STERICALLY CROWDED HETEROCYCLES. V. INCORPORATION OF MELAMINE AND ADENINE MOIETIES INTO IMIDAZO[1,2]HETEROAROMATIC MOLECULES

Richard KUBIK and Josef KUTHAN[1,*]

Department of Organic Chemistry, Prague Institute of Chemical Technology, 166 28 Prague 6, Czech Republic; e-mail: [1] kuthan@vscht.cz

Received December 18, 1995
Accepted January 26, 1996

Melamine and adenine react with 2,4,6-triphenylpyrylium perchlorate to corresponding quaternary pyridinium salts **1** and **2**, respectively. Ferricyanide oxidation of salt **1** in alkaline medium gave (*Z*)-3-(2,4-diamino-7-phenylimidazo[1,2-*a*][1,3,5]triazin-6-yl]-1,3-diphenylprop-2-en-1-one (**3**). Analogous oxidation of perchlorate **2** afforded (*Z*)-3-(8-phenylimidazo[1,2-*f*]-4*H*-purin-7-yl)-1,3-diphenylprop-2-en-1-one (**5**).
Key words: Ferricyanide oxidation; Sterically crowded heterocycles.

Ferricyanide oxidations of quaternary 2,4,6-triphenylpyridinium salts having in the position 1 a pyridin-2-yl-like group have been found to afford sterically crowded, and therefore racemic, imidazo[1,2-*a*]pyridines[1,2] and imidazo[1,2-*a*]pyrimidines[3]. In this communication, some experiments are reported which make possible to use the procedure as a simple approach to two analogous imidazo[1,2-*a*][1,3,5]triazine and imidazo[1,2-*f*]purine derivatives. The former heterocyclic system has been synthesized by several procedures[4] but none of them was an oxidation. Similarly, none of scarce approaches to imidazo[1,2-*f*]purine derivatives[5–7] is based on an oxidative procedure.

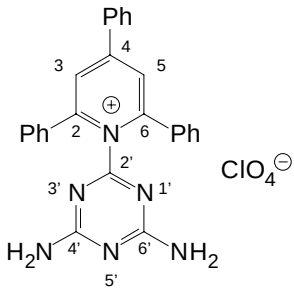
To obtain the starting pyridinium salts **1** and **2** we have applied the generally used procedure based on the ring-opening-ring-closure transformation of pyrylium salts with primary amines[8]. Thus, melamine as well as adenine have been really found to react as typical heteroaromatic primary amines to give expected perchlorates **1** and **2** in good yields by heating with 2,4,6-triphenylpyrylium perchlorate in dimethylformamide.

Application of the ferricyanide oxidation[9] to pyridinium salts **1** and **2** might be considered to be problematic especially in the first case, where oxidizable amino groups are present in the 1-substituent. Hence somewhat surprisingly, expected unsaturated ketones **3** and **4** of (*Z*)-configuration were not only identified but also isolated from the

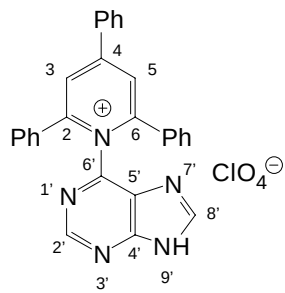
* The author to whom correspondence should be addressed.

reaction mixtures although no special improvement of the original oxidation procedure[10] had to be used. This finding offers a chance to apply the extended Decker oxidation[9] to more structurally variable heterocyclic substrates than it has originally been expected. In addition, the reported incorporation of the melamine and adenine moieties into the fused heterocyclic systems in compounds **3** and **4** may enrich chemistry of the parent compounds[11,12] by a new versatile type of chemical transformations.

