Structural Assembly of Rigid Hydroxycarboxylic Acid Frameworks –
Solid State Structures of Two Substituted 6-Hydroxy-trans-3-hexenoic Acids

Martin Berlekamp, Gerhard Erker*, Roland Fröhlich
Organisch-Chemisches Institut der Universität Münster, Corrensstraße 40,
D-48149 Münster, Germany
Z. Naturforsch. 51b, 1649–1654 (1996); received May 29, 1996
Crystal Engineering, Structural Networks, Staple Structures, Hydrogen Bonding,
Template Synthesis

5-(1-Hydroxy-cyclohexyl)-trans-3-pentenoic acid (2a) and 5-(2-hydroxy-2-indanyl)-trans-3-
pentenoic acid (2b) both exhibit associated structures in the solid state that contain strictly
alternating repetitive -OH/HO2C- hydrogen bonded arrays. The (2a)ₙ structure is helical,
whereas the association of 2b leads to a three dimensional assembly of tube-like (2b)ₙ structures. In contrast, the related sterically shielded 6,6-diphenyl-6-hydroxy-trans-3-hexenoic acid
(2c) exhibits only a conventional carboxylic acid dimer structure in the solid state.

Introduction

It is an interesting task to search for specific
rules of assembling simple organic molecules by
multiple hydrogen bonding to form organic solid
state systems [1]. This may lead to an advanced
crystal engineering of novel organic chemistry
based materials [2] and could possibly open new
designs to ways of designing organic catalyst systems [3]. In
this context we have investigated the solid state
structural chemistry of a variety of 6,6-disubstituted
6-hydroxy-trans-3-hexenoic acids [4]. These
are systems that contain two functional groups of
hydrogen bonding potential that are strictly sepa-
rated from each other by the rigid trans-alkene
spacer. Therefore, such monomeric building
blocks assemble intermolecularly by forming re-
petitive -OH/HO2C- hydrogen bond linkages
when crystallized [5]. It has turned out that the
specific supramolecular structural type is very sen-
sitively dependent on the nature of the substitu-
ents at the 6-position of the hydroxycarboxylic
acid chain. Choosing the right substitution pattern thus
allows for an easy way to control the overall prop-
erties of the structural assemblies derived from
these organic molecules in the solid state.

As a typical example, the 5-(1-hydroxy-cyclo-
pentyl)- and -(3-cyclopentenyl)-trans-3-pentenoic
acids 1a-1c all form ribbon-like assemblies in the
solid state, exhibiting cyclic 12-membered ring ar-
rays of alternating -OH/-CO₂H/-OH/-CO₂H func-
tional groups (see Scheme 1) [4,6]. We have now
found that small specific alterations of the cyclic
substituents at the end of the hydroxycarboxylic
acid chain are sufficient to change this cyclic
pattern of hydrogen bonds to two different types of
related linear (-OH/-CO₂H)_n assemblies. For
each of these two structural patterns a specific ex-
ample is presented and depicted in this article.

Results and Discussion

The specific examples looked at in this study are the ε-hydroxy-β,γ-unsaturated carboxylic acids 2a
and 2b. Both were prepared by means of an orga-
nometallic template reaction in the course of
which a ketone (here cyclohexanone or 2-inda-
none, respectively) were CC-coupled with butadiene and a CO₂-equivalent at the bis(cyclopentadienyl)zirconium unit [4,7]. For this purpose (butadiene)zirconocene (3) [8] was treated with hexacarbontungsten to give 4 which then in turn was reacted with cyclohexanone to give the nine-membered metallacycle 5, isolated in 95% yield. Subsequently, pyridine-N-oxide was added, then water. Conventional workup of the reaction mixture furnished 5-(1-hydroxycyclohexyl)-trans-3-pentenoic acid (2a) in 59% yield. 5-(2-Hydroxy-2-indanyl)-trans-3-pentenoic acid (2b) was obtained analogously from coupling 2-indanone with (butadiene)zirconocene and W(CO)₆, followed by oxidative hydrolysis, as was recently described by us in the literature [4] (see Scheme 2).

\[
\begin{array}{c}
\text{(butadiene)zirconocene (3)} \xrightarrow{\text{W(CO)₆}} \text{(butadiene)zirconocene (4)} \\
\end{array}
\]

Scheme 2.

