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Molecular Complexes of Phenols with Dicyclohexylamine

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Abstract—The Mannich reaction of 2,4-di-*tert*-butylphenol with dicyclohexylamine was found to involve formation of a stable 1:1 molecular complex between the phenol and amine. The complex does not change on melting, sublimation, and chromatography on silica gel. Its structure was determined by X-ray analysis. Stable 1:1 complexes of dicyclohexylamine with a series of substituted phenols were synthesized; exceptions were 2,6-disubstituted phenols with bulky substituents.

Phenol version of the Mannich reaction, i.e., *ortho*-aminomethylation by the action of formaldehyde and secondary amine in the system 2,4-di-*tert*-butyl-phenol–CH_2O–HNR_2, occurs under mild conditions and yields the corresponding Mannich bases with various substituents on the nitrogen atom (Scheme 1).

Scheme 1.
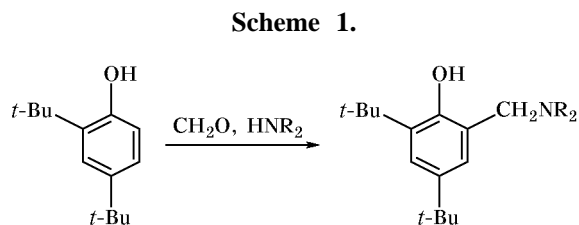
Dimethylamine, diethylamine, didecylamine, bis-(2-hydroxyethyl)amine, morpholine, and piperidine were successfully used as amine component. An exception was dicyclohexylamine which gave rise to an unexpected product, 1:1 phenol–amine molecular complex **I**. Its structure was established by X-ray analysis. The complex is very stable, and it does not change on melting, sublimation, and column or thin-layer chromatography on silica gel. Its dissociation into the components occurs only under electron impact: the mass spectrum contains peaks belonging to the molecular ions of 2,4-di-*tert*-butylphenol and dicyclohexylamine. Decomposition of the complex can also be effected by the action of an acid, e.g., HCl.

We have found that the formation of a stable 1:1 complex with dicyclohexylamine is not a specific property of only 2,4-di-*tert*-butylphenol; however,

the ability to form such complexes depends on the substituents in the *ortho* positions with respect to the hydroxy group. No complexes with dicyclohexylamine were obtained from phenols having bulky substituents (*t*-Bu or Ar) in both *ortho* positions or groups capable of forming strong intramolecular hydrogen bond with the hydroxy proton (CHO, CH_2NR_2). Presumably, the above two factors hamper complex formation between dicyclohexylamine and 2,2′,4,4′-tetrabutylbisphenol, while its homolog in which the aryl fragments are separated by a methylene bridge, 2,4-di-*tert*-butyl-6-(2-hydroxy-3,5-di-*tert*-butyl)benzylphenol, gives a 2:1 complex with dicyclohexylamine via participation of two OH groups.

Most of the isolated complexes are crystalline substances; however, some stable complexes are liquids which do not decompose above the boiling point.
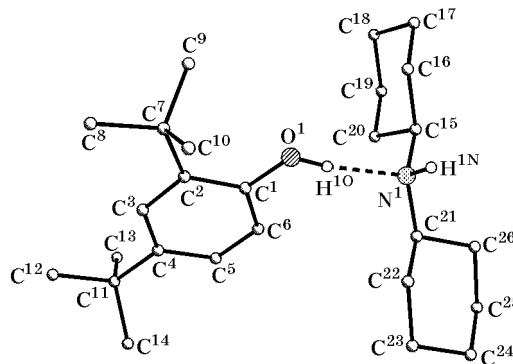
Structure of the 1:1 molecular complex of 2,4-di-*tert*-butylphenol with dicyclohexylamine.

Table 1. Coordinates of atoms ($\times 10^4$) and their equivalent isotropic temperature factors (B_{eq}; isotropic for hydrogen atoms, B_{iso}) in the structure of complex **I**

