

Unexpected dipivaloylation of 9-lithiated fluorene: formation of 1-(fluoren-9-ylidene)-2,2-dimethylpropyl pivalate

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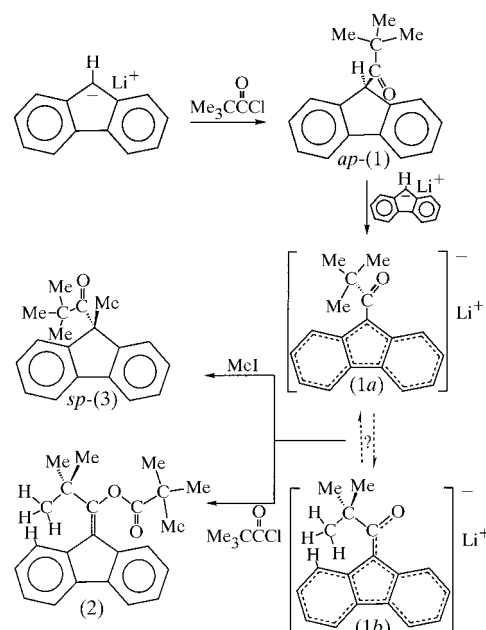
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Treatment of 9-lithiated fluorene with pivaloyl chloride provided *ap*-9-pivaloylfluorene, (1), the major product, and a minor product ultimately identified as the title compound, C₂₃H₂₆O₂, (2). The latter was also formed directly, but slowly, from 9-lithiated-(1) treated with pivaloyl chloride. Although (1) exists exclusively as its less sterically restricted *ap* rotamer, its *sp*²-hybridized anion sterically impedes reaction at the 9-position from either face. While 9-lithiated-(1) is exclusively, but slowly, 9-methylated with methyl iodide, reaction with pivaloyl chloride, also slow, leads only to the O-acylated product, (2). The protons of the *tert*-butyl-C=C moiety approach a proton on the fluorene ring to well within the sum of their van der Waals radii, resulting in significant molecular compression, strain and distortion. For example, distortion in the moiety C=C(O)(C) is exhibited by the enlargement of C=C—C angle to 130.6(2)° at the expense of the corresponding 'equivalent' C=C—O angle, which is compressed to 116.46(19)°.

Comment

9-Pivaloylfluorene, (1), exists as a rotamerically specific compound, the *ap* configuration being exclusive both in the solution and crystalline forms on steric grounds (Meyers *et al.*, 1991). Its lithiated anion, (1a), is sterically hindered to attack, kinetically retarding methylation, which is also retarded thermodynamically by the steric hindrance associated with both of the potentially produced 9-methylated rotamers. Thus, our initial attempts to methylate 9-Li-(1) with CH₃I or (CH₃)₂SO₄ in ether failed (Manohar, 1986; Meyers & Manohar, 1987; Meyers *et al.*, 1993, 1989, 1992; Meyers, 1990). Methylation was successful, but slow, when carried out at higher temperatures with CH₃I in tetrahydrofuran (THF), and

provided exclusively the lesser sterically hindered *sp* rotamer of 9-methyl-9-pivaloylfluorene, (3) (Meyers *et al.*, 2000).



Generally, diacylation of the 9-fluorenyl anion is difficult to avoid. The initially formed 9-acylfluorene, being many powers of 10 more acidic than fluorene (Bordwell & Harrelson, 1987; Bordwell & Satish, 1993), rapidly transfers its residual 9-H to the 9-fluorenyl anion, and the resulting 9-acyl-9-fluorenyl anions, which are commonly enolic, are subsequently C- and O-acylated (*cf.* Naik *et al.*, 1988; Rouzaud *et al.*, 1965; Von & Wagner, 1944; Miller & Bachman, 1935; Greenhow *et al.*, 1953; Scherf & Brown, 1961). Caine (1979) has reviewed C- versus O-acylations and alkylations of metallated ketone enolates.

