N-(2-Hydroxy-1,1-dimethylethyl)-3-methylbenzamide

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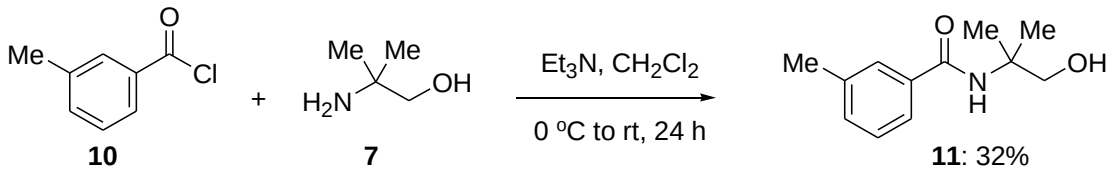
General Methods

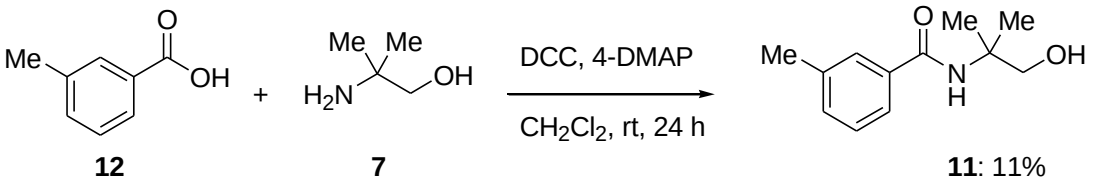
All chemicals, reagents and solvents were purchased from chemical companies (Sigma-Aldrich Chemie GmbH, Taufkirchen, Germany) and were used as received without prior purification. Reactions that required dry conditions were performed in an inert atmosphere with Ar gas. Syringes and needles for the transfer of reagents were oven dried and cooled in a desiccator over silica gel before use. The reaction's progress was monitored by thin-layer chromatography (TLC) on glass plates pre-coated with Merck silica gel. TLC plates were examined under UV lamplight (UVGL-58 Handheld 254/365 nm). Büchi-USA rotary evaporators were used to evaporate solvents using appropriate temperatures. Flash column chromatography was performed using silica gel (Kieselgel) (70–230) mesh as an adsorbent. The purified products were characterized using analyses NMR (^{1}H NMR, ^{13}C NMR), IR, mass spectra and melting points. Melting points were recorded on the GallenKamp-MPd350.bm2.5 melting point apparatus (Gallenkamp, Kent, UK). Attenuated total-reflectance IR spectra were recorded on pure samples on Agilent Technologies Cary 630 FTIR (Agilent, Santa Clara, CA, USA). ^{1}H NMR spectra were recorded in $CDCl_3$ on JEOL ECX-400 spectrometers (JEOL Ltd, Tokyo, Japan). ^{1}H NMR chemical shifts (δ) were assigned in part per million (ppm) downfield using an internal standard trimethylsilane (TMS) and were referenced to $CDCl_3$, δ = 7.24. Abbreviations s, d, t, q, quin, sept and m refer to singlet, doublet, triplet, quartet, quintet, septet and multiplet, respectively. Chemical shifts in ^{13}C spectra (175 MHz) were quoted in ppm and referenced to the central line of the $CDCl_3$ triplet, δ C 77.0. Coupling constants (*J*) were recorded in hertz (Hz). GC-MS spectra were obtained using an Agilent mass spectrometer (Agilent, Santa Clara, CA, USA). Elemental analysis was performed using an EuroEA Elemental Analyzer (configuration CHN (EuroVector Instruments & Software, Milano, Italy) with a calibration type of K-factor. Single-crystal X-ray structure determinations were performed at room temperature on a Stoe IPS II diffractometer using monochromatic Mo−K_α radiation (λ = 0.71073 Å). A multiscan absorption correction was applied. The data reduction, including an empirical absorption correction using spherical harmonics, implemented in LANA. The crystal structures were solved by direct methods using the online version of WinGX and then refined by full-matrix least-squares (SHELXL2014) on F^2. The nonhydrogen atoms were refined anisotropically. All of the hydrogen atoms were positioned geometrically in idealized positions and refined with the riding model approximation, with Uiso(H) = 1.2 or 1.5 Ueq(C). The molecular graphics the program MERCURY from the CSD package was used.

