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Spirally twisted imidazolium iminyl ylide structures from 1,2-rearrangements in reactions of imidazolium dicyanomethanide 1,3-dipoles with maleic anhydride: new perspectives on the Boekelheide–Fedoruk ring expansions

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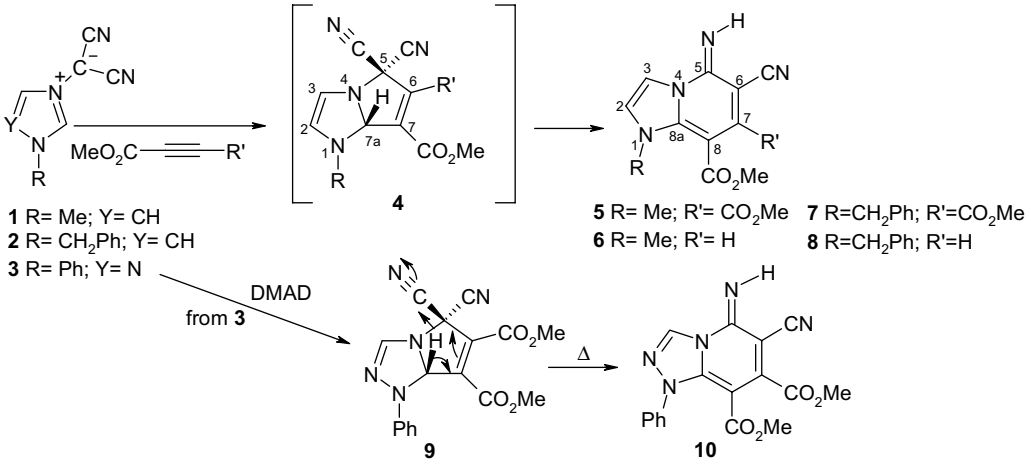
Abstract—The reactions of 1-substituted-imidazolium-3-dicyanomethanides with maleic anhydride gave new ylide products from a Michael reaction and 1,2-rearrangements. These experiments, combined with theoretical calculations, provide an interesting new perspective on the Boekelheide–Fedoruk ring expansions.

1. Introduction

The reaction of 1-substituted imidazolium dicyanomethanides **1** with dimethyl acetylenedicarboxylate (DMAD), which gives imidazo[2,3-*a*]pyridines **5** by an interesting ring-expansion of the cycloadducts **4**, was first reported by Boekelheide and Fedoruk (Scheme 1).[1] Our interest in azinium dicyanomethanides[2] attracted us to this rearrangement which we feel merits revisiting. Earlier it was thought that such



Scheme 1.

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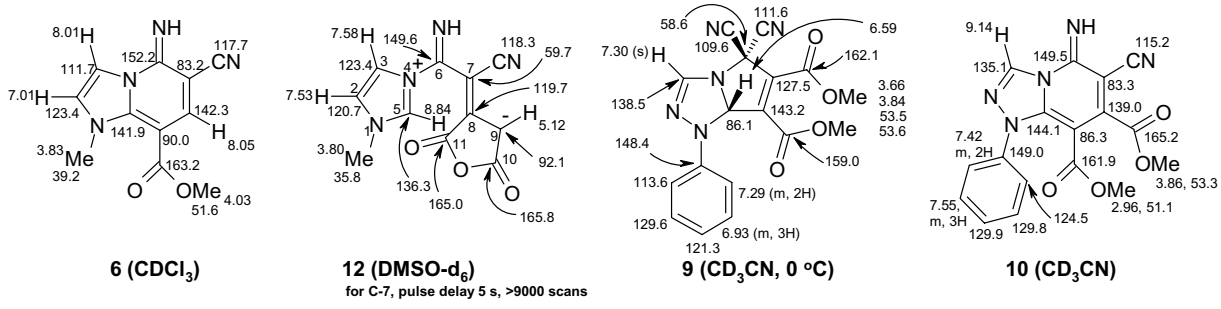


Figure 1. Proton and carbon-13 NMR signals (JEOL GXFT-400), assignments supported by DEPT, NOEDS and calculated[8] shifts.

ring-expansion rearrangements occurred in the 6,5-fused ring cycloadducts of azinium-*N*-dicyanomethanides[3] but this proved not to be the case.[4] The proposed mechanism of the ring expansion **4**→**5** involved anion formation by loss of the bridgehead H(7a) proton, cleavage of the N(4)–C(5) bond and attack by the N-(4) anion on the nitrile carbon, that is, a conjugated E1cb type process followed by a 6-*exo-dig* ring closure. Herein, from new results using maleic anhydride (MA) as the dipolarophile, we show that, (i) the bridgehead H-(7a) proton is not necessary for the rearrangement and, (ii) the ring-expansion is not a necessary part of the rearrangement. To date the only cycloadduct intermediate isolated[5] in these ring expansion reactions has been the unstable species **9** from Huisgen cycloaddition of the 1,2,4-triazolium substrate **3** with DMAD. Thiazolium *N*-dicyanomethanides react with alkenes to give stable saturated cycloadducts,[6] such as **13** (S instead of NMe).