Atom	x	y	z	B_{eq}/B_{iso}, Å^2	Atom	x	y	z	B_{eq}/B_{iso}, Å^2
O^1	1527(1)	3581(1)	299(1)	23(1)	H^{9B}	2201(17)	2957(16)	–855(10)	43(5)
N^1	1196(1)	5731(1)	798(1)	17(1)	H^{9C}	2036(17)	1873(16)	–1418(11)	45(5)
C^1	2198(1)	2849(1)	714(1)	18(1)	H^{10A}	244(14)	2208(14)	–240(8)	26(4)
C^2	2426(1)	1776(1)	446(1)	17(1)	H^{10B}	163(14)	1139(13)	–784(9)	26(4)
C^3	3092(1)	1056(1)	903(1)	19(1)	H^{10C}	222(15)	983(14)	84(9)	31(4)
C^4	3537(1)	1334(1)	1601(1)	19(1)	H^{12A}	3410(20)	–929(17)	1761(11)	50(5)
C^5	3307(1)	2409(1)	1840(1)	21(1)	H^{12B}	4660(20)	–718(19)	1248(14)	68(7)
C^6	2652(1)	3149(1)	1406(1)	21(1)	H^{12C}	4690(20)	–1168(19)	2106(12)	64(6)
C^7	1924(1)	1392(1)	–303(1)	19(1)	H^{13A}	6120(18)	387(18)	2413(11)	51(5)
C^8	2295(1)	191(1)	–469(1)	27(1)	H^{13B}	5674(19)	1662(18)	2360(11)	55(6)
C^9	2411(1)	2127(1)	–916(1)	27(1)	H^{13C}	5910(20)	918(19)	1599(14)	69(7)
C^{10}	525(1)	1436(1)	–306(1)	22(1)	H^{14A}	4295(19)	–22(18)	3161(11)	55(6)
C^{11}	4272(1)	519(1)	2079(1)	24(1)	H^{14B}	3850(20)	1280(20)	3082(14)	80(8)
C^{12}	4245(2)	–662(1)	1769(1)	48(1)	H^{14C}	2920(20)	195(19)	2829(12)	69(7)
C^{13}	5609(1)	897(1)	2117(1)	35(1)	H^{15}	1996(13)	7199(13)	554(8)	23(4)
C^{14}	3786(2)	500(2)	2853(1)	46(1)	H^{16A}	1192(13)	6499(12)	–541(8)	19(3)
C^{15}	2135(1)	6421(1)	453(1)	18(1)	H^{16B}	2101(13)	5491(13)	–477(8)	22(3)
C^{16}	2011(1)	6280(1)	–375(1)	22(1)	H^{17A}	2894(14)	6812(13)	1301(9)	27(4)
C^{17}	2989(1)	6934(1)	–770(1)	27(1)	H^{17B}	2825(15)	7728(15)	–722(9)	34(4)
C^{18}	4264(1)	6609(1)	–498(1)	28(1)	H^{18A}	4387(15)	5808(15)	–625(9)	32(4)
C^{19}	4393(1)	6737(1)	328(1)	30(1)	H^{18B}	4883(16)	7043(14)	–734(9)	35(4)
C^{20}	3411(1)	6085(1)	721(1)	25(1)	H^{19A}	5203(16)	6517(14)	488(9)	33(4)
C^{21}	1104(1)	5816(1)	1601(1)	17(1)	H^{19B}	4324(16)	7542(16)	460(9)	39(4)
C^{22}	44(1)	5087(1)	1833(1)	24(1)	H^{20A}	3543(13)	5281(13)	628(8)	23(4)
C^{23}	–47(1)	5048(1)	2664(1)	31(1)	H^{20B}	3512(15)	6203(14)	1241(9)	30(4)
C^{24}	–142(1)	6207(1)	2985(1)	32(1)	H^{21}	1889(13)	5507(12)	1824(8)	18(3)
C^{25}	907(1)	6938(1)	2743(1)	27(1)	H^{22A}	151(15)	4337(14)	1645(9)	31(4)
C^{26}	967(1)	6986(1)	1910(1)	23(1)	H^{22B}	–722(14)	5404(14)	1618(8)	26(4)
H^{1N}	458(14)	5903(12)	576(8)	18(3)	H^{23A}	718(16)	4682(15)	2877(9)	34(4)
H^{1O}	1464(18)	4249(18)	504(11)	49(5)	H^{23B}	–771(17)	4621(15)	2796(10)	39(5)
H^3	3239(14)	307(13)	733(8)	24(4)	H^{24A}	–913(16)	6524(15)	2823(10)	35(4)
H^5	3610(14)	2636(14)	2333(9)	27(4)	H^{24B}	–142(18)	6200(17)	3515(11)	51(5)
H^6	2505(15)	3916(14)	1564(9)	30(4)	H^{25A}	1710(16)	6647(14)	2939(9)	32(4)
H^{8A}	1970(15)	–358(15)	–106(9)	33(4)	H^{25B}	840(15)	7683(16)	2940(9)	37(4)
H^{8B}	3194(15)	128(14)	–476(9)	30(4)	H^{26A}	1647(15)	7434(14)	1761(8)	27(4)
H^{8C}	1947(16)	–7(15)	–947(10)	40(5)	H^{26B}	215(15)	7313(14)	1691(9)	29(4)
H^{9A}	3294(17)	2054(15)	–940(10)	38(5)					

Thus phenols can be divided into two groups with respect to dicyclohexylamine: those forming and not forming molecular complexes. This difference may be used, e.g., for separation of mixtures of substituted phenols, as well as for extraction of phenols from mixtures with other substances and from various phenol-containing media.

