Formylation of an indolenine: 2-(diformylmethylidene)-3,3-dimethyl-2,3-dihydro-1H-indole

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Reaction of 2,3,3-trimethyl-3H-indole with dimethylformamide/POCl$_3$ and then aqueous NaOH produces 2-(diformylmethylidene)-2,3-dihydro-3,3-dimethylindole, $C_{13}H_{13}NO_2$. The crystal structure shows the molecule to be planar, with the exception of the two methyl groups, which lie above and below the plane.

Comment

Reaction of the 3,3-disubstituted 3H-indole, (1), with the Vilsmeier reagent (dimethylformamide and POCl$_3$) (Cheng *et al.*, 1999, 2002; Fischer *et al.*, 1925; Jutz, 1976; Vilsmeier & Haack, 1927) gave compound (2), the product of N-formylation (Fritz, 1959). Further reaction of (2) with the Vilsmeier reagent and subsequent alkaline hydrolysis produced compound (4) (Fritz, 1959). Formation of this product presumably involves the intermediate N,C-diformyl derivative (3), from which the N-formyl group is then hydrolytically removed.
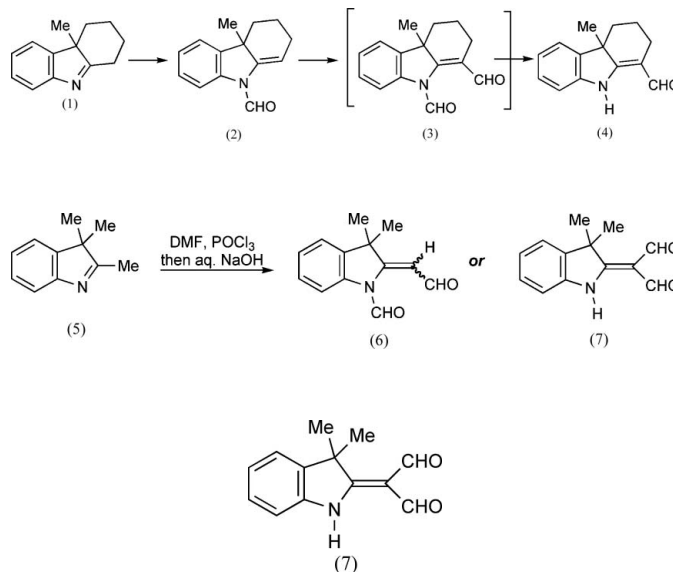
According to this previous work, we expected that the 2,3,3-trimethylindolenine, (5) (2,3,3-trimethyl-3H-indole), would react with the Vilsmeier reagent to form an N-formylated product. However, when (5) was subjected to the Vilsmeier conditions, at 323 K, followed by aqueous alkaline hydrolysis, a diformyl product was obtained in 56% yield. On the basis of the earlier work (Fritz, 1959), it appeared that (5) had been converted into (6). However, ^{1}H NMR analysis of the diformyl product showed the presence of an NH H atom, inconsistent with structure (6). In order to define the structure, crystals
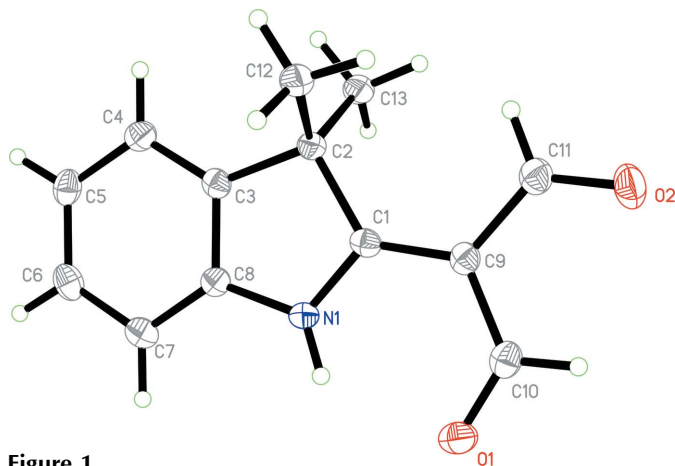
Figure 1
A plot of (7), with displacement ellipsoids drawn at the 50% probability level.

were grown and subjected to X-ray analysis, which showed the product to be the title compound, (7) (Fig. 1).