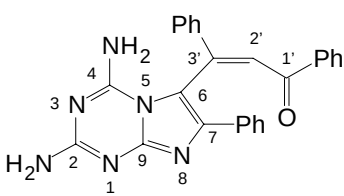
The structures **1**, **2**, **3** and **4** have been assigned to the prepared substances in agreement with their IR, ^{1}H and ^{13}C NMR spectra as well as correct elemental analyses. However, different tautomers could not unambiguously recognized by the identification methods and all prepared compounds have been drawn only in one of their more probable tautomeric forms[4,11–13].



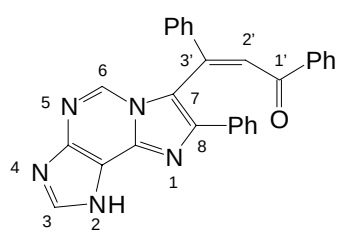
1



2



3



4

EXPERIMENTAL

The temperature data are uncorrected. Melting points were determined on a Boetius block. NMR spectra (δ, ppm; *J*, Hz) were taken on a GEMINI 300 HC instrument at 297 K in hexadeuteriodimethyl sulfoxide unless stated otherwise. The working frequency was 300 MHz for ^{1}H and 75 MHz for ^{13}C. IR spectra ($\tilde{\nu}$, cm^{-1}) were measured on a FTIR NICOLET 740 spectrometer.

1-(4,6-Diamino[1,3,5]triazin-2-yl)-2,4,6-triphenylpyridinium Perchlorate (**1**)

A mixture of 2,4,6-triphenylpyrylium perchlorate[14] (2.0 g, 4.9 mmol) and melamine (0.65 g, 5.2 mmol) in dry dimethylformamide (10 ml) was refluxed for 45 min. After cooling the crude salt was precipitated with water (100 ml) and recrystallized from ethanol (charcoal). Yield 2.0 g (79%) of perchlorate **1**, m.p. 308–310 °C. For $C_{26}H_{21}ClN_6O_4$ (516.9) calculated: 60.41% C, 4.09% H, 16.26% N; found: 60.27% C, 4.32% H, 16.08% N. ^{1}H NMR spectrum: 7.30 brs, 2 H (NH_2); 7.33 brs, 2 H (NH_2); 7.51–7.76 m, 13 H (Ph2, Ph6 and *m*,*p*-Ph4); 8.35 d, 2 H, *J* = 7.7 (*o*-Ph4); 8.65 s, 2 H (H-3 and H-5). ^{13}C NMR spectrum: 125.54 CH (C-3 and C-5), 128.45 CH (*m*-Ph2 and *m*-Ph6), 129.13 CH (*o*-Ph4), 129.36 CH (*o*-Ph2 and *o*-Ph6), 129.54 CH (*m*-Ph4), 131.04 CH (*p*-Ph2 and *p*-Ph6), 131.82 C (*i*-Ph2 and *i*-Ph6), 132.76 CH (*p*-Ph4), 133.31 C (*i*-Ph4), 153.51 C (C-2 and C-6), 156.69 C (C-4), 164.48 C (C-2′), 166.51 C (C-4′ and C-6′).

2,4,6-Triphenyl-1-[9(7)*H*-purin-6-yl]pyridinium Perchlorate (**2**)

Reaction of 2,4,6-triphenylpyrylium perchlorate[14] (2.0 g, 4.9 mmol) and adenine (0.7 g, 5.2 mmol) was performed in the same way as mentioned above but the reaction time was only 15 min. Yield 2.2 g (85%) of perchlorate **2**, m.p. 217–220 °C (ethanol). For $C_{28}H_{20}ClN_5O_4$ (526.0) calculated: 63.94% C, 3.83% H, 13.22% N; found: 63.70% C, 3.85% H, 12.94% N. ^{1}H NMR spectrum: 3.4 brs (NH); 7.24–7.45 m, 10 H (Ph2 and Ph6); 7.66–7.79 m, 3 H (*m*,*p*-Ph4); 8.43 d, 2 H, *J* = 7.2 (*o*-Ph4); 8.76 s, 1 H (H-2′ or H-8′); 8.81 s, 1 H (H-2′ or H-8′); 8.84 s, 2 H (H-3 and H-5). ^{13}C NMR spectrum: 125.69 CH (C-3 and C-5), 129.15 CH (*m*-Ph2 and *m*-Ph6), 129.24 CH (*o*-Ph2 and *o*-Ph6), 129.33 CH (*o*-Ph4), 129.66 CH (*m*-Ph4), 130.83 CH (*p*-Ph2 and *p*-Ph6), 131.34 C (*i*-Ph2 and *i*-Ph6), 133.09 CH (*p*-Ph4), 133.21 C (*i*-Ph4), 155.41 C (C-2 and C-6), 157.73 C (C-4). Three additional signals were recognized provided the recording time was increased. Two of those (106.86 and 150.93) were of extremely low intensities and the third one (149.14) was broad probably due to a tautomerism.

