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Thermodecarbonylation of α-substituted cycloalkanones: a convenient one-carbon ring contraction method

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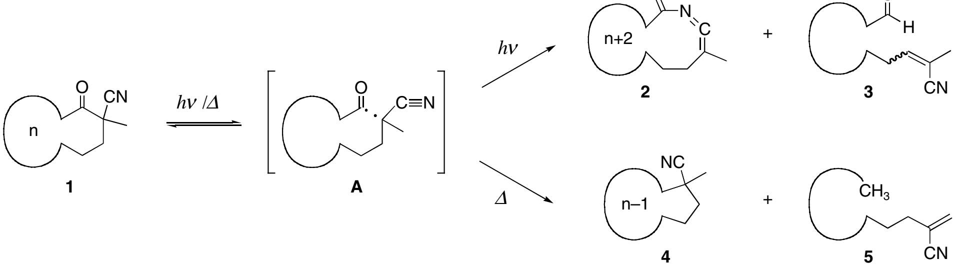
Abstract—A new and very convenient one-carbon ring contraction method is reported. Pyrolysis of α-substituted cycloalkanones at 600–650 °C under flow conditions produces the ring contracted compounds under loss of carbon monoxide. Substrates varying in ring size and nature of the α-substituent have been investigated.

In recent years, much attention has been paid to the photochemical reaction of cyclic ketones, which upon irradiation undergo Norish type-I cleavage to give acyclic 1,ω-enals by disproportionation.[1] On the other hand, it is well known that appropriate substitution in 2-position allows for ring expansion reactions.[2] Thus, 2-cyano-2-methylcycloalkanones **1** are reported to yield upon irradiation ($n + 2$) ring expanded *N*-acylketenimine derivatives **2**,[3] besides the principal products, being α,β-unsaturated cyanoaldehydes **3** (Scheme 1).[4]

In connection with our investigations aimed at the design and development of novel diradical-mediated ring expansion[5] and ring opening reactions[6] by means of flash vacuum pyrolysis (FVP),[7] we were interested to explore the hitherto unknown thermal behavior of 2-cyanocycloalkanones. The instigating question of the present study was directed at whether **1** undergoes clean α-cleavage upon FVP, and if this was the case, whether recombination within the generated α-acyl ω-cyanoalkyl diradical **A** provides access to cyclic *N*-acylketenimines of type **2**.[8]

In a test run 2-cyano-2-methylcyclododecanone (**1**, $n = 12$) was heated in a flow reactor system at 550 °C to afford a 2:1 mixture of two compounds, which were readily purified by column chromatography. To our surprise, no traces of the expected ($n + 2$) ring expanded ketenimine **2** and cyanoaldehyde **3**, respectively, could be detected. Instead, the major component turned out to be ($n - 1$) *ring contracted* 1-methylcycloundecanecarbonitrile (**4**) (60%) while the minor component proved



Scheme 1. Photochemical reaction (reported) versus thermal gas-phase reaction (new) of 2-cyano-2-methylcycloalkanones **1**.

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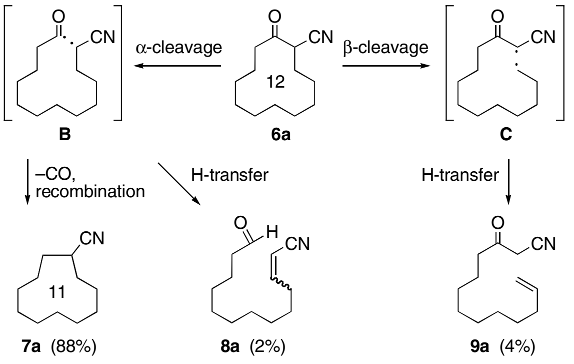
to be acrylonitrile **5** (30%) (Scheme 1).[9] This finding intimates a mechanism involving the expulsion of carbon monoxide within intermediate **A**. The resulting decarbonylated α-alkyl ω-cyanoalkyl diradical may relax either way, giving **4** by recombination or **5** by intramolecular disproportionation. In contrast to the photochemical reaction, the formation of the thermodynamically less favored terminal olefin **5** involves hydrogen abstraction from the more readily accessible methyl group. It is noteworthy to state that no traces of the decarbonylated form of **3** could be detected.

Given the ready availability of 2-cyanocycloalkanones[10] and the promising performance of **1** in the above-mentioned thermal reaction, we next turned our interest to the scope of this simple but preparatively very useful ring contraction methodology. In order to suppress competing hydrogen transfer reactions we subjected a number of substrates lacking the additional methyl group at C2 to FVP. As exemplified in the case of 2-cyanocyclododecanone (**6a**), FVP at 600 °C proceeded smoothly to afford the desired one-carbon ring contracted nitrile **7a** in good yield along with trace amounts of (*E*/*Z*)-1,13-cyanoaldehyde **8a** and 1,3-cyanoketone **9a**. As indicated in Scheme 2, the latter presumably arises through initial β-cleavage and subsequent hydrogen abstraction within the resulting diradical species **C**. Notwithstanding the high reactor temperatures the spectroscopic data provided no evidence for the presence of the decarbonylated form of **8a**. Furthermore, the product ratio proved to be unaffected by varying the reactor temperatures. However, temperatures above 700 °C adversely affected the overall yield due to increasing amounts of low boiling fragmentation products.