In light of the difficulty in methylating (1) and the fact that the pivaloyl group is much bulkier than simple alkyl or acyl groups, dipivaloylation of (1) was considered improbable. In an earlier study (Meyers *et al.*, 1991), THF solutions of 9-fluorenyllithium and an equivalent of pivaloyl chloride were maintained at *ca* 200 K under argon for a period of time and then allowed to warm up slowly prior to work-up. We isolated *ap*-(1) (*ca* 60% yield) and fluorene as the 'exclusive' products, although thin-layer chromatography (TLC) indicated trace amounts of another product. When pivaloyl chloride was added to the 9-fluorenyllithium-THF solution at a temperature of *ca* 253 K, which was then allowed to rise to 273 K prior to work-up, the other product, previously detected by TLC, was isolated in larger amounts. It was unequivocally characterized as the title compound, (2), the exclusive dipivaloylation product (Fig. 1 and Scheme). That the formation of (2) is quite sensitive to the reaction conditions is demonstrated by the fact that in several attempts to prepare it directly from the reaction of 9-Li-(1) with pivaloyl chloride in THF solution at 200 K under argon, the usual result was exclusive recovery of (1) on work-up. When the pivaloyl chloride was added after the 9-Li-(1)/THF solution had warmed to *ca* 250 K and slowly allowed to reach and remain at room temperature, at least 20% yield of (2) was obtained.

The X-ray study shows that (2) is a compressed and distorted molecule, which is apparent from Fig. 1 and quantitatively expressed by the selected geometric parameters in Table 1. The major source of the distortion derives from the impinging of the fluorene ring on the C18 and C19 methyl groups, the distance between H8 and H19A of only 2.01 Å, and that between H8 and H18C of 2.04 Å, being well within the sum of the van der Waals radii. As a result, angle C9—C10—C16 is 14.1 (4)° larger than the corresponding angle C9—C10—O1; angle C8a—C9—C10 is 4.9 (4)° greater than its corresponding angle C9a—C9—C10; angle C18—C16—C19 is forced to be 7.6 (4) and 6.6 (4)° larger, respectively, than the corresponding angles C17—C16—C19 and C17—C16—C18; and the skeletal planarity associated with sp^2 -hybridized C atoms is reduced, torsion angles C8a—C9—C10—C16 and C9a—C9—C10—C16, respectively, being 4.3 (4) and 4.4 (2)° away from planarity compared with the corresponding torsion angles C9a—C9—C10—O1 and C8a—C9—C10—O1, which reflect almost perfect planarity.

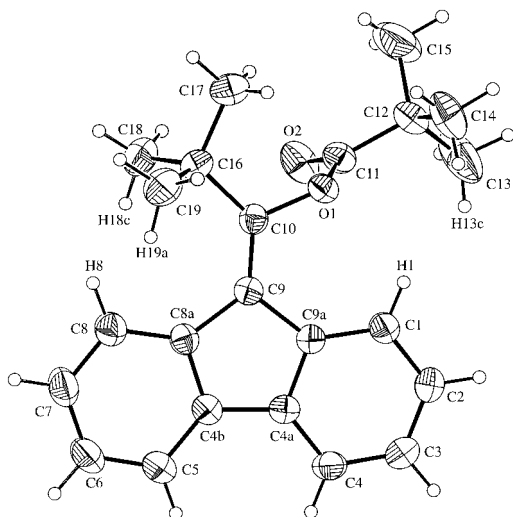


Figure 1
The molecular structure and atom-numbering scheme for (2) with displacement ellipsoids at the 30% probability level.

The pK_a in dimethyl sulfoxide of 14.0 for (1) compared to 10.8 for 9-acetylfluorene and 22.6 for fluorene (Bordwell & Harrelson, 1987; Bordwell & Satish, 1993) suggests that, for steric reasons, the (1)-anion has little enolate structure, *i.e.* it is better represented by (1a) than (1b). This suggestion led Bordwell to say, '...Your 9-pivaloylfluorene is exceptional; evidently overlap of the p orbital of the C=O bond with the radical is almost completely inhibited', and '...The negligible change in bond dissociation energy for 'BuC=O indicates that the C=O bond in the radical is orthogonal to the p orbital holding the odd electron. The 4 pK_{HA} -unit increase *versus* PhC=O shows that the 9-pivaloylfluorene anion is being stabilized only by a field/inductive effect'. If enolate anion (1b) does not exist, the reaction of 9-Li-(1) with pivaloyl chloride leading to (2) may involve non-enolate anion (1a) and a non-nucleophilic electron-transfer mechanism.