In the solid state, the molecule of (7) is planar, with the exception of the two methyl groups, which lie above and below the plane. The greatest deviation from the least-squares plane through atoms C1–C11/N1/O1/O2 is 0.052 (1) Å for C2.

Further examples of this interesting conversion, together with the utilization of such diformyl compounds for heterocyclic ring synthesis, will be described in a forthcoming paper.

Experimental

To dimethylformamide (10 ml) cooled in an ice bath, phosphorus oxychloride (6 ml, 66 mmol) was added dropwise with stirring over a period of 2 h at below 298 K. After the addition was complete, a solution of trimethylindolenine, (5) (12.6 mmol), in dimethylformamide (10 ml) was added dropwise. The cooling bath was removed and the reaction mixture was stirred at 323 K for 2 h. The resulting solution was added to ice-cooled water, the pH was adjusted to 8.0 by the addition of aqueous NaOH (35%) and the mixture was extracted with ethyl acetate (3 × 30 ml). The organic layer was washed with hot water and dried over Na_2SO_4. The solvent was evaporated and the resulting crude product was purified by column chromatography on silica gel, eluting with ethyl acetate–toluene (1:5 v/v), to give the pure diformyl compound, (7), as yellow crystals.

Crystal data

$C_{13}H_{13}NO_2$	$D_x = 1.329$ Mg m^{-3}
$M_r = 215.24$	Mo $K\alpha$ radiation
Monoclinic, $P2_1/c$	Cell parameters from 1781
$a = 12.1488$ (13) Å	reflections
$b = 12.2273$ (13) Å	$\theta = 2.4–26.3°$
$c = 7.3404$ (8) Å	$\mu = 0.09$ mm^{-1}
$\beta = 99.329$ (2)°	$T = 100$ (2) K
$V = 1076.0$ (2) Å^3	Prism, yellow
$Z = 4$	$0.65 \times 0.50 \times 0.50$ mm

Data collection

Bruker SMART CCD area-detector diffractometer	1729 reflections with $I > 2\sigma(I)$
φ and ω scans	$R_{int} = 0.051$
Absorption correction: none	$\theta_{max} = 26.4°$
4520 measured reflections	$h = -14 \rightarrow 14$
2177 independent reflections	$k = -15 \rightarrow 10$
	$l = -6 \rightarrow 9$

Refinement

Refinement on F^2	H atoms treated by a mixture of
$R[F^2 > 2\sigma(F^2)] = 0.036$	independent and constrained
$wR(F^2) = 0.095$	refinement
$S = 0.99$	$w = 1/[\sigma^2(F_o^2) + (0.0477P)^2]$
2177 reflections	where $P = (F_o^2 + 2F_c^2)/3$
151 parameters	$(\Delta/\sigma)_{max} < 0.001$
	$\Delta\rho_{max} = 0.26$ e Å^{-3}
	$\Delta\rho_{min} = -0.16$ e Å^{-3}

Table 1
Hydrogen-bond geometry (Å, °).

$D—H\cdots A$	$D—H$	$H\cdots A$	$D\cdots A$	$D—H\cdots A$
N1—H1N$\cdots$O1	0.858 (16)	2.075 (16)	2.7021 (15)	129.3 (13)
N1—H1N$\cdots$O2^i	0.858 (16)	2.157 (16)	2.8254 (15)	134.4 (14)

Symmetry code: (i) $-x + 1, y + \frac{1}{2}, -z + \frac{1}{2}$.

The H atom bonded to atom N1 was found by difference Fourier methods and refined isotropically. H atoms bonded to C atoms were included in calculated positions, using the riding method, with C—H distances of 0.95–0.98 Å and $U_{iso}(H) = 1.2U_{eq}(C)$, or $1.5U_{eq}(C)$ for methyl groups. The methyl groups were allowed to rotate but not to tip.

Data collection: *SMART* (Bruker, 2001); cell refinement: *SAINT* (Bruker, 2002); data reduction: *SAINT*; program(s) used to solve structure: *SHELXS97* (Sheldrick, 1997); program(s) used to refine structure: *SHELXL97* (Sheldrick, 1997); molecular graphics: *SHELXTL* (Bruker, 2001); software used to prepare material for publication: *SHELXTL*.