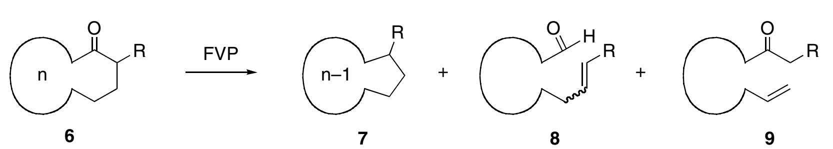


Scheme 2.

To study the generality of this new ring contraction procedure, we examined the reaction of 2-cyanocycloalkanones, which differed in the ring size (Table 1). In agreement with the results obtained with **6a**, FVP of the large-ring substrates **6b**,**c** produced the corresponding ring contracted nitriles **7b**,**c** in good-to-excellent yields (entries 2 and 3). Passing to the medium ring substrate **6d** provided the corresponding nitrile **7d** in only 63% yield while the yields of the acyclic side products appeared to be unaffected (entry 4). This trend was even more pronounced in the case of the eight-membered **6e**, which upon FVP at 640 °C afforded equal amounts of ring contracted and ring opened products (entry 5). In remarkable contrast, 2-cyanocyclohexanone produced only trace amounts of the desired cyclopentanecarbonitrile when heated in the range of 600–750 °C.

In order to extend the general applicability of the ring contraction method we extended our investigations to substrates bearing different α-substituents. Thus, 2-methoxy- and 2-trimethylsilyloxy ketones **6f** and **6g**, respectively, reacted in a similar manner to give the corresponding ring contracted compounds as the sole products besides considerable amounts of recovered starting material (entries 6 and 7). Fortunately, the conversion rate of either reaction could be improved by resubjecting the crude pyrolyzate to the same reaction conditions (recycling procedure). For reasons of decreasing radical stabilizing ability, FVP of **6h**,**i** proceeded rather sluggishly (entries 8 and 9). However, the desired 11-membered products could be isolated in moderate yields

Table 1. Effect of ring size and α-substitution on FVP-mediated ring contraction of cycloalkanones **6**



Entry	*n*	R	Compound	Temperature (°C)[a]	**7** (%Yield)[b]	**8** (%Yield)[c]	**9** (%Yield)[c]
1	12	CN	**a**	600	88	2	4
2	14	CN	**b**	620	82	2	3
3	15	CN	**c**	600	89	1	3
4	10	CN	**d**	620	63	2	4
5	8	CN	**e**	640	24	8[b]	16[b]
6	12	OMe	**f**	610	70[d] (43)	0	0
7	12	$OSiMe_3$	**g**	610	58[d] (34)	0	0
8	12	Me	**h**	650	42[d] (27)	0	0
9	12	CH_2SiMe_3	**i**	630	51[d] (30)	0	0

[a] Optimized temperatures.

[b] Yield of isolated material.

[c] Yield determined by GC.

[d] Via recycling procedure. Numbers in parentheses indicate the yields obtained after the first run.

when the recycling procedure was applied. Interestingly, substrates **6f–i** produced no open-chain disproportionation products.

In summary, we have developed a convenient one-carbon ring contraction methodology based on thermal decarbonylation. In the case of 2-cyanocycloalkanones, the corresponding ring contracted nitriles are produced in good-to-excellent yields, accompanied with trace amounts of acyclic disproportionation products. This procedure appears to be fairly general, as variations in ring size and α-substitution are well tolerated. In particular, the ready availability of low-priced C-12 substrates allows for the preparation of common but otherwise difficult-to-achieve 11-membered carbocyclic systems. Further studies are in progress.

Acknowledgement

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9. FVP reactions were performed in a flow reactor system using a quartz tube (1 m long) heated by a tube furnace (1 m with six different temperature zones, which can be separately adjusted). After evacuation of the apparatus with a high-vacuum oil pump ($2–4 \times 10^{-2}$ mbar), 2-cyano-2-methylcyclododecanone (**1**, $n = 12$; 5.0 g, 22.6 mmol) was directly distilled through the preheated reactor tube (550 °C; estimated contact time <1 s). A flow of nitrogen gas was adjusted from 1.5 L/h. At the end of the reactor unit the isomerization products were collected in a trap, which was cooled with liquid N_2. After all of the starting material had been distilled (ca. 45 min), the apparatus was vented and the frozen products were transferred to a bulb using Et_2O as solvent. The resulting solution was dried over anhydrous $MgSO_4$, filtered, and evaporated under reduced pressure. Purification by flash chromatography on silica gel (hexane/AcOEt 50:1) afforded **4** (2.62 g, 60%) and **5** (1.31 g, 30%). Data of **4**: IR (film): 2254, 2233 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ 1.86–1.76 (m, 2H), 1.70–1.61 (m, 2H), 1.59–1.32 (m, 16H), 1.30 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 125.4, 36.0, 23.6, 26.8, 26.1, 25.6, 25.2, 21.6. Data of **5**: IR (film): 2255, 2225 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ 5.82 (br s, 1H), 5.69 (br s, 1H), 2.24 (t, $J = 7.4$ Hz, 2H), 1.55 (quint., $J = 7.2$ Hz, 2H), 1.30–1.27 (m, 14H), 0.88 (t, $J = 6.7$ Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 129.9, 123.5, 118.7, 34.6, 31.8, 29.4, 29.3, 29.2, 29.1, 28.6, 27.5, 22.6, 14.1.
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