2. Results

We have prepared compounds **5**–**10**, including the new examples **6**–**8** and confirmed their structures by proton and carbon-13 NMR spectra (Fig. 1). The structures of compounds **5**–**8** and **10** have a characteristic structural signature, an embedded enediamine unit (atoms C-8, C-8a, N-1, N-4) which causes exceptional deshielding of the enamine α-carbon (C-8a, 140–150 ppm in carbon-13 NMR) and exceptional shielding of the enamine β-carbon (C-8, 80–90 ppm) due to the resonance forms. When we used *N*-phenylmaleimide (NPM) the initial cycloadduct **13**, underwent in situ oxidation and rearranged to the ring-expanded product **14** (77%) (Scheme 2). An X-ray structure[7] of the orange plate-like crystals of **14** (mp >300 °C, from MeCN) showed a flat molecule with the 5-imino proton *syn* coplanar with the 6-cyano group at a distance of 2.809 Å from the triple bond (Fig. 2). With maleic anhydride (MA) as the dipolaro-

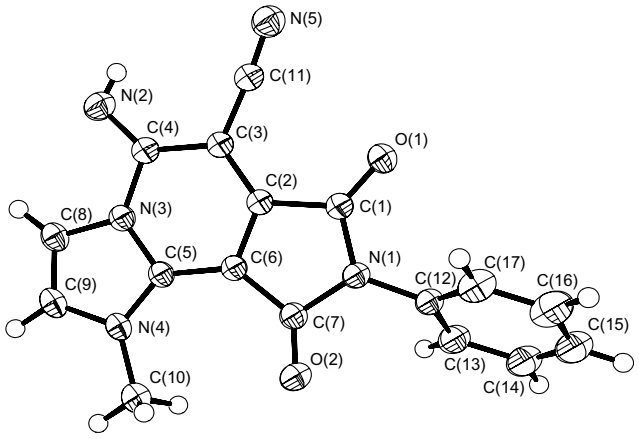
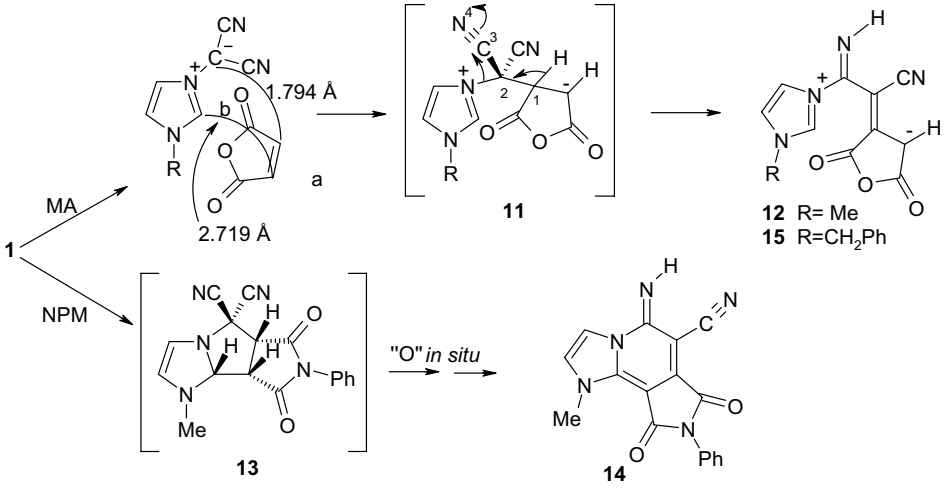
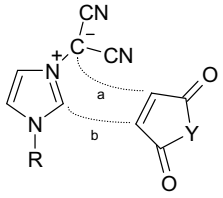


Figure 2. X-ray crystal structure of **14**.



Scheme 2.