Single crystals of 2a were obtained from pentane. The X-ray crystal structure analysis of 2a confirms the presence of a trans-configured CC-double bond (C3-C4 1.326(9) Å). The hydroxy group is located at C6. In the crystal it occupies an equatorial position at the cyclohexyl chair. It is the intermolecular assembly of the 2a monomers in the solid state that makes this hydroxycarboxylic acid so remarkable. A schematic view of the regular orientation of monomeric building blocks to form this assembly is depicted in Fig. 1.

It can be seen that this assembly has led to an organized structure that exhibits staples of cyclohexyl ring systems. Also the pentenoic acid side chains have become oriented in a nicely parallel arrangement. The monomeric units of 2a are held together in this structural orientation by strong intermolecular hydrogen bonds. The hydrogen bond pattern shows a strict alternation of the alcohol -OH functions and the -CO₂H groups. The specific hydrogen bonding pattern can best be visualized by formally constructing a pathway that leads the viewer through the structure as it is depicted in Fig. 1. The Figure shows a section of the crystal structure that contains three layers of individual molecules in the macroscopic assembly. Let us start at the south-west corner of the picture. The alcoholic -OH group at the top layer cyclohexyl ring (molecule A) is hydrogen bonded to a carboxylic acid of the second layer of the adjacent south-east staple (molecule B). This carboxylic acid function is then connected by a hydrogen bond to the cyclohexyl -OH of the next molecule (molecule C, located in the north-east section of the drawing) within the same layer. This -OH (of molecule C) then binds to the carboxylic C=O of molecule D, also located in the second layer (central position in Fig. 1), whose carboxylic -OH then binds to the cyclohexyl -OH of molecule A’ (located northwest); then this pattern is continued infinitely in a symmetry equivalent manner. 2a thus forms a heli-
cal suprastructure in the crystal. In this case the chiral organization results in a spontaneous resolution of the (2a) arrays (acentric space group P2\textsubscript{1}2\textsubscript{1}2\textsubscript{1}); thus only one helical arrangement (M) is observed in the investigated crystal (see Fig. 1).

The hydroxyhexenoic acid 2b also forms an organized structure in the solid state where the intermolecular array of hydrogen bonds leads to an infinitely extended suprastructure. Again, there is a strict alternation of -OH and -CO\textsubscript{2}H functional groups linked together. However, in 2b this leads to a very different overall structural type as compared to 2a (and also very different from 1). The -OH/-CO\textsubscript{2}H/-OH/-CO\textsubscript{2}H-- linkage is arranged in a pair of almost coplanar subunits, which are interlinked by covalent hydrocarbyl bridges of the hexenoic acid frameworks. This bonding situation is illustrated in Fig. 2 that exhibits a characteristic section of the overall suprastructure, containing two pairs of 2b entities. It shows that the alcoholic -OH group of molecule C is hydrogen bonded to the hydrogen bond acceptor C=O of the carboxylic acid function of molecule D. Complementary to that the -OH group of molecule D is hydrogen bonded to the -CO\textsubscript{2}H group of molecule C. The latter is then linked with the alcoholic -OH function of molecule A, that again is hydrogen bonded with the molecule B -CO\textsubscript{2}H group and so forth.

Fig. 3 shows that this special pattern of intermolecular hydrogen bond interlinkages results in the formation of a channel type structure. The individual channels are formed by the cross-linking of the substituted 6-hydroxy-trans-3-hexenoic acid units. Each channel is composed of two sides of symmetry equivalent infinite -CO\textsubscript{2}H/-OH chains that are oriented parallel to each other. The top and bottom of the channels is then made up of the hydrocarbyl frameworks of the molecular 2b entities. In this arrangement the 2-indanyl moieties are oriented away from the central channel structures and oriented parallel to the hydrocarbyl top and bottom sections of the channels. This leads to the formation of individual channel structures that are all oriented parallel to each other to make up the overall crystal structure. In this arrangement the annulated arene groups of the indanyl side groups become oriented in close to parallel pairwise stacks as is seen in Fig. 3.

For a comparison, we have also carried out the X-ray crystal structure analysis of 6,6-diphenyl-6-hydroxy-trans-3-hexenoic acid 2c. This compound had been prepared previously by a template synthesis, analogously as depicted in Scheme 2, starting from benzophenone. In this case the alcoholic -OH group is nicely tucked in a hydrocarbyl niche, made up by the bulky phenyl substituents and the hydrocarbon chain. This sterical shielding prevents the 6-OH group from becoming involved in the hydrogen bonding pattern. Consequently, compound 2c only exhibits the normal carboxylic acid dimer structure [9].

