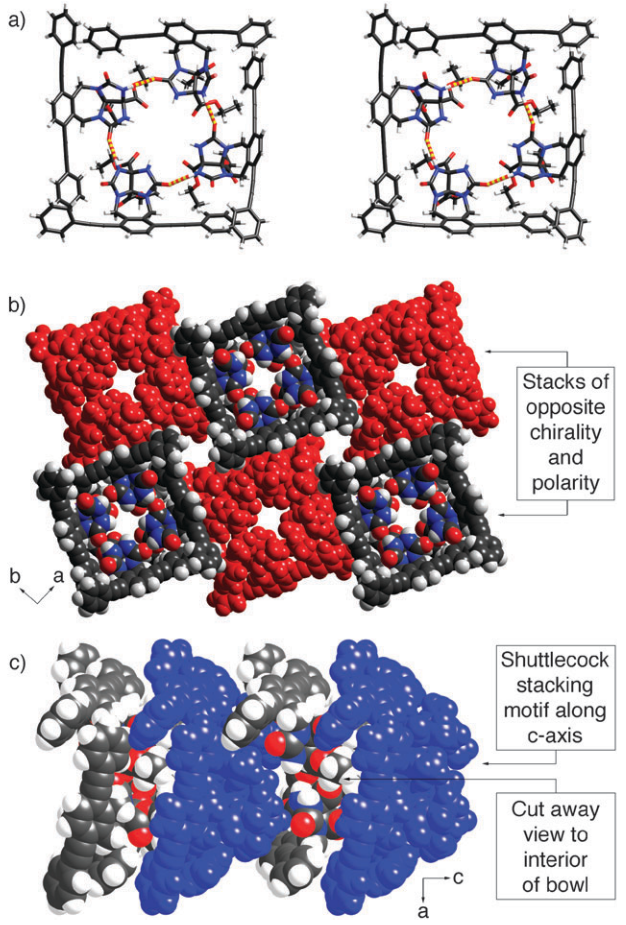

Fig. 4 (a) Details of the hydrogen bonds and C–H· · ·π interactions in the bowl-shaped structural unit of **1**. For the sake of clarity, H atoms not involved in these interactions have been omitted. (b) Space filling model of the packing of $(\mathbf{1})_4$ in the crystal. (c) Stacking of $(\mathbf{1})_4$ along the *c*-axis. Color code: C, grey; O, red; N, blue; H-bonds, red-yellow striped.

Notes and references

‡ *Crystallographic data*: Single crystals of $\mathbf{1}\cdot(H_2O)_{1.6}$ suitable for X-ray diffraction were grown from the anhydrous CH_2Cl_2. The intensities of 2844 independent reflections with $I > 2\sigma(I)$ were measured on a Bruker Smart Apex CCD area-detector diffractometer with Mo-Kα radiation ($\lambda = 0.71073$ Å). The structure was solved by direct methods and refined on F^2 using SHELXL-97. All the non-hydrogen atoms were refined anisotropically. Carbon bound H-atoms were located at the geometrical positions whereas H-atoms bonded to nitrogen were found from the difference Fourier maps with two constraints of N–H = 0.86(1) Å and thermal parameters of $U_{\mathrm{iso}}(H) = 1.2U_{\mathrm{eq}}(N)$. During the refinement, five separate larger residual peaks (within 1.2–2.0 e Å^{-3}) were crystallographically assigned to water molecules. One was located at the general position, two lying on the 4-fold axis and the other two on the 2-fold axis in space group $P4/n$. Further refinement results in several short contacts between them. So the contribution of the solvent molecules to the diffraction pattern was subtracted using the SQUEEZE procedure of PLATON. The result indicated that the solvent-accessible void in the unit cell has a volume of 799.8 Å^3 (consisting of about 12.3% of the crystal volume, equally distributed across four cavities). The residual electron density count amounted to 134 e per unit cell, corresponding to nearly 13 molecules of H_2O (the content of each of the four cavities per unit cell being equivalent about 3.2 molecules of H_2O, *i.e.* every molecule of **1** being distributed with 1.6 water molecules. *Crystal data* for $\mathbf{1}\cdot(H_2O)_{1.6}$: $C_{34}H_{31.2}N_4O_{7.6}$, M_r = 617.40, tetragonal, space group $P4/n$, a = 27.2293(7), b = 27.2293(7), c = 8.7855(4) Å, Z = 8, V = 6513.9(4) Å^3, D_c = 1.200 g cm^{-3}, μ = 0.084 mm^{-1}, $\theta_{\max}$ = 25.00°, $F(000)$ = 2592, reflections collected/unique, 61 089/5726 (R_{int} = 0.1657), final R indices [$I > 2\sigma(I)$] R_1 = 0.0685, wR_2 = 0.1603, R indices (all data) R_1 = 0.1366, wR_2 = 0.1810, GOF = 0.927 for all data. CCDC 671165 and 671166 for $\mathbf{1}\cdot(H_2O)_{1.6}$ and $\mathbf{1}\cdot$DMF, respectively.

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12. Compound **1**: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.65–7.36 (m, 12H), 6.17 (s, 2H), 5.83 (d, J = 16.0, 2H), 4.35 (d, J = 16.0, 2H), 4.29 (q, J = 6.8, 2H), 4.16 (q, J = 6.8, 2H), 1.33 (t, J = 6.8, 3H), 1.21 (t, J = 6.8, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): 165.9, 165.8, 157.2, 138.6, 131.7, 131.4, 128.6, 128.4, 123.5, 122.8, 95.5, 87.0, 82.6, 73.7, 63.4, 63.2, 41.8, 14.0, 13.7. MS (ESI): m/z 589 ([M + H]$^+$), 611 ([M + Na]$^+$) (calc. 588.20).
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