Ethoxycarbonylation of the 7-Methylpyrrolotetrazolide Ion Revisited

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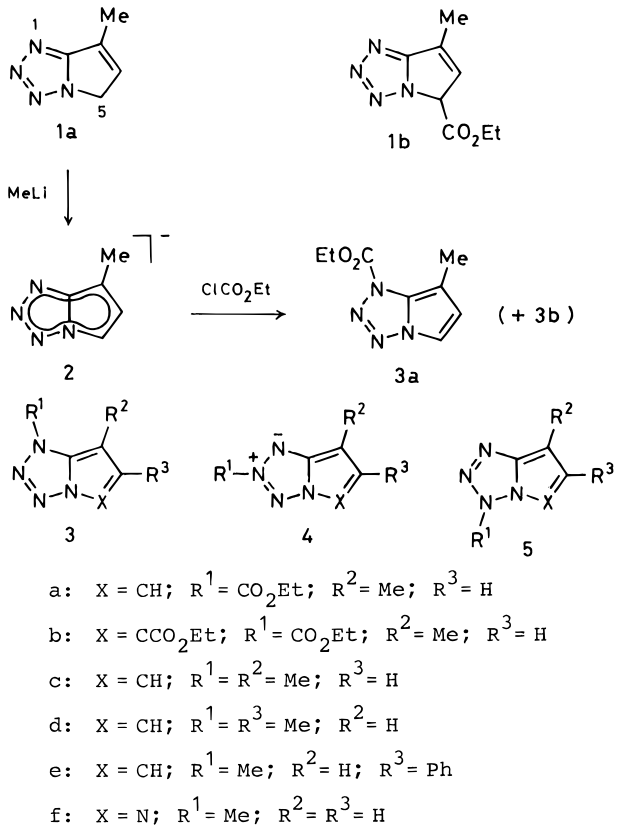
In a recent study on the alkylation and acylation of certain polyazapentalenide ions Dulcere and co-workers[1] reported that treatment of the title anion **2** with ethyl chloroformate led to an acyl derivative that they believed was compound **1b**. Because of our current interest in pyrrolotetrazole chemistry,[2] we looked at this result more closely and found that some of the published characterization data[1] are scarcely compatible with the claimed structure: A compound of that kind would require a ^{13}C NMR spectrum akin to that of the starting bicycle **1a** (see Table 1), but the set of peaks provided[1]—δ 10.7 (q), 14.0 (q), 65.1 (t), 102.2 (d), 120.9 (d), 127.7 (s), 147.3 (s), and 165.7 ppm (s)—does not contain a high-field-shifted doublet necessary for the sp^3-hybridized C(5) atom nor does it show a second singlet downfield from δ 160 ppm, which would indicate an ester group attached to that position.

For clarification we repeated the title reaction, assuming that **2** is preferentially *N*-acylated and thus a 10π-aromatic system is formed. Indeed, from a series of experiments we uniformly obtained an isomer of **1b**, viz. **3a** (40% yield), and as a second component we isolated traces of the congener **3b** (Scheme 1).[3] The 1*H*-pyrrolotetrazole structure of these derivatives follows from a comparison of their ^{13}C NMR spectra with that of the model compound **3c**[4] (see Table 1). Chemical shift differences regarding C(5), C(7), and C(7a) as observed with the couple **3a**/**3c** are due to the ethoxycarbonyl ligand at N(1). This acceptor group somewhat inhibits the normal π-electron delocalization so as to shield C(7a)[5] and to deshield C(5) and C(7) relative to **3c**. In compound **3b**, owing to the ester function at C(5), all of the ring carbon atoms are more deshielded than in **3a**.[6] Additional support for the 1*H*-isomeric system present in our acylation products comes from the models **4e**,**f** and **5f**: These compounds, which represent the 2*H*- and 3*H*-series, respectively, are characterized by a low-field-shifted singlet for C(7a). The resonances of **3a**,**b** that appear in that region (i.e., at δ 147.3 and 146.7 ppm), however, do not refer to C(7a) but arise from the N(1)-attached carbonyl groups.[7] It may be added that the formation of a compound of type **5** (i.e. **5a**) by substitution of **2** would have been unlikely for thermodynamic reasons.[8]

Scheme 1



From the foregoing it is consistent to expect that the original ^{13}C NMR data[1] fully match ours found for **3a**. As shown by a final comparison, this is actually the case with six out of eight peaks. Lack of conformity, however, concerns three points: (i) absence of the singlet at δ 90.9 ppm [for C(7)], (ii) quotation of a singlet at δ 165.7 ppm, and (iii) different multiplicity of the signal at δ 127.7 ppm. Perhaps this latter peak stems from compound **3b** as an impurity (see Table 1) and has erroneously been taken for a singlet while the proper singlet at δ 123.5 ppm [for C(7a) of **3a**], which is in fact very small, had been overlooked. The other two shortcomings (i, ii) are not comprehensible in our view.