Method a: Synthesis of N-(1-hydroxy-2-methylpropan-2-yl)-3-methylbenzamide from 3-methylbenzoyl chloride



3-Methylbenzoyl chloride (**10)** (1.30 mL, 9.86 mmol) was added dropwise under an atmosphere of N_2 into a cold (0 ^{0}C ice-water bath) solution of 2-amino-2-methylpropan-1-ol **(7)** (0.50 mL, 5.2 mmol), in CH_2Cl_2 (20 mL). Et_3N (1.40 mL, 10.0 mmol) was then added to the 0 ^{0}C mixture under N_2. The mixture was stirred for 1 h at 0 ^{0}C, allowed to warm up to room temperature and then stirred for an additional 23 h. To the reaction mixture, aqueous saturated $NaHCO_3$ solution (20 mL) was added. The mixture was extracted with CH_2Cl_2 (3 × 20 mL). The combined organic extracts were dried over anhydrous $MgSO_4$ and filtered. The evaporation of the solvents under reduced pressure followed by flash chromatography (SiO_2) using hexane: Et_2O (5:1) gave the title compound (**11**) as white crystals after recrystallization from CH_2Cl_2: hexane (0.66 g, 62%). R_f = 0.12 (Pet. Ether: EtOAc (1:1)), mp = 81-83C. ^{1}H NMR (400 MHz, $CDCl_3$): 7.52 (s, 1H), 7.49 (d, *J*=2.3 Hz, 1H), 7.48 (d, *J*=1.9 Hz 1H), 7.28 Hz (dd, *J*=3.8, 3.3 Hz, 1H), 7.25 (s, 1H), 6.24 (s, 1H), 3.66 (s, 2H), 2.37 (s, 3H), 1.39 (s, 6H). ^{13}C NMR (176 MHz, $CDCl_3$): = 168.8, 138.6, 134.8, 132.5, 128.6, 127.7, 123.9, 70.8, 56.5, 24.8, 24.4. IR (film): ν max/cm^{-1}: 3340, 3198, 2924, 1627, 1535, 1548, 1481. Elemental analysis calculated: C (69.54), H (8.27), N (6.76), found (average of two runs): C (69.329), H (8.171), N (6.530).

Method b: Synthesis of N-(1-hydroxy-2-methylpropan-2-yl)-3-methylbenzamide from 3-methylbenzoic acid



To a mixture of 3-methylbenzoic acid (**12**) (0.71 g, 5.2 mmol), 2-amino-2-methylpropan-1-ol (**7**) (0.50 ml, 5.2 mmol) and DCC (1.07 g, 5.2 mmol) in CH_2Cl_2 (100 mL), DMAP (0.20 g, 1.6 mmol) was added. The mixture was stirred at room temperature for 24 h. To the reaction mixture, aqueous saturated $NaHCO_3$ solution (50 mL) was added. The mixture was extracted with CH_2Cl_2 (3 × 50 mL). The combined organic extracts were dried over anhydrous $MgSO_4$ and filtered. The evaporation of the solvents under reduced pressure followed by flash chromatography (SiO_2) using hexane: Et_2O (5:1) gave the title compound (**11)** as a white crystal after recrystallization from CH_2Cl_2: hexane (0.11 g, 11%).