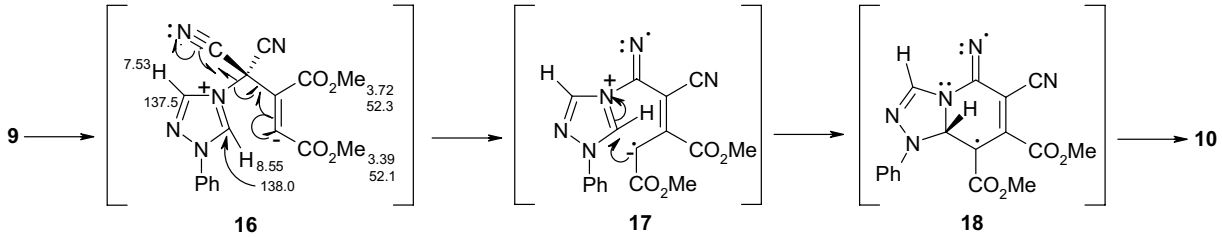
Table 1. Calculated reaction energies (ΔE_R), activation energies (E_a) and distances[8]



Entry		Cycloaddition reaction		Cycloadducts		Transition states		
	Y		ΔE_R (kJ mol^{-1})	*a* (Å)	*b* (Å)	E_a (kJ mol^{-1})	*a* (Å)	*b* (Å)
1	O	*endo*	−5.94	1.600	1.633	44.6	1.794	2.719
2	O	*exo*	−5.95	1.603	1.604	57.38	2.050	2.132
3	O	E_{diff}	0.01	—	—	−12.78	—	—
4	O	*exo*/*endo*	1.00	—	—	0.01	—	—
5	NH	*endo*	−18.12	1.596	1.618	52.77	1.914	2.430
6	NH	*exo*	−25.53	1.597	1.592	54.90	2.194	2.046
7	NH	E_{diff}	6.41	—	—	−2.13	—	—
8	NH	*exo*/*endo*	12.02	—	—	0.44	—	—
9	NPh	*endo*	−17.81	1.598	1.620	49.43	2.122	2.100
10	NPh	*exo*	−23.00	1.595	1.592	56.89	2.193	2.056
11	NPh	E_{diff}	5.19	—	—	−7.46	—	—
12	NPh	*exo*/*endo*	7.48	—	—	0.06	—	—

phile, the reaction changed to a potentially two step cycloaddition but the second step failed to complete. The products were the ylides **12** and **15** in which the 1,2-rearrangement has still occurred (Scheme 2, Fig. 1). The NMR spectra of these products clearly showed the simple intact imidazolium unit, the imine unit bonded to the imidazole N-3 and the altered maleic anhydride unit (Fig. 1). This rearrangement may be a 1,2-sigmatropic process, but it could also parallel the Stevens rearrangement which involves short lived caged diradicals.

The products **12** and **15** were initially stable at ambient temperature but on standing, they decomposed to imidazole-containing gums. Theoretical calculations[8] of the transition state for their formation suggest that the structures are twisted so that the maleic anhydride unit spirals under the imidazolium ring. Calculated[8] transition states for the reactions of compound **1** with maleic anhydride, maleimide and *N*-phenylmaleimide (NPM) are shown in Table 1. For NPM the reaction is a normal Huisgen cycloaddition with both new bonds *a* and *b* almost equally developed in the transition state (*a*, 2.122 Å; *b*, 2.100 Å) and a favoured *endo* stereochemistry (Table 1, entries 9 and 10). With maleic anhydride the results are quite different. The activation energy E_a is significantly lower for the favoured *endo* approach where only one bond is formed, *a*, 1.794 Å versus *b*, 2.719 Å (Table 1, entry 1 and Scheme 2). The normal 1,3-dipolar cycloaddition where both new bonds a and b are well formed (Table 1, entry 2) for maleic anhydride has Ea 12.78 kJ higher and involved an *exo*-approach. Hence, the experimental and theoretical results are in good agreement. Effectively, with maleic anhydride the reaction has changed to a Michael reaction but the Boekelheide–Fedoruk type rearrangement has still occurred.[9] A possible, but now unlikely sigmatropic ring expansion mechanism is shown by the arrows in **9** (Scheme 1). The NMR data for compound **9** (Fig. 1) were measured at 0 °C in CD_3CN. The temperature was then raised to that of the probe (19 ± 1 °C) and proton spectra were measured at 30 min intervals, with C-13 spectra being accumulated between the intervals, over 16 h. The signals for **9** declined while those of **10** grew. In addition an intermediate, showing four simple singlet signals (which appeared at δH 8.55, 7.53, 3.72 OMe, 3.39 OMe, with 8.55 drifting upfield) was seen to develop, reaching a maximum at ca. 6 h, and then decline and disappear as the spectra fully changed to **10**. This intermediate was also seen to develop and decline in the C-13 NMR spectra but due to the large number of close and overlapping signals, assignments were tenuous. The C-13 signals which we believe to be associated with the proton signals are shown in structure **16** (Scheme 3).