Experimental

Preparation of (2): method *A*, from fluorene. To a stirred solution of fluorene (MCB; 2.095 g, 12.63 mmol) in freshly distilled THF (12.5 ml) in a flame-dried three-necked round-bottomed flask maintained under argon and cooled to 210 K, a molar equivalent of *n*-BuLi (Aldrich; in hexane) was added using a syringe. The orange-brown suspension that formed was stirred for 20 min while the temperature was allowed to rise to 253 K. Pivaloyl chloride (Sigma; 1.93 g, 16.0 mmol) in a few ml of THF was then added using a syringe; the mixture immediately transformed into a clear yellow solution. After 20 min, the cooling bath was removed and stirring was continued for 90 min at room temperature. Column chromatography: fraction 1, *ca* 50% recovery of fluorene; fraction 2, an unidentified product; fraction 3, *ca* 40 mol% of (1). The unidentified product melted at 402–403 K (uncorrected). Recrystallization from hexane provided thick colorless monoclinic crystals, m.p. 404–405 K (uncorrected, no decomposition), characterized as (2) by X-ray diffraction. IR (concentrated chloroform): 1745 cm^{-1} (*s*), C—O—C=O; 1172, 1158 (*m*, doublet), 1120, 1110 (*s*, doublet), and 1080 (*s*), C—O—C=O. NMR (Varian VXR 300, 300 MHz 1H , 75 MHz ^{13}C , $CDCl_3$), 1H : δ 1.58 [*s*, 9H, C=CC(CH₃)₃], 1.47 [*s*, 9H, OC(O)C(CH₃)₃]; ^{13}C : δ 177.0 (O—C=O), 161.0 (C=C—O), 141.0 (C=C—O), 39.5 and 37.5 (C12 and C16), 29 and 28 (C17,18,19 and C13,14,15). Method *B*, from *ap*-9-pivaloylfluorene, (1). General procedure, example: to a solution of (1) in anhydrous THF maintained under argon at about 200 K, a molar equivalent of *n*-BuLi in hexane was added using a syringe. The stirred solution was allowed to warm to 250 K, a molar equivalent of pivaloyl chloride was added, and the cooling bath was removed. The mixture slowly reached room temperature. Work-up as described above provided (2) along with recovered (1). Yields of (2) depended on reaction time, but were at least 20% for relatively short periods.

Crystal data

$C_{23}H_{26}O_2$
 $M_r = 334.44$
Monoclinic, $P2_1/n$
 $a = 11.1247$ (15) Å
 $b = 10.4604$ (10) Å
 $c = 16.6259$ (14) Å
 $\beta = 93.951$ (9)°
 $V = 1930.1$ (4) Å³
 $Z = 4$

$D_x = 1.151$ Mg m⁻³
Mo $K\alpha$ radiation
Cell parameters from 24 reflections
 $\theta = 18.8$ – 20.9 °
 $\mu = 0.072$ mm⁻¹
 $T = 296$ K
Prism, colorless
 $0.54 \times 0.49 \times 0.43$ mm

Data collection

Rigaku AFC-5S diffractometer
 ω scans
3589 measured reflections
3401 independent reflections
2019 reflections with $I > 2\sigma(I)$
 $R_{int} = 0.017$
 $\theta_{max} = 25.01$ °

$h = 0 \rightarrow 13$
 $k = 0 \rightarrow 12$
 $l = -19 \rightarrow 19$
3 standard reflections
every 100 reflections
intensity decay: 0.2%

Refinement

Refinement on F^2
 $R[F^2 > 2\sigma(F^2)] = 0.050$
 $wR(F^2) = 0.153$
 $S = 1.029$
3401 reflections
233 parameters
H-atom parameters constrained
 $w = 1/[\sigma^2(F_o^2) + (0.0734P)^2 + 0.2129P]$
where $P = (F_o^2 + 2F_c^2)/3$

$(\Delta/\sigma)_{max} < 0.001$
 $\Delta\rho_{max} = 0.17$ e Å⁻³
 $\Delta\rho_{min} = -0.16$ e Å⁻³
Extinction correction: SHELXL97 (Sheldrick, 1997)
Extinction coefficient: 0.017 (2)

Table 1
Selected geometric parameters (°).

C8a—C9—C10	129.9 (2)	C10—C16—C17	111.8 (2)
C9a—C9—C10	125.0 (2)	C10—C16—C18	109.6 (2)
C9—C10—C16	130.6 (2)	C10—C16—C19	109.5 (2)
C9—C10—O1	116.46 (19)	C13—C12—C14	108.9 (3)
C18—C16—C19	113.4 (2)	C15—C12—C14	108.9 (3)
C17—C16—C19	105.8 (2)	C15—C12—C13	110.3 (3)
C17—C16—C18	106.8 (2)		
C8a—C9—C10—C16	4.3 (4)	C8—C8a—C9—C9a	−177.8 (3)
C9a—C9—C10—O1	0.6 (3)	C8a—C9—C9a—C1	−176.5 (2)
C9a—C9—C10—C16	−175.6 (2)	C2—C1—C9a—C9	179.1 (2)
C8a—C9—C10—O1	−179.4 (2)		

The rotational orientations of the methyl groups were refined by the circular Fourier method available in *SHELXL97* (Sheldrick, 1997). All H atoms are riding.