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Crystal data

$C_{13}H_{13}NO_2$	$D_x = 1.329$ Mg m^{-3}
$M_r = 215.24$	Melting point = 118–120 K
Monoclinic, $P2_1/c$	Mo $K\alpha$ radiation, $\lambda = 0.71073$ Å
$a = 12.1488$ (13) Å	Cell parameters from 1781 reflections
$b = 12.2273$ (13) Å	$\theta = 2.4$–26.3°
$c = 7.3404$ (8) Å	$\mu = 0.09$ mm^{-1}
$\beta = 99.329$ (2)°	$T = 100$ K
$V = 1076.0$ (2) Å^3	Prismatic, yellow
$Z = 4$	$0.65 \times 0.50 \times 0.50$ mm
$F(000) = 456$	

Data collection

Bruker SMART CCD area-detector diffractometer	1729 reflections with $I > 2\sigma(I)$
Radiation source: fine-focus sealed tube	$R_{int} = 0.051$
Graphite monochromator	$\theta_{max} = 26.4°$, $\theta_{min} = 1.7°$
φ and ω scans	$h = -14 \rightarrow 14$
4520 measured reflections	$k = -15 \rightarrow 10$
2177 independent reflections	$l = -6 \rightarrow 9$

Refinement

Refinement on F^2	Secondary atom site location: difference Fourier map
Least-squares matrix: full	
$R[F^2 > 2\sigma(F^2)] = 0.036$	Hydrogen site location: inferred from neighbouring sites
$wR(F^2) = 0.095$	H atoms treated by a mixture of independent and constrained refinement
$S = 0.99$	
2177 reflections	$w = 1/[\sigma^2(F_o^2) + (0.0477P)^2]$ where $P = (F_o^2 + 2F_c^2)/3$
151 parameters	
0 restraints	$(\Delta/\sigma)_{max} < 0.001$
Primary atom site location: structure-invariant direct methods	$\Delta\rho_{max} = 0.26$ e Å^{-3}
	$\Delta\rho_{min} = -0.16$ e Å^{-3}

Special details

Geometry. All e.s.d.'s (except the e.s.d. in the dihedral angle between two l.s. planes) are estimated using the full covariance matrix. The cell e.s.d.'s are taken into account individually in the estimation of e.s.d.'s in distances, angles and torsion angles; correlations between e.s.d.'s in cell parameters are only used when they are defined by crystal symmetry. An approximate (isotropic) treatment of cell e.s.d.'s is used for estimating e.s.d.'s involving l.s. planes.

Refinement. Refinement of F^2 against ALL reflections. The weighted R-factor wR and goodness of fit S are based on F^2, conventional R-factors R are based on F, with F set to zero for negative F^2. The threshold expression of $F^2 > \sigma(F^2)$ is used only for calculating R-factors(gt) *etc*. and is not relevant to the choice of reflections for refinement. R-factors based on F^2 are statistically about twice as large as those based on F, and R- factors based on ALL data will be even larger.

Fractional atomic coordinates and isotropic or equivalent isotropic displacement parameters (Å^2)

	x	*y*	*z*	U_{iso}*/U_{eq}
O1	0.41864 (8)	0.59632 (7)	0.17572 (13)	0.0248 (2)
O2	0.45038 (8)	0.30192 (7)	0.41990 (14)	0.0291 (3)
N1	0.64031 (10)	0.59216 (9)	0.16885 (15)	0.0175 (3)
H1N	0.5812 (14)	0.6311 (13)	0.141 (2)	0.034 (5)*
C1	0.63698 (10)	0.49488 (10)	0.25163 (16)	0.0164 (3)
C2	0.75649 (11)	0.44847 (10)	0.29030 (17)	0.0175 (3)
C3	0.82031 (11)	0.53649 (10)	0.20644 (16)	0.0173 (3)
C4	0.93209 (11)	0.54392 (10)	0.19213 (18)	0.0205 (3)
H4	0.9828	0.4877	0.2394	0.025*
C5	0.96879 (12)	0.63560 (11)	0.10687 (18)	0.0225 (3)
H5	1.0456	0.6425	0.0974	0.027*
C6	0.89476 (11)	0.71681 (11)	0.03570 (18)	0.0239 (3)
H6	0.9216	0.7781	−0.0235	0.029*
C7	0.78199 (11)	0.71067 (10)	0.04888 (17)	0.0218 (3)
H7	0.7310	0.7663	0.0004	0.026*
C8	0.74801 (11)	0.61946 (10)	0.13616 (16)	0.0169 (3)
C9	0.53856 (11)	0.44934 (10)	0.29297 (17)	0.0176 (3)
C10	0.43321 (11)	0.50492 (11)	0.24412 (17)	0.0209 (3)
H10	0.3687	0.4669	0.2672	0.025*
C11	0.53515 (12)	0.34386 (11)	0.37930 (18)	0.0226 (3)
H11	0.6029	0.3040	0.4067	0.027*
C12	0.79827 (11)	0.44121 (11)	0.49983 (17)	0.0220 (3)
H12A	0.8754	0.4147	0.5216	0.033*
H12B	0.7509	0.3905	0.5557	0.033*
H12C	0.7950	0.5138	0.5553	0.033*
C13	0.76813 (11)	0.33804 (10)	0.19465 (19)	0.0219 (3)
H13A	0.7362	0.3438	0.0636	0.033*
H13B	0.7284	0.2814	0.2527	0.033*
H13C	0.8472	0.3185	0.2068	0.033*