Scheme 3.

We tentatively suggest that the intermediate may be the ylide **16** resulting from cleavage of the C(7)–C(7a) bond of **9**. In parallel to the formation of **12** and **15**, this may undergo 1,2-rearrangement to the ylide diradical **17** which ring closes (RORC) and aromatises to **10** (Scheme 3).

3. Conclusion

The mechanism of the thermal ring expansions of the unstable Huisgen cycloadducts formed in the reactions of azolium-*N*-dicyanomethanide 1,3-dipoles with alkyne dipolarophiles has been reassessed. The most likely mechanism is heterolysis of the C7–C7a bond generating a ylide intermediate, possessing resonance-stabilised termini, which undergoes 1,2-rearrangement followed by ring closure.

Acknowledgements

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7. Crystal structure determination for structure **14**. Crystal data, $C_{17}H_{11}N_5O_2$, $M = 317.31$, monoclinic, $a = 7.134(2)$, $b = 24.240(2)$, $c = 8.589(2)$ Å, $\beta = 93.23(5)°$, $V = 1482.9(6)$ Å^3, space group $P21/a$, $Z = 4$, Dc 1.421 Mg/m^3, $\mu = 0.099$ mm^{-1}, $F(000) = 656$, unique reflections = 2789 [R(int) = 0.0155], observed $I > 2\sigma I = 1838$, data/restraints/parameters = 2789/219. The final $R_1 = 0.0734$ and $wR_2 = 0.1232$ (all data). Crystallographic data (excluding structure factors) for the structures in this paper have been deposited with the Cambridge Crystallographic Data Centre as supplementary publication number CCDC 601383. Copies of the data can be obtained, free of charge, on application to CCDC, 12 Union Road, Cambridge CB2 1EZ, UK [fax: +44 (0)1223336033 or e-mail: deposit@ccdc.cam.ac.uk].
8. *Theoretical calculations*: All geometry optimisations used the B3LYP/6-31G(d) theoretical method and analytical frequencies to characterise minima, as found in Gaussian03. The computer output can be obtained at http://camchem.rutgers.edu/~burke as well as calculated NMR chemical shifts.
9. Typical examples: *Synthesis of 1-methyl-imidazolium-3-dicyanomethanide* **1.**

To a solution of tetracyanoethylene oxide (TCNEO) (1.74 g, 12.1 mmol) in ethyl acetate (15 ml) at 0 °C, 1-methylimidazole (0.96 ml, 12.1 mmol), neat or in EtOAc (3.0 ml), was added dropwise with stirring. When the addition was complete, a pale brown solid separated from the solution. The product **1** (1.15 g, 65%), mp 143–144 °C (from ethanol using Norit) was filtered off and washed with cold ethyl acetate. The filtrate rapidly turned dark brown. Attempts to isolate more product or starting material from the filtrate by removing the solvent under reduced pressure led to a brown sticky residue due to decomposition of TCNEO. Compound **1**: Anal. Calcd for $C_7H_6N_4$: C, 57.55; H, 4.1; N, 38.35. Found: C, 57.45; H, 3.95; N, 38.2. IR (Nujol mull): 2180 cm^{-1} and 2134 cm^{-1} (CN); δ_H NMR (400 MHz, DMSO-d_6): 3.88 (s, 3H, CH_3), 7.70 (dd, J, 1.4 Hz, 2H, H-4 and H-5), 9.15 (s, 1H, H-2); δ_C NMR (100 MHz, DMSO-d_6): 35.8 (CH_3), 60.3 (C^-), 123.2 (two CN), 123.5 (C-5), 124.4 (C-4), 137.5 (C-2); (for C^- pulse delay, 3s, 17,000 scans).