Experimental Section[11]

Ethoxycarbonylation of the Anion 2. In accordance with ref 1, compound **1a** (0.366 g, 3 mmol) was dissolved in anhydrous THF (7.5 mL) under a nitrogen atmosphere. After the solution was cooled to −60 °C, methyllithium in ether (2.5 mL, 4 mmol) was added. The solution was stirred for 30 min and then allowed to warm to −20 °C and 15 min later again cooled to −60 °C, whereupon ethyl chloroformate (0.5 mL, ca. 5.3 mmol) was added. After gradual warming to −20 °C (within 2 h), the mixture was poured into ice/ether (10 g/30 mL) and the organic layer treated as previously described.[1] Chromatography on silica gel [ether−light petroleum (bp 30−40 °C), 1:1] first gave

(1) Dulcere, J.-P.; Tawil, M.; Santelli, M. *J. Org. Chem.* **1990**, *55*, 571.

(2) (a) Moderhack, D.; Decker, D. *14th International Congress of Heterocyclic Chemistry*, Antwerp, 1993; Abstracts of Papers, PO3-211, and references cited therein. (b) Moderhack, D.; Decker, D. *Heterocycles* **1994**, *37*, 683.

(3) Formed through lithiation of **3a** or of (nondetectable) **1b**.

(4) Prepared from **1a** in analogy to: Babichev, F. S.; Romanov, N. N. *Ukr. Khim. Zh.* **1973**, *39*, 49; *Chem. Abstr.* **1973**, *78*, 111229m. The 1*H*-isomeric structure of **3c** is demonstrated by means of **3d**, which has been made by an unambiguous route (cf. ref 2b).

(5) Compare the influence exerted by an N(1)-attached carbamoyl group on the chemical shift of C(5) in 4,5-dihydro-1*H*-tetrazol-5-ones: Tsuge, O.; Urano, S.; Oe, K. *J. Org. Chem.* **1980**, *45*, 5130.

(6) Cf. Abraham, R. J.; Lapper, R. D.; Smith, K. M.; Unsworth, J. F. *J. Chem. Soc., Perkin Trans. 2* **1974**, 1004.

(7) Cf. Begtrup, M.; Elguero, J.; Faure, R.; Camps, P.; Estopá, C.; Ilavský, D.; Fruchier, A.; Marzin, C.; de Mendoza, J. *Magn. Reson. Chem.* **1988**, *26*, 134.

(8) Ege, G.; Heck, R.; Gilbert, K.; Irngartinger, H.; Huber-Patz, U.; Rodewald, H. *J. Heterocycl. Chem.* **1983**, *20*, 1629.

(9) Moderhack, D.; Holtmann, B. Manuscript in preparation (compound made in analogy to the procedure outlined in ref 2b).

(10) Alcalde, E.; Claramunt, R. M.; Elguero, J.; Saunderson Huber, C. P. *J. Heterocycl. Chem.* **1978**, *15*, 395.

(11) For a synopsis of analytical instruments used, see: Moderhack, D. *Liebigs Ann.* **1996**, 777.

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Table 1. Comparison of ^{13}C NMR Data of Educts 1a and 2, Products 3a,b, and Selected Model Compounds 3c,d, 4e,f, and 5f[a]

compd	C(5)	C(6)	C(7)	C(7a)	Me and/or CO_2Et	ref
1a	50.3 (t)	135.0 (d)	127.9	164.0	12.4 (q)	1
2	90.5 (d)	115.0 (d)	79.1	146.5	12.1 (q)	1
3a	102.2 (d)	120.9 (d)	90.9	123.5	10.7 (q), 14.3 (q), 65.1 (t), 147.3	this work
3b	108.9	127.7 (d)	93.9	128.2	10.9 (q), 14.2 (q), 14.5 (q), 60.6 (t), 65.9 (t), 146.7, 159.0	this work
3c	99.2 (d)	119.4 (d)	83.1	129.6	9.4 (q), 34.4 (q)	this work
3d	99.7 (d)	129.8[b]	74.0 (d)	132.9[b]	13.5 (q), 34.3 (q)	2b[c]
4e	94.2 (d)	135.6[d]	76.2 (d)	147.0	41.2 (q)	9
4f[e]		146.8 (d)	80.8 (d)	149.8[f]	42.4 (q)	10
5f[g]		145.2 (d)	86.6 (d)	152.0	36.1 (q)	8

[a] Spectra were measured in $CDCl_3$ (**1a**, **3a**−**d**, **4e**, **5f**) and DMSO-d_6 (**2**), respectively (solvent for **4f** not mentioned); chemical shifts are in δ relative to internal TMS; unspecified signals are singlets. [b] Discerned by means of a C,H-COLOC experiment. [c] In ref 2b data were omitted. [d] Shift value can be exchanged with 136.7 [C(1) of Ph]. [e] In ref 10 the compound was erroneously viewed as **5f**; the structure was revised in ref 8. [f] Cf. δ 138.4 in the case of 1*H*-isomer **3f** (ref 10; solvent not specified). [g] 3*H*-Pyrrolotetrazoles are still unknown.

