Thermal Behaviour of Dipolarophile-containing Acyl Azides: Intramolecular Cycloaddition *versus* Curtius Rearrangement

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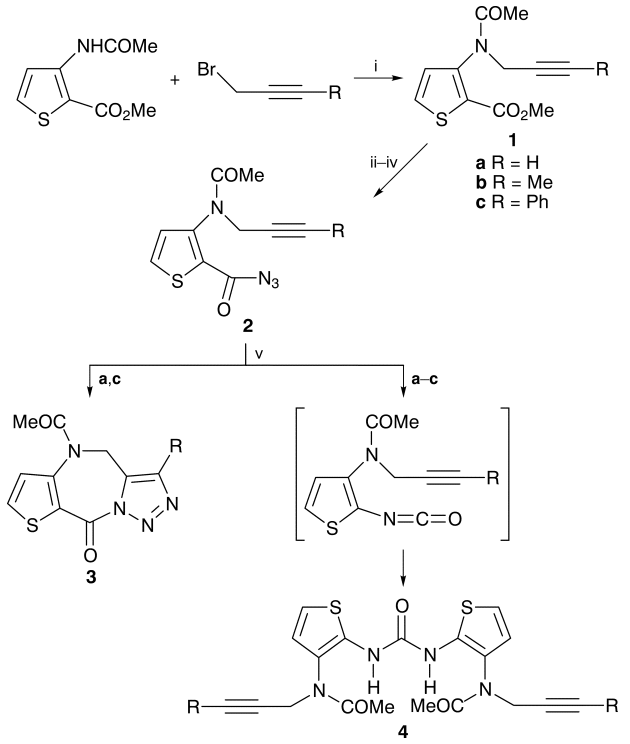
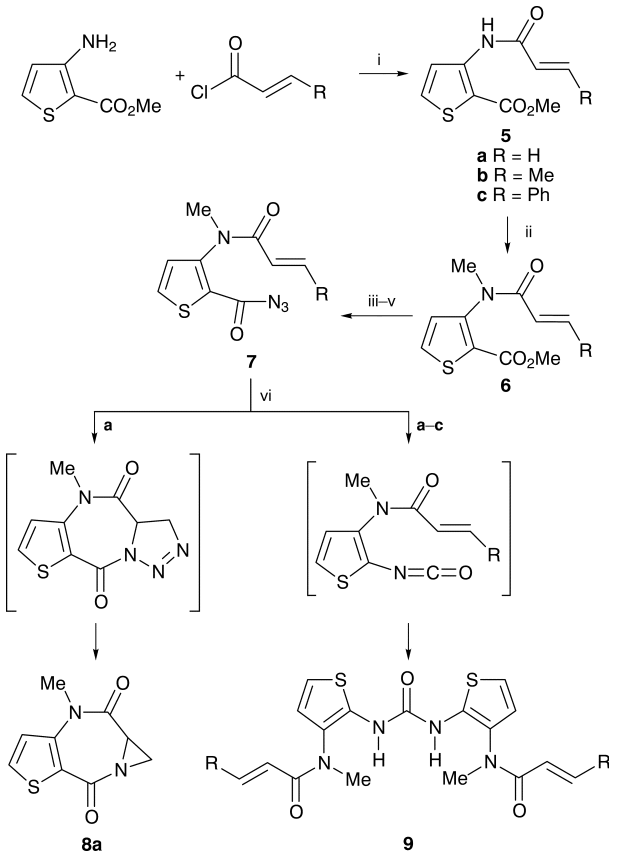
The thermal reaction of a series of alkynyl- or alkenoyl-containing acyl azides involves competition between intramolecular azide cycloaddition and Curtius rearrangement.

As a part of our research dealing with intramolecular azide cycloadditions,[3] we were interested in examining the behaviour of acyl azides **2** and **7** to establish the degree of competition between intramolecular cycloaddition and Curtius rearrangement. The choice of such thiophene-based substrates was dictated by the fact that the thieno-[2,3-*f*][1,2,3]triazolo[5,1-*c*][1,4]diazepine skeleton, which is unreported in the literature, could represent a valuable target in medicinal chemistry, owing to its structural similarity with some anxiolytic drugs.[4]



Scheme 1 *Reagents and conditions*: i, K_2CO_3, BTAC, acetone, heat; ii, KOH, MeOH, heat; iii, EtOCOCl, acetone, 0 °C; iv, NaN_3, 0 °C; v, toluene, heat



Scheme 2 *Reagents and conditions*: i, Et_3N, toluene, heat; ii, MeI, K_2CO_3, BTAC, acetone, heat; iii, KOH, MeOH, heat; iv, EtOCOCl, acetone, 0 °C; v, NaN_3, 0 °C; vi, toluene, heat

Table 1 Thermal reaction of acyl azides **2** and **7**[a]

Compd.	Time (*t*/h)	Product yield (%)				Eluent
		3	**4**	**8**	**9**	
2a	8	60	10	–	–	Et_2O
2b	4	0	85	–	–	AcOEt–Light petroleum[b] (2:1)
2c	5	30	40	–	–	Et_2O
7a	3	–	–	30	10	Et_2O
7b	4	–	–	0	75	AcOEt–Light petroleum[b] (4:1)
7c	3	–	–	0	95	–

[a]Boiled under reflux in toluene solution (0.05 M). [b]Bp 40–60 °C.

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Heat treatment of acyl azides **2** and **7**, synthesized as depicted in Schemes 1 and 2, was carried out in boiling toluene. Reaction times, products, eluents and yields are summarized in Table 1.

Our results shows that the substituent R plays a key role in determining the competition between the two possible routes. The intramolecular cycloaddition pathway actually predominates over the Curtius rearrangement if R = H. Steric encumbrance owing to R hinders the intramolecular approach of the reactive π systems in parallel planes that is required for concerted cycloadditions.[11] Consequently, the powerful driving force exerted by the loss of molecular nitrogen makes the Curtius rearrangement the main or exclusive pathway for R other than H.

Techniques used: IR, ^{1}H NMR, mass spectrometry, elemental analysis

References: 11

Schemes: 2

Table 2: Characterisation of compounds **3**, **4**, **8** and **9**

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