EXPERIMENTAL

The ^{1}H NMR spectra were recorded on a Bruker WH-250 spectrometer. The mass spectrum of complex **I** was obtained on a Hitachi M-80 A instrument (electron impact, 70 eV). Crystals of **I** were analyzed by the X-ray diffraction method using a Syntex $P2_1$

Table 2. Complexes of substituted phenols with dicyclohexylamine
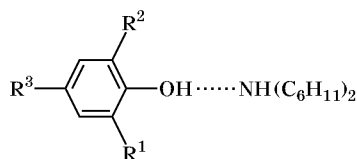
Complex no.	R^1	R^2	R^3	Yield, %	Phenol–dicyclo-hexylamine ratio	mp or bp, °C (solvent or *p*, mm)
I	*t*-Bu	H	*t*-Bu	88	1:1	86–87 (hexane)
II	H	H	H	98	1:1	64–65 (hexane)
III	*t*-Bu	CHO	*t*-Bu	0	–	–
IV	*t*-Bu	Br	*t*-Bu	84	1:1	39–40 (hexane)
V	*t*-Bu	CH$_2$NMe$_2$	*t*-Bu	0	–	–
VI	*t*-Bu	3,5-Di-*tert*-butyl-2-hydroxyphenyl	*t*-Bu	0	–	–
VII	*t*-Bu	3,5-Di-*tert*-butyl-2-hydroxybenzyl	*t*-Bu	65	1:2	120–121 (ethanol), subl.
VIII	*t*-Bu	*t*-Bu	H	0	–	–
IX	Cl	Cl	H	91	1:1	144–145 (hexane–chloroform)
X	Me	Me	H	79	1:1	137–138 (20), 31–32 (hexane)
XI	*t*-Bu	H	H	87	1:1	117–118 (14)

diffractometer. C$_{14}$H$_{22}$O·C$_{12}$H$_{23}$N (**I**) (C$_{26}$H$_{45}$NO, *M* 387.63); monoclinic crystals with the following unit cell parameters (153 K): *a* = 10.977(3), *b* = 12.059(4), *c* = 18.328(6) Å; β = 91.43(2)°; *V* = 2425(1) Å^3; space group *P*2$_1$/*c*; *Z* = 4; d_{calc} = 1.063 g/cm^3. Total of 6595 reflections were measured at 153 K (λMoK$_\alpha$ radiation, 2θ$_{max}$ = 63.84°) from a 0.6×0.5×0.3-mm single crystal. Averaging of equivalent reflections gave 6267 independent reflections [*R*(int) = 0.0254] which were used in structure determination and refinement. The structure was solved by the direct method; all atoms were localized from the difference syntheses of electron density and were refined with respect to F_{hkl}^2 by the least-squares procedure in anisotropic approximation for non-hydrogen atoms and isotropic approximation for hydrogen atoms. The final divergence factors were R_1 = 0.0468 [calculated from F_{hkl} for 4629 reflections with $I > 2\sigma(I)$] and wR_2 = 0.1363 (calculated from F_{hkl}^2 for all 5840 reflections used in the refinement); GOF 0.997; 433 refined parameters. All calculations were performed using SHELXTL PLUS 5 software package. The coordinates of atoms are given in Table 1, and the structure of complex **I** with atom numbering is shown in figure.

The molecules of 2,4-di-*tert*-butylphenol and di-cyclohexylamine are linked through strong hydrogen bond O^1–H^{1O}···N^1: O^1···N^1 2.776(2) Å , H^{1O}···N^1 1.89(2) Å, ∠O^{1}H^{1O}N^1 170.7(4)°). The H^{1N} atom is not involved in hydrogen bonding; the shortest H^{1N}···O^{1A} distance to the oxygen atom in the molecule related to the initial one through a symmetry center is 2.75(2) Å [N^1···O^{1A} 3.656(2) Å). The geometric parameters (bond lengths and bond angles) of the 2,4-di-*tert*-butylphenol and dicyclohexylamine fragments have standard values.

The reaction mixtures were analyzed by thin-layer chromatography using Silufol UV-254 plates.

A mixture of equimolar amounts (0.001 mol) of the corresponding phenol and dicyclohexylamine in 40 ml of ethanol was heated for 2 h under reflux. The solution was evaporated, and the residue was recrystallized. The structure of the products was confirmed by elemental analysis and ^{1}H NMR spectroscopy (in CDCl$_3$ and DMSO-d_6). Liquid complexes **X** and **XI** were distilled under reduced pressure.

The yields and melting (or boiling) points of complexes **I**–**XI** are given in Table 2.