1-(ethoxycarbonyl)-7-methyl-1*H*-pyrrolotetrazole (**3a**) (0.230 g; 40%): mp 71−73 °C (plates; chloroform−light petroleum);[12] IR (KBr) 3140, 1745, 1620 cm^{-1}; UV max (MeOH) 228 (lg ϵ = 4.029), 260 (3.614), 349 (3.221) nm; ^1H NMR ($CDCl_3$) δ 1.51 (3, t, J = 7.2 Hz), 2.33 (3, s), 4.59 (2, q, J = 7.2 Hz), 6.50 (1, d, J = 3.0 Hz), 7.11 (1, d, J = 3.0 Hz); ^{13}C NMR (see Table 1); mass spectrum *m*/*e* 195 (10), 194 (100), 150 (21), 149 (13), 122 (89), 93 (49), 67 (82).[13] Anal. Calcd for $C_8H_{10}N_4O_2$: C, 49.48; H, 5.19; N, 28.85. Found: C, 49.52; H, 5.19; N, 28.79. Heating of this material in boiling chloroform for 90 min led to full recovery. Further elution afforded **1,5-bis(ethoxycarbonyl)-7-methyl-1*H*-pyrrolotetrazole** (**3b**) (0.037 g; 4.6%): mp 76−78 °C (prisms; chloroform−light petroleum); IR (KBr) 1775, 1705, 1615 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.40 (3, t, J = 7.1 Hz), 1.54 (3, t, J = 7.1 Hz), 2.35 (3, s), 4.40 (2, q, J = 7.1 Hz), 4.64 (2, q, J = 7.1 Hz), 7.22 (1, s); ^{13}C NMR (see Table 1); mass spectrum *m*/*e* 266 (24), 194 (34), 166 (13), 122 (19), 93 (100). Anal. Calcd for $C_{11}H_{14}N_4O_4$: C, 49.62; H, 5.30; N, 21.04. Found: C, 49.44; H, 5.36; N, 20.62.

Attempted Conversion of 3a into 3b. To the acyl derivative **3a** (0.194 g, 1 mmol), dissolved in anhydrous THF (2.5 mL), was added methyllithium in ether (1.25 mL, 2 mmol) at −60 °C; after the mixture was stirred for 1 h at −20 °C, ethyl chloroformate (0.30 mL, 3.2 mmol) was added at −60 °C and the mixture stirred for another 4 h at this temperature. Workup as described above yielded a crude product that contained **3a** and **3b** in a ratio ca. 85:15 (^1H NMR analysis). Direct treatment of **3a** with ethyl chloroformate (i.e., without prior lithiation) had no effect.

1,7-Dimethyl-1*H*-pyrrolotetrazole (**3c**). A mixture of compound **1a**[1] (0.49 g, 4 mmol) and dimethyl sulfate (2.52 g, 20 mmol) was kept at ambient temperature for 24 h. Then the solution was washed with ether (4 × 20 mL) and the residue diluted with water (10 mL). After careful addition of aqueous sodium carbonate (10 mL, 4 mmol) and another 30 min of standing the product was extracted with dichloromethane (3 × 30 mL). Filtration over silica gel (chloroform−ethyl acetate, 4:1), followed by addition of light petroleum, gave 0.11 g (20%) of the pyrrolotetrazole **3c** as fine needles: mp 55−56 °C; IR (KBr) 3145, 1645 cm^{-1}; ^1H NMR ($CDCl_3$) δ 2.27 (3, s), 4.04 (3, s), 6.49 (1, d, J = 2.8 Hz), 7.04 (1, d, J = 2.8 Hz); ^{13}C NMR (see Table 1); mass spectrum *m*/*e* 136 (100), 107 (80), 93 (53), 80 (64). Anal. Calcd for $C_6H_8N_4$: C, 52.93; H, 5.92; N, 41.15. Found: C, 52.78; H, 6.04; N, 41.28.

The mother liquor of **3c** showed the presence of minor quantities of **2,7-dimethyl-2*H*-pyrrolotetrazole** (**4c**): ^1H NMR ($CDCl_3$) δ 2.34 (3, s), 4.30 (3, s), 6.72 (1, d, J = 2.5 Hz), 7.03 (1, d, J = 2.5 Hz); ^{13}C NMR ($CDCl_3$) δ 10.4 (q), 41.2 (q), 95.2 (d), 121.1 (d) [singlets for C(7) and C(7a) not observed]. Attempts to isolate the compound failed.

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(12) Material described in ref 1 has mp 58−59 °C.
(13) Peaks at *m*/*e* 168 and 143 (quoted in ref 1) were not observed.