(*Z*)-3-(2,4-Diamino-7-phenylimidazo[1,2-*a*][1,3,5]triazin-6-yl)-1,3-diphenylprop-2-en-1-one (**3**)

A solution of potassium ferricyanide (2 g, 6.1 mmol) and potassium hydroxide (0.5 g, 8.9 mmol) in water (10 ml) was added to a boiling suspension of perchlorate **1** (1 g, 1.9 mmol) and ethanol (50 ml). The reaction mixture was stirred under reflux for 15 min and then poured to ice–water (150 ml) and extracted with chloroform (4 × 40 ml). The collected organic layers were washed with water (100 ml), dried with sodium sulfate and evaporated. The residue was chromatographed on a silica gel column (50 g silica gel) in acetone. Fractions containing ketone **3** were collected, evaporated and the crude product was recrystallized from ethanol; yield 0.35 g (42%) of yellow crystals, m.p. 270–272 °C. For $C_{26}H_{20}N_6O$ (432.5) calculated: 72.21% C, 4.66% H, 19.43% N; found: 72.24% C, 4.69% H, 19.32% N. ^{1}H NMR spectrum: 6.55 brs, 2 H (2- or 4-NH_2); 6.93 brs, 2 H (2- or 4-NH_2); 7.05–7.19 m, 7.34–7.68 m, 7.91–7.99 m, 16 H (H-2′, Ph1′, Ph3′ and Ph7). ^{13}C NMR spectrum: 112.67 C (C-7), 127.09 CH, 127.12 CH, 127.78 CH, 128.02 CH, 128.18 CH, 128.22 CH, 128.48 CH, 128.75 CH, 130.16 CH, 132.82 CH, 133.69 C, 137.79 C, 138.62 C, 141.24 C and 141.69 C (C-3′ and C-6), 151.32 C and 152.83 C (C-2 and C-4), 160.56 C (C-9), 189.14 C (C-1′). IR spectrum (KBr): 3 443 and 3 321 (NH), 1 643 (C=C–C=O).

(*Z*)-3-(8-Phenylimidazo[1,2-*f*]-4*H*-purin-7-yl)-1,3-diphenylprop-2-en-1-one (**4**)

A solution of potassium ferricyanide (1.0 g, 3.0 mmol) and potassium hydroxide (0.25 g, 4.5 mmol) in water (5 ml) was added to a boiling suspension of perchlorate **2** (0.5 g, 0.95 mmol) and ethanol (25 ml). The reaction mixture was stirred under reflux for 15 min and then poured to ice–water (100 ml), acidified with concentrated hydrochloric acid to pH 8–9 and extracted with chloroform (3 × 25 ml).