Atomic displacement parameters (Å^2)

	U^{11}	U^{22}	U^{33}	U^{12}	U^{13}	U^{23}
O1	0.0231 (5)	0.0236 (5)	0.0268 (5)	0.0046 (4)	0.0010 (4)	0.0003 (4)
O2	0.0291 (6)	0.0220 (5)	0.0380 (6)	−0.0075 (5)	0.0104 (5)	−0.0016 (4)
N1	0.0162 (6)	0.0153 (6)	0.0208 (6)	0.0026 (5)	0.0029 (4)	0.0009 (5)

C1	0.0203 (7)	0.0135 (6)	0.0147 (6)	0.0009 (5)	0.0009 (5)	−0.0033 (5)
C2	0.0169 (7)	0.0152 (6)	0.0197 (7)	0.0005 (5)	0.0007 (5)	0.0000 (5)
C3	0.0205 (7)	0.0152 (6)	0.0157 (6)	−0.0007 (5)	0.0019 (5)	−0.0031 (5)
C4	0.0202 (7)	0.0197 (7)	0.0212 (7)	0.0024 (6)	0.0018 (5)	−0.0048 (6)
C5	0.0190 (7)	0.0254 (7)	0.0243 (7)	−0.0038 (6)	0.0073 (6)	−0.0050 (6)
C6	0.0294 (8)	0.0218 (7)	0.0222 (7)	−0.0052 (6)	0.0096 (6)	0.0006 (6)
C7	0.0258 (8)	0.0192 (7)	0.0208 (7)	0.0014 (6)	0.0049 (6)	0.0017 (5)
C8	0.0176 (7)	0.0173 (6)	0.0162 (6)	0.0008 (5)	0.0035 (5)	−0.0034 (5)
C9	0.0184 (7)	0.0166 (6)	0.0176 (6)	−0.0016 (5)	0.0018 (5)	−0.0037 (5)
C10	0.0196 (7)	0.0232 (7)	0.0199 (7)	−0.0026 (6)	0.0031 (5)	−0.0045 (6)
C11	0.0218 (7)	0.0199 (7)	0.0259 (7)	−0.0023 (6)	0.0027 (6)	−0.0038 (6)
C12	0.0217 (7)	0.0204 (7)	0.0227 (7)	−0.0005 (6)	−0.0003 (6)	0.0020 (6)
C13	0.0212 (7)	0.0162 (7)	0.0278 (7)	0.0016 (6)	0.0022 (6)	−0.0018 (6)

Geometric parameters (Å, º)