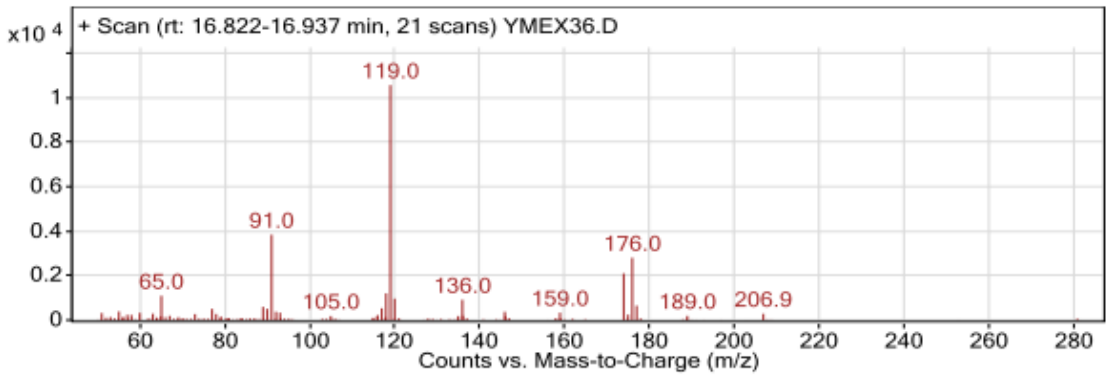


Figure S1. GC-MS of the title compound.

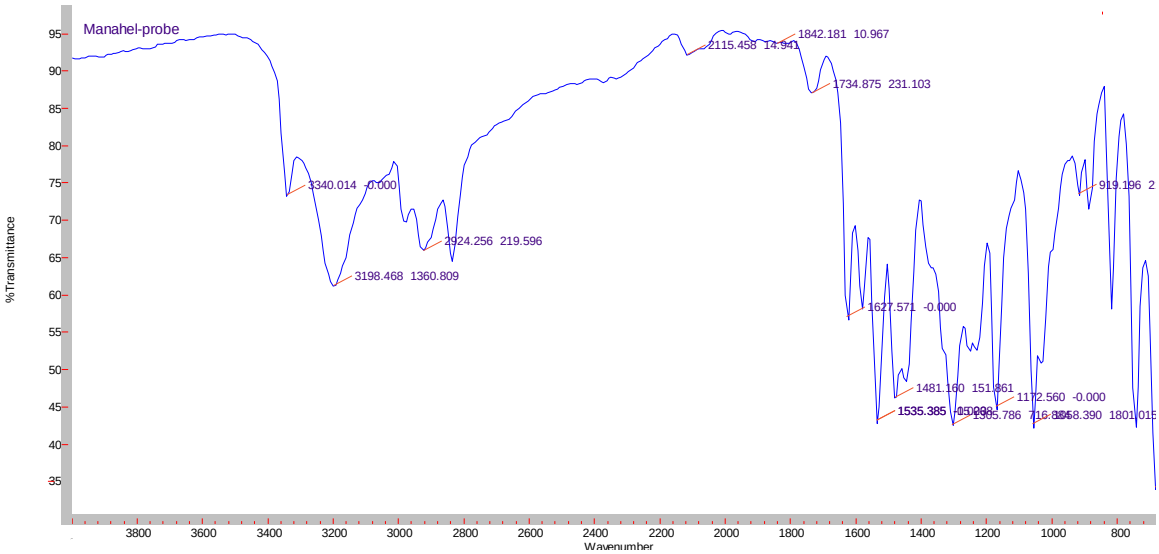


Figure S2. IR Spectrum of the title compound.