The collected organic layers were washed with water (75 ml), dried with sodium sulfate and evaporated at diminished pressure. The residue was chromatographed on a silica gel column (40 g silica gel, dichloromethane–acetone 3 : 1). Fractions containing ketone **4** were collected, evaporated at diminished pressure and the crude product was dissolved in a minimum amount of diethyl ether. The solution was allowed to stand for 24 h, the formed orange crystals were sucked off and dried in vacuo, yield 0.25 g (60%) of ketone **4**, m.p. 164–166 °C. For $C_{28}H_{19}N_5O$ (441.5) calculated: 76.18% C, 4.34% H, 15.86% N; found: 75.96% C, 4.42% H, 15.65% N. ^{1}H NMR spectrum ($CDCl_3$): 6.80 brs, 1 H (NH); 7.21–7.33 m, 6 H (*m*,*p*-Ph8, *m*,*p*-Ph3′); 7.34–7.56 m, 4 H (H-2′ and *m*,*p*-Ph1′); 7.51 dd, 2 H, J = 7.5 and ≈1.7 (*o*-Ph3′); 7.56–7.62 m, 2 H (*o*-Ph8); 7.63 s, 1 H (H-3); 7.69 d, 2 H, J = 7.2 (*o*-Ph1′); 8.46 s, 1 H (H-6). ^{13}C NMR spectrum ($CDCl_3$): 118.23 C (C-8), 128.17 CH, 128.61 CH, 128.95 CH, 129.33 CH, 129.38 CH, 129.54 CH, 129.60 CH, 130.02 CH, 131.41 CH, 132.68 C, 133.58 CH, 138.02 C, 139.21 C, 140.80 C, 145.13 C, 190.76 (C-1′). Increasing of the recording time resulted in the observation of five additional signals (104.84, 113.45, 134.65, 138.15 and 150.06) but their assignment to C or CH was imposible because of too low intensities. IR spectrum ($CHCl_3$): 3 104 (NH), 1 661 (C=C–C=O).

This work was supported within the project No. 203/93/0320 of the Grant Agency of the Czech Republic. The authors are indebted to the staff of Central Laboratories (Prague Institute of Chemical Technology) for the elemental analyses and measurement of IR spectra.

REFERENCES

1. Bohm S., Kubik R., Hradilek M., Nemecek J., Husak M., Kratochvil M., Kuthan J.: Collect. Czech. Chem. Commun. *60*, 115 (1995).
2. Kubik R., Bohm S., Ruppertova I., Kuthan J.: Collect. Czech. Chem. Commun. *61*, 126 (1996).
3. Bohm S., Kubik R., Novotny J., Ondracek J., Kratochvil B., Kuthan J.: Collect. Czech. Chem. Commun. *56*, 2326 (1991).
4. Montgomery J. A., Secrist J. A., III in: *Comprehensive Heterocyclic Chemistry* (K. T. Potts, Ed.), Vol. 5, Part. 4A, p. 657. Pergamon Press, Oxford 1984.
5. Chheda G. B., Hall R. H.: Biochemistry *5*, 2082 (1966).
6. Shaw G., Smallwood B. M.: J. Chem. Soc., C *1970*, 2206.
7. Sattsangi P. D., Barrio J. R., Leonard N. J.: J. Am. Chem. Soc. *102*, 770 (1980).
8. Balaban A. T., Dinculescu A., Dorofeenko G. N., Fischer G. W., Koblik A. V., Mezheritskii V. V., Schroth W.: Adv. Heterocycl. Chem., Suppl. *2* (1982).
9. Kuthan J.: Heterocycles *37*, 1347 (1994).
10. Nesvadba P., Kuthan J.: Collect. Czech. Chem. Commun. *47*, 1494 (1982).
11. Shaw G. in: *Comprehensive Heterocyclic Chemistry* (K. T. Potts, Ed.), Vol. 5, Part 4A, p. 499. Pergamon Press, Oxford 1984.
12. Quirke J. M. E. in: *Comprehensive Heterocyclic Chemistry* (A. J. Boulton and A. McKillop, Eds), Vol. 3, Part 2B, Section 2.20.3.8, p. 475. Pergamon Press, Oxford 1984; and references therein.
13. Elguero J., Marzin C., Katritzky A. R., Linda P.: Adv. Heterocycl. Chem., Suppl. *1*, 502 (1976).
14. Allan J. A., Reynolds G. A.: J. Org. Chem. *33*, 1102 (1968).