1-Benzyl-imidazolium-3-dicyanomethanide **2** was similarly prepared (73%), mp 177–179 °C (from ethanol), Anal. Calcd for $C_{13}H_{10}N_4$: C, 70.25; H, 4.55; N, 25.21; Found: C, 69.85; H, 4.55; N, 24.78.; IR (cm^{-1}) 2160, 2180 (J, 1.4 Hz, CN); δ_H NMR (400 MHz, DMSO-d_6): 5.32 (s, 2H, benzyl CH_2), 7.59–7.42 (m, 5H, Ph), 7.66 (s, 1H, H-5), 7.75 (s, 1H, H-4), 9.36 (s, 1H, H-2); δ_C NMR (100 MHz, DMSO-d_6): 52.1 (benzyl CH_2), 122.6 (C-5), 123.0 (two CN), 124.7 (C-4), 128.3 (C-3′), 128.7 (C-4′), 129.0 (C-2′), 134.9 (C-1′), 136.4 (C-2).

Synthesis of 1-methyl-5-imino-6-cyano-8-methoxycarbonyl-imidazo-[1,2-a] pyridine **6**.

A solution of **1** (0.28 g, 1.92 mmol) in acetonitrile (10 ml) was treated with methyl propiolate (0.17 ml, 1.92 mmol), stirred at 0–5 °C (ice-bath) for 72 h and the solvent removed under reduced pressure to give a crude dark brown solid (0.42 g, 95%); fractional crystallisation from EtOH gave **6** as a pale yellow solid mp 155–157 °C (51%) and a dark red gum. Anal. Calcd for $C_{11}H_{10}N_4O_2$: C, 57.4; H, 4.4; N, 24.3; Found: C, 57.4; H, 4.5; N, 24.7. IR (cm^{-1}) 3107 (NH), 2204 (CN), 1723 (C=O), 1613 (C=N); δ_H, δ_C NMR Figure 1. Compounds **7**, mp 131–133 °C and **8**, mp 190–191 °C were similarly prepared. (Due to contamination by a dark-red gum, compound **7** was better prepared by the method described for **9** below).

Imidazolium ylides **12** *and* **15**.

A solution of **1** (0.5 g, 3.42 mmol) in acetonitrile (10 ml) was treated with a solution of maleic anhydride (0.33 g, 3.42 mmol) in acetonitrile, and the mixture stirred at room temperature for 3 h. The solution was then evaporated under reduced pressure at a temperature below 35 °C. Addition of ether to the residue gave a brown solid, compound **12** (0.62 g, 72%), mp 180–181 °C (from acetonitrile). Anal. Calcd for $C_{11}H_8N_4O_3$: C, 54.1; H, 3.3; N, 22.95. Found: C, 54.35; H, 3.6; N, 22.7%. IR (cm^{-1}) 3330 (N–H), 2175 (CN), 1792, 1734 (C=O); δ_H, δ_C NMR Figure 1. Evaporation of the ethereal filtrate led only to isolation of an oily residue. Compound **15** was prepared similarly but under N_2 with the stirring continued for 27 h. Compound **15**, a sticky brown solid, (0.33 g, 86%). δ_H NMR (400 MHz, CD_3CN): 5.24 (s, 1H, H-9), 5.31 (s, 2H, benzyl CH_2), 7.27–7.39 (m, 7H, H-2, H-3 and Ph), 8.52 (s, 1H, H-5), 9.8–11.62 (br, 1H, moisture sensitive NH); δ_C NMR (100 MHz, CD_3CN) 52.4 (benzyl CH_2), 62.2 (C-7), 92.2 (C-9), 118.8 (CN), 119.5 (C-8), 121.5 (C-2), 121.8 (C-3), 128.5 (C-2′), 134.2 (C-1′), 129.1 (C-4′), 129.3 (C-3′), 135.4 (C-5), 150.0 (C-6), 165.4, 166.1 (C=O); (for C-7 pulse delay 4 s, 12,800 scans).

Synthesis of compounds **9** *and* **10** (cf Ref. 5).

A solution of **3** (0.37 g, 1.77 mmol) in DMF (20 ml), cooled to 0 °C, was treated with DMAD (0.218 ml, 1.77 mmol),

and allowed to stand at 0 °C for 4.5 h, then filtered and the filtrate added to ice-cold water. The resulting brown product **9** (0.44 g, 71%) was collected on a jacketed sintered glass funnel at −5 °C, washed with EtOH (10 × 1 ml, 0 °C) and Et_2O (3 × 1 ml, 0 °C) δ_H, δ_C NMR at 0 °C see Figure 1.

When a solution of **9** (0.2 g, 0.5 mmol) in CH_3CN (15 ml) was stirred at 50 °C for 2 h and ambient temperature for 50 h, and then evaporated under reduced pressure, **10** was obtained in 80% yield, mp 167 °C, lit.,[5] mp 172–174 °C; δ_H NMR, δ_C NMR see Figure 1.