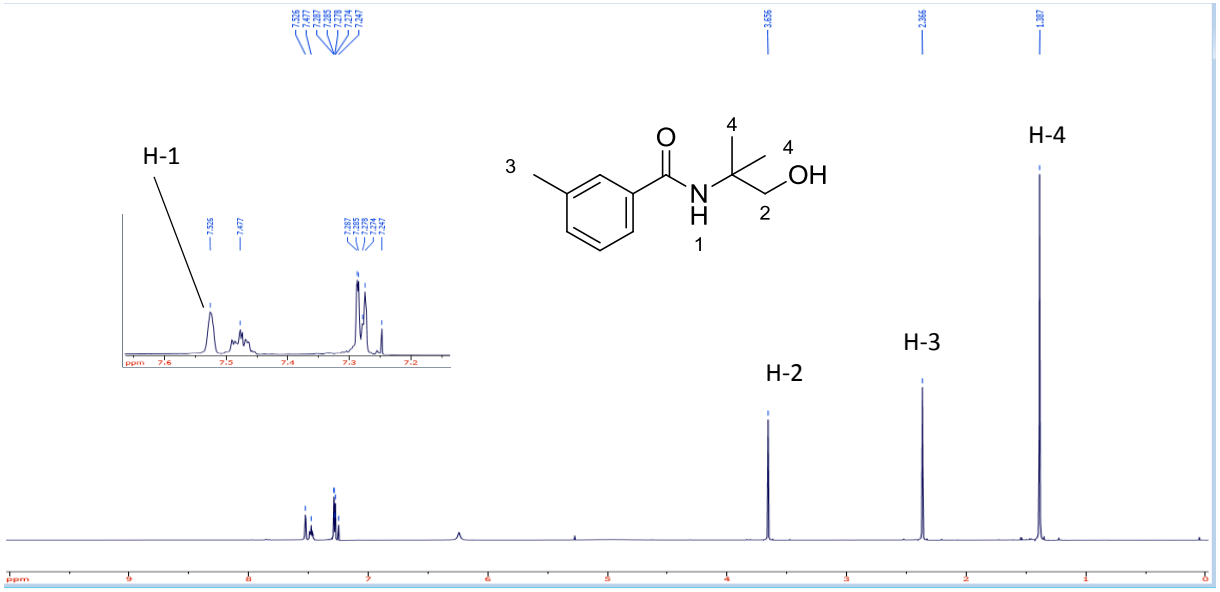


Figure S3. [1]H NMR Spectrum of the title compound.

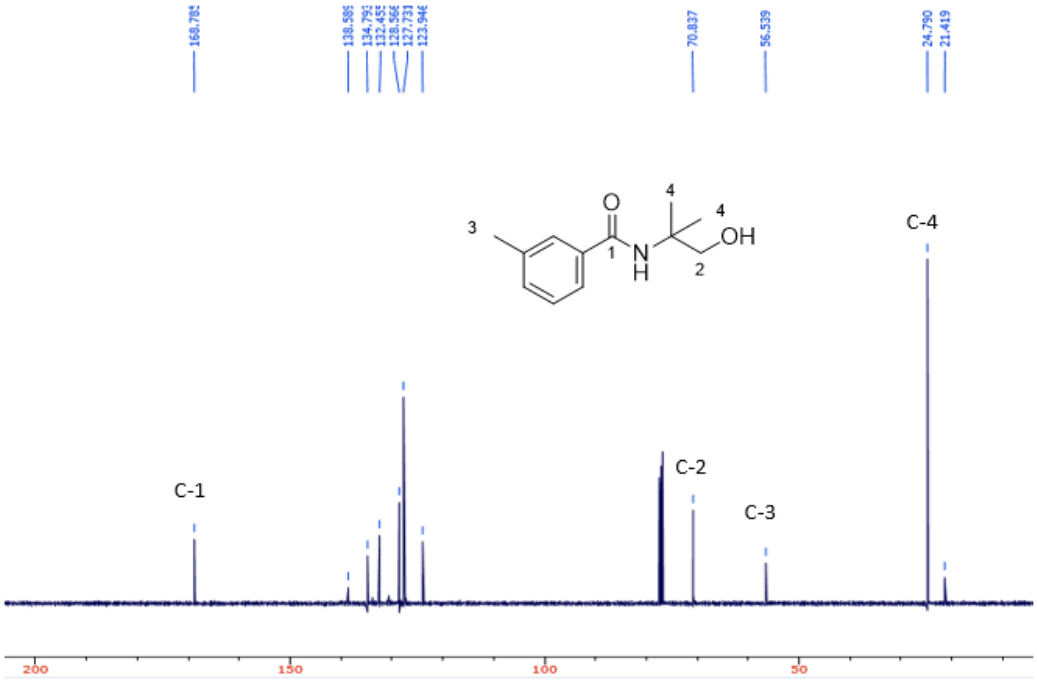


Figure S4. [13]C NMR Spectrum of the title compound.