This study shows that the actually assembled supramolecular structure of the differently substituted 6-hydroxy-trans-3-hexenoic acids 2 depends very much on the substituent pattern that was chosen. It will be investigated whether the different types of supramolecular structural assemblies will exhibit different characteristic physical properties [10] that many eventually lead to the design of novel organic solid state materials.

**Experimental Section**

The synthesis of 2b and 2c had previously been described by us[4,7b]. Single crystals for the X-ray crystal structure determination were obtained from pentane at +4°C (2b) or toluene at ambient temperature (2c). For additional general informa-
tion including a listing of instrumentation used for physical characterization see ref. 4 and 7a,b.

Reaction of 4 with cyclohexanone, formation of 5

14.9 g (23.7 mmol) of 4 were suspended in 300 ml of toluene. Cyclohexanone (2.36 g, 24.0 mmol) was added and the mixture stirred for 8h at room temperature. A solid residue was removed by filtration, then the solvent was evaporated from the clear filtrate in vacuo. The remaining yellow solid was washed with pentane (2 x 50 ml) and dried in vacuo to yield 16.4 g (95%) of 5. Crystals of 5 were obtained at -18°C (2d) from toluene, m.p. 190°C (decomp.). $^1$H NMR (CDCl$_3$, 200 MHz): $\delta$ 6.32, 6.24 (s, each 5H, Cp), 5.1–4.8 (m, 2H, CH=CH), 4.56 (dd, $^2$J = 18.1 Hz, $^3$J = 3.3 Hz, 1H) and 2.96 (dd, $^2$J = 18.1 Hz, $^3$J = 9.7 Hz, 1H, C(carbene)-CH$_2$), 2.43 (m, 1H), 1.8–1.3 (m, 11H, CH$_2$). $^{13}$C NMR (CDCl$_3$, 50 MHz): $\delta$ 332.1 (carbene-C), 204.8 (trans-CO), 199.6 (cis-CO), 132.7, 126.9 (CH=CH), 113.3, 113.2 (Cp), 85.7 (quart. C), 71.7 (carbene-CH$_2$), 45.6 (=CH-CH$_2$), 41.4, 36.8, 25.8, 23.3, 23.0 (CH$_2$). IR (KBr): $\tilde{\nu}$ = 2058, 1953, 1925, 1899 cm$^{-1}$ (CO).

Analysis for C$_{26}$H$_{26}$O$_7$WZr (725.6)
Calcd C 43.04 H 3.61%,
Found C 42.97 H 3.69%.

$(3E)$-5-(1-Hydroxycyclohexyl)-3-pentenoic acid 2a

31.8 ml of a 0.63 M pyridine-N-oxide solution (20.2 mmol) in THF was added to a solution of 14.6 g (30.1 mmol) of 5 in 300 ml of THF, then 0.73 ml of water was added. The mixture was stirred for 2.5h at room temperature, then an additional 2 ml portion of water was added and the solvent removed in vacuo. The residue was suspended in 500 ml of ether and the product extracted with saturated aqueous potassium carbonate solution (4 x 70 ml). The combined aqueous extracts were washed with ether (3 x 70 ml) and then acidified with conc. aqueous HCl to pH 1. The product was extracted with ether (5 x 100 ml), the combined organic phases were washed with brine (3 x 10 ml) and water (3 x 10 ml) and dried over magnesium sulfate. The solvent was then removed in vacuo to yield 2a as an oil (2.34 g, 59%), that was solified in pentane at -30°C, m.p. 26°C. $^1$H NMR (CDCl$_3$, 200 MHz): $\delta$ 6.4 (br. s, 2H, OH), 5.63 (m, 2H, CH=...
Table I. Details of the X-ray crystal structure analyses of 2a, 2b, and 2c.

Table II. Selected bond lengths (Å) and angles (°) for 2a, 2b, and 2c.

Fig. 5. Projections of the monomeric units of 2a and 2b in the crystal with atom numbering scheme.

Acknowledgements

Financial support from the Fonds der Chemischen Industrie, the Wissenschaftsministerium des Landes Nordrhein-Westfalen, and the Krupp-Stiftung is gratefully acknowledged.