Data collection and cell refinement: *MSC/AFC Diffractometer Control Software* (Molecular Structure Corporation, 1996); data reduction: *TEXSAN* (Molecular Structure Corporation, 1997); program(s) used to solve structure: *SHELXS97* (Sheldrick, 1997); program(s) used to refine structure: *TEXSAN* and *SHELXL97*; software used to prepare material for publication: *TEXSAN*, *SHELXL97* and *PLATON* (Spek, 2000).

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Supplementary data for this paper are available from the IUCr electronic archives (Reference: BK1551). Services for accessing these data are described at the back of the journal.

References

- Bordwell, F. G. & Harrelson, J. (1987). Personal communication (CYM).
 Bordwell, F. G. & Satish, A. V. (1993). Personal communication (CYM).
 Caine, D. (1979). *Carbon–Carbon Bond Formation*, Vol. 1, edited by R. L. Augustine, pp. 85–352. New York: Marcel Dekker.
 Greenhow, E. J., White, E. N. & McNeil, D. (1953). *J. Chem. Soc.* pp. 3099–3105.
 Johnson, C. K. (1965). *ORTEP*. Report ORNL-3794. Oak Ridge National Laboratory, Tennessee, USA.
 Manohar, S. K. (1986). MS thesis, Southern Illinois University, USA.
 Meyers, C. Y. (1990). *Symposium on Asymmetric Induction/Organic Synthesis*, American Chemical Society Midwest Regional Meeting, Manhattan, Kansas, USA. Paper No. 113.
 Meyers, C. Y., Chan-Yu-King, R., Wahner, A. P., Carr, S. E. & Robinson, P. D. (1989). *Symposium on Carbanion Chemistry*, Canadian Society of Chemistry, Ottawa, Canada. Abstract No. 12.
 Meyers, C. Y., Lutfi, H. G. A., Carr, S. E., Robinson, P. D., Saha, S. & Hua, D. H. (1992). *Third International Symposium on Carbanion Chemistry*, Gallipoli (Lecce), Italy. Abstracts, paper No. SO 7.
 Meyers, C. Y., Lutfi, H. G., Varol, P., Hou, Y. & Robinson, P. D. (2000). *Acta Cryst.* **C56**. In the press.
 Meyers, C. Y., Lutfi, H. G., Varol, P. & Robinson, P. D. (1993). American Chemical Society National Meeting, Denver, USA. Abstracts, ORGN 345.
 Meyers, C. Y. & Manohar, S. K. (1987). American Chemical Society National Meeting, Denver, USA. Abstracts, ORGN 260.
 Meyers, C. Y., Wahner, A. P., Manohar, S. K., Carr, S. E., Chan-Yu-King, R. & Robinson, P. D. (1991). *Acta Cryst.* **C47**, 1236–1239.
 Miller, H. F. & Bachman, B. (1935). *J. Am. Chem. Soc.* **57**, 766–771.
 Molecular Structure Corporation (1996). *MSC/AFC Diffractometer Control Software*. MSC, 3200 Research Forest Drive, The Woodlands, TX 77381, USA.
 Molecular Structure Corporation (1997). *TEXSAN*. MSC, 3200 Research Forest Drive, The Woodlands, TX 77381, USA.
 Naik, S. N., Pandey, B. & Ayyangar, N. R. (1988). *Synth. Commun.* **18**, 625–632.
 Rouzaud, J., Cauquil, G. & Boyer, J. (1965). *Bull. Soc. Chim. Fr.* pp. 2345–2353.
 Scherf, G. W. H. & Brown, R. K. (1961). *Can. J. Chem.* **39**, 1613–1618.
 Sheldrick, G. M. (1997). *SHELXS97* and *SHELXL97*. University of Göttingen, Germany.
 Spek, A. L. (2000) *PLATON*. University of Utrecht, The Netherlands.
 Von, I. & Wagner, E. C. (1944). *J. Org. Chem.* **9**, 155–169.