EuroEA Elemental Analyser

AutoRun name : YOUSEF DR HAMMED STUDENT - (279)
Date of Analysis : 03 Nov 2019
Time of Analysis : 13:51:36

Operator : Alberto Paglia
Operator Group : GRP1
Configuration : CHN

Calibration Type : K-Factor

Results Summary for Element %

#	Type	Name	N %	C %	H %	S %	O %	Weight (mg)
1	Byp	Bypass-1	-	-	-	-	-	-
2	Byp	Bypass-2	-	-	-	-	-	-
3	Std	Acetanilide-1	10.357	71.062	6.654	-	-	0.853
4	Std	Acetanilide-2	10.369	71.116	6.771	-	-	0.962
5	Smp	YMEX 10-1	6.488	69.267	8.081	-	-	0.715
6	Smp	YMEX 10-2	6.571	69.391	8.260	-	-	0.788

Figure S5. Elemental analysis of the title compound.

checkCIF/PLATON report

Structure factors have been supplied for datablock(s) I

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No syntax errors found. CIF dictionary Interpreting this report

Datablock: I

Bond precision: C-C = 0.0158 A Wavelength=0.71073

Cell: a=18.380(4) b=10.170(2) c=6.0800(12)
alpha=90 beta=90 gamma=90
Temperature: 298 K

	Calculated	Reported
Volume	1136.5(4)	1136.5(4)
Space group	P n a 21	P n a 21
Hall group	P 2c -2n	P 2c -2n
Moiety formula	C12 H17 N O2	?
Sum formula	C12 H17 N O2	C12 H17 N O2
Mr	207.27	207.26
Dx,g cm-3	1.211	1.211
Z	4	4
Mu (mm-1)	0.082	0.082
F000	448.0	448.0
F000'	448.20	
h,k,lmax	20,11,6	20,11,6
Nref	1639[911]	1348
Tmin,Tmax	0.984,0.984	0.991,0.992
Tmin'	0.984	

Correction method= # Reported T Limits: Tmin=0.991 Tmax=0.992
AbsCorr = MULTI-SCAN

Data completeness= 1.48/0.82 Theta(max)= 23.248

R(reflections)= 0.0851(884) wR2(reflections)= 0.1861(1348)

S = 1.166 Npar= 138

The following ALERTS were generated. Each ALERT has the format
test-name_ALERT_alert-type_alert-level.
Click on the hyperlinks for more details of the test.

Alert level B

THETM01_ALERT_3_B The value of sine(theta_max)/wavelength is less than 0.575
Calculated sin(theta_max)/wavelength = 0.5554
PLAT023_ALERT_3_B Resolution (too) Low [sin(theta)/Lambda < 0.6].. 23.25 Degree
PLAT029_ALERT_3_B _diffrn_measured_fraction_theta_full value Low . 0.952 Why?

PLAT340_ALERT_3_B Low Bond Precision on C-C Bonds ..... 0.01582 Ang.

Alert level C

ABSTY02_ALERT_1_C An _exptl_absorpt_correction_type has been given without a literature citation. This should be contained in the _exptl_absorpt_process_details field.
Absorption correction given as multi-scan
STRVA01_ALERT_4_C Flack parameter is too small
From the CIF: _refine_ls_abs_structure_Flack -1.700
From the CIF: _refine_ls_abs_structure_Flack_su 1.000
PLAT048_ALERT_1_C MoietyFormula Not Given (or Incomplete) ..... Please Check
PLAT089_ALERT_3_C Poor Data / Parameter Ratio (Zmax < 18) ..... 6.28 Note
PLAT911_ALERT_3_C Missing FCF Refl Between Thmin & STh/L= 0.555 44 Report
PLAT915_ALERT_3_C No Flack x Check Done: Low Friedel Pair Coverage 66 %
PLAT978_ALERT_2_C Number C-C Bonds with Positive Residual Density. 0 Info