O1—C10	1.2262 (16)	C5—H5	0.9500
O2—C11	1.2296 (16)	C6—C7	1.3910 (19)
N1—C1	1.3393 (16)	C6—H6	0.9500
N1—C8	1.4082 (17)	C7—C8	1.3822 (17)
N1—H1N	0.858 (16)	C7—H7	0.9500
C1—C9	1.3963 (18)	C9—C10	1.4420 (18)
C1—C2	1.5417 (18)	C9—C11	1.4406 (18)
C2—C3	1.5144 (18)	C10—H10	0.9500
C2—C13	1.5390 (17)	C11—H11	0.9500
C2—C12	1.5421 (17)	C12—H12A	0.9800
C3—C4	1.3818 (18)	C12—H12B	0.9800
C3—C8	1.3856 (17)	C12—H12C	0.9800
C4—C5	1.3920 (18)	C13—H13A	0.9800
C4—H4	0.9500	C13—H13B	0.9800
C5—C6	1.3840 (19)	C13—H13C	0.9800
C1—N1—C8	112.64 (11)	C6—C7—H7	121.7
C1—N1—H1N	121.0 (10)	C7—C8—C3	122.98 (12)
C8—N1—H1N	126.4 (10)	C7—C8—N1	128.74 (12)
N1—C1—C9	122.86 (12)	C3—C8—N1	108.27 (11)
N1—C1—C2	108.28 (11)	C1—C9—C10	120.99 (12)
C9—C1—C2	128.85 (11)	C1—C9—C11	122.64 (12)
C3—C2—C1	101.10 (10)	C10—C9—C11	116.33 (12)
C3—C2—C13	110.31 (10)	O1—C10—C9	126.49 (13)
C1—C2—C13	113.11 (10)	O1—C10—H10	116.8
C3—C2—C12	109.81 (10)	C9—C10—H10	116.8
C1—C2—C12	110.65 (10)	O2—C11—C9	124.41 (13)
C13—C2—C12	111.39 (10)	O2—C11—H11	117.8
C4—C3—C8	119.67 (12)	C9—C11—H11	117.8
C4—C3—C2	130.68 (12)	C2—C12—H12A	109.5
C8—C3—C2	109.65 (11)	C2—C12—H12B	109.5
C3—C4—C5	118.52 (12)	H12A—C12—H12B	109.5

C3—C4—H4	120.7	C2—C12—H12C	109.5
C5—C4—H4	120.7	H12A—C12—H12C	109.5
C6—C5—C4	120.76 (13)	H12B—C12—H12C	109.5
C6—C5—H5	119.6	C2—C13—H13A	109.5
C4—C5—H5	119.6	C2—C13—H13B	109.5
C5—C6—C7	121.47 (12)	H13A—C13—H13B	109.5
C5—C6—H6	119.3	C2—C13—H13C	109.5
C7—C6—H6	119.3	H13A—C13—H13C	109.5
C8—C7—C6	116.57 (12)	H13B—C13—H13C	109.5
C8—C7—H7	121.7		
C8—N1—C1—C9	−178.12 (11)	C5—C6—C7—C8	−0.11 (19)
C8—N1—C1—C2	2.49 (14)	C6—C7—C8—C3	−0.71 (18)
N1—C1—C2—C3	−2.13 (12)	C6—C7—C8—N1	179.96 (12)
C9—C1—C2—C3	178.53 (12)	C4—C3—C8—C7	0.73 (18)
N1—C1—C2—C13	−120.06 (12)	C2—C3—C8—C7	−179.21 (11)
C9—C1—C2—C13	60.60 (17)	C4—C3—C8—N1	−179.82 (11)
N1—C1—C2—C12	114.17 (11)	C2—C3—C8—N1	0.24 (14)
C9—C1—C2—C12	−65.18 (16)	C1—N1—C8—C7	177.63 (12)
C1—C2—C3—C4	−178.83 (12)	C1—N1—C8—C3	−1.77 (14)
C13—C2—C3—C4	−58.89 (17)	N1—C1—C9—C10	1.32 (19)
C12—C2—C3—C4	64.25 (17)	C2—C1—C9—C10	−179.42 (11)
C1—C2—C3—C8	1.10 (12)	N1—C1—C9—C11	178.96 (11)
C13—C2—C3—C8	121.04 (11)	C2—C1—C9—C11	−1.8 (2)
C12—C2—C3—C8	−115.82 (11)	C1—C9—C10—O1	−4.9 (2)
C8—C3—C4—C5	0.09 (18)	C11—C9—C10—O1	177.36 (12)
C2—C3—C4—C5	−179.98 (12)	C1—C9—C11—O2	178.99 (12)
C3—C4—C5—C6	−0.88 (19)	C10—C9—C11—O2	−3.28 (19)
C4—C5—C6—C7	0.9 (2)		

Hydrogen-bond geometry (Å, º)

D—H···*A*	*D*—H	H···*A*	*D*···*A*	*D*—H···*A*
N1—H1*N*···O1	0.858 (16)	2.075 (16)	2.7021 (15)	129.3 (13)
N1—H1*N*···O2ⁱ	0.858 (16)	2.157 (16)	2.8254 (15)	134.4 (14)

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