Alert level G

PLAT003_ALERT_2_G Number of Uiso or Uij Restrained non-H Atoms ... 12 Report
PLAT007_ALERT_5_G Number of Unrefined Donor-H Atoms ..... 2 Report
PLAT032_ALERT_4_G Std. Uncertainty on Flack Parameter Value High . 1.000 Report
PLAT177_ALERT_4_G The CIF-Embedded .res File Contains DELU Records 1 Report
PLAT178_ALERT_4_G The CIF-Embedded .res File Contains SIMU Records 1 Report
PLAT180_ALERT_4_G Check Cell Rounding: # of Values Ending with 0 = 3 Note
PLAT380_ALERT_4_G Incorrectly? Oriented X(sp2)-Methyl Moiety ..... C4 Check
PLAT860_ALERT_3_G Number of Least-Squares Restraints ..... 91 Note
PLAT883_ALERT_1_G No Info/Value for _atom_sites_solution_primary . Please Do !
PLAT916_ALERT_2_G Hooft y and Flack x Parameter Values Differ by . 1.47 Check
0 **ALERT level A** = Most likely a serious problem - resolve or explain
4 **ALERT level B** = A potentially serious problem, consider carefully
7 **ALERT level C** = Check. Ensure it is not caused by an omission or oversight
10 **ALERT level G** = General information/check it is not something unexpected
3 ALERT type 1 CIF construction/syntax error, inconsistent or missing data
3 ALERT type 2 Indicator that the structure model may be wrong or deficient
8 ALERT type 3 Indicator that the structure quality may be low
6 ALERT type 4 Improvement, methodology, query or suggestion
1 ALERT type 5 Informative message, check

checkCIF publication errors

Alert level A

PUBL004_ALERT_1_A The contact author’s name and address are missing, _publ_contact_author_name and _publ_contact_author_address.
PUBL005_ALERT_1_A _publ_contact_author_email, _publ_contact_author_fax and _publ_contact_author_phone are all missing.
At least one of these should be present.
PUBL006_ALERT_1_A _publ_requested_journal is missing
e.g. ’Acta Crystallographica Section C’
PUBL008_ALERT_1_A _publ_section_title is missing. Title of paper.
PUBL009_ALERT_1_A _publ_author_name is missing. List of author(s) name(s).
PUBL010_ALERT_1_A _publ_author_address is missing. Author(s) address(es).
PUBL012_ALERT_1_A _publ_section_abstract is missing.
Abstract of paper in English.

Alert level G

PUBL017_ALERT_1_G The _publ_section_references section is missing or empty.
7 **ALERT level A** = Data missing that is essential or data in wrong format
1 **ALERT level G** = General alerts. Data that may be required is missing

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You should attempt to resolve as many as possible of the alerts in all categories. Often the minor alerts point to easily fixed oversights, errors and omissions in your CIF or refinement strategy, so attention to these fine details can be worthwhile. In order to resolve some of the more serious problems it may be necessary to carry out additional measurements or structure refinements. However, the nature of your study may justify the reported deviations from journal submission requirements and the more serious of these should be commented upon in the discussion or

experimental section of a paper or in the "special_details" fields of the CIF. *checkCIF* was carefully designed to identify outliers and unusual parameters, but every test has its limitations and
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not guarantee there are no aspects of the results needing attention. It is up to the individual to critically assess their own results and, if necessary, seek expert advice.
If level A alerts remain, which you believe to be justified deviations, and you intend to submit this
CIF for publication in a journal, you should additionally insert an explanation in your CIF using the Validation Reply Form (VRF) below. This will allow your explanation to be considered as part
of the review process.

Validation response form

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# start Validation Reply Form
_vrf_PUBL004_GLOBAL
;
PROBLEM: The contact author’s name and address are missing,
RESPONSE: ...
;
_vrf_PUBL005_GLOBAL
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PROBLEM: _publ_contact_author_email, _publ_contact_author_fax and
RESPONSE: ...
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PROBLEM: _publ_requested_journal is missing
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RESPONSE: ...
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PROBLEM: _publ_author_name is missing. List of author(s) name(s).
RESPONSE: ...
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PROBLEM: _publ_section_abstract is missing.
RESPONSE: ...
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# end Validation Reply Form
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PLATON version of 07/08/2019; check.def file version of 30/07/2019

Datablock I - ellipsoid plot