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THERMAL REARRANGEMENT OF ALLYLIC CYANAMIDES

Carmen Betancor, Reyes Carrau, Cosme G. Francisco and Ernesto Suárez*

Instituto de Productos Naturales Orgánicos del C.S.I.C.
Carretera de La Esperanza 2, La Laguna, Tenerife, Spain.

Summary: The allylic rearrangement of cyanamides has been achieved by pyrolysis in solution at temperatures between 125 and 190 °C. This rearrangement was also observed during the thermal opening of the aziridine ring in cyanoaziridines. This allylic transposition constitutes a formal method for the 1,3-isomerization of allylic amines.

Although the 1,3-isomerization of allylic alcohols and allylic alcohol derivatives has been the subject of numerous studies[1] and also plays an important role in several synthetic processes,[2] the 1,3-isomerization of allylic amine derivatives has received comparatively little attention.

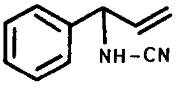
The growing importance[3] of primary allylic amines in organic synthesis and the presence of this group in many naturally occurring compounds[4] led us to study the 1,3-rearrangement of allylic amine derivatives, a reaction which should be useful in synthetic organic chemistry. The sole reaction of this type previously reported is the isomerization of allylic azides and has scarcely been used in organic synthesis.[5]

Cyanamides that can be easily obtained from the corresponding amines[6,7] are versatile compounds that eventually can be transformed into isoureas,[8] ureas,[6a,9] tioureas,[10] ketones,[7] or hydrolyzed to amines.[11]

Herein we describe a new and efficient rearrangement of allylic cyanamides as well as the thermal opening of cyanoaziridines. Hence, through the above mentioned transformation of amines into cyanamides and viceversa, starting from an allylic amine it is possible to get the isomeric allylic amine.

Allylic cyanamides undergo, as shown in the table, clean rearrangement to give the allylically transposed cyanamides when heated in solution, at low concentration (1-5 mg/ml), and at temperatures between 125 and 190 °C under argon. High yields are observed except in the case of linalyl-cyanamide (**3**) due to the unstability of the geranyl- and neryl-cyanamide mixture (**4**) obtained at the reaction temperature.

In the case of 5α-cholest-1-ene-3α-cyanamide (**7**) the equilibrium is reached after 3.5 h. at 190 °C and an equimolecular mixture of 5α-cholest-2-ene-1α-cyanamide (**8**) and starting material was obtained.



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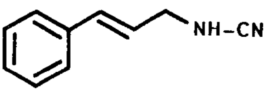

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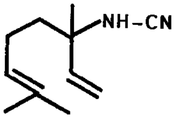

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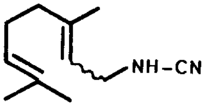

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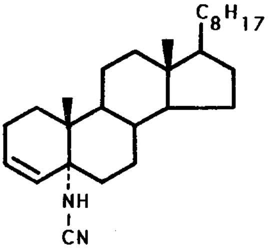

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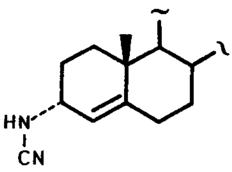

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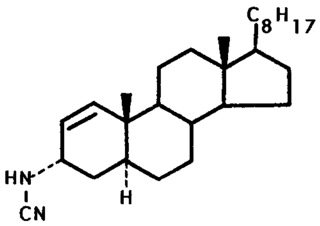

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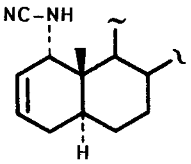

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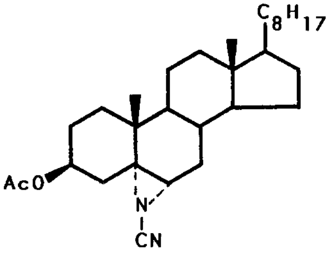

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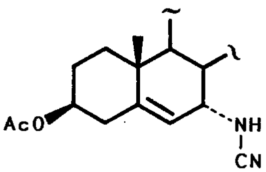

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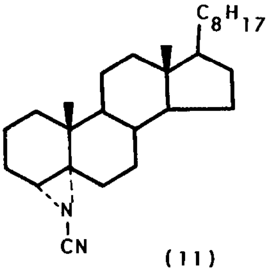

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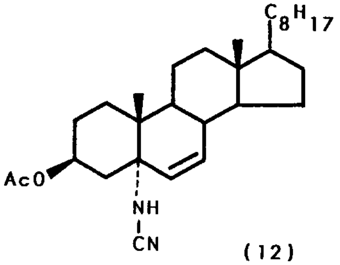

(12)

The allylic rearrangement of cyanamides is also observed during the thermal opening of cyanoaziridines (9 and 11). As far as we know the thermal behaviour of cyanoaziridines has not been previously reported[12]. The pyrolytic opening of the aziridine ring in 9 and 11 afforded allylcyanamides 10 and 6 respectively. The reaction probably occurs with conformational control to give the 5α-axial cyanamides 12 and 5, which under the reaction conditions rearrange to the isolated allylcyanamides 10 and 6.

These results can be rationalized on the basis of a [3,3] -sigmatropic rearrangement (Scheme) which resembles that of allyl thyocyanates to allyl isothiocyanates.[13] The equilibrium between cyanamide and the intermediate carbodiimide is well documented.[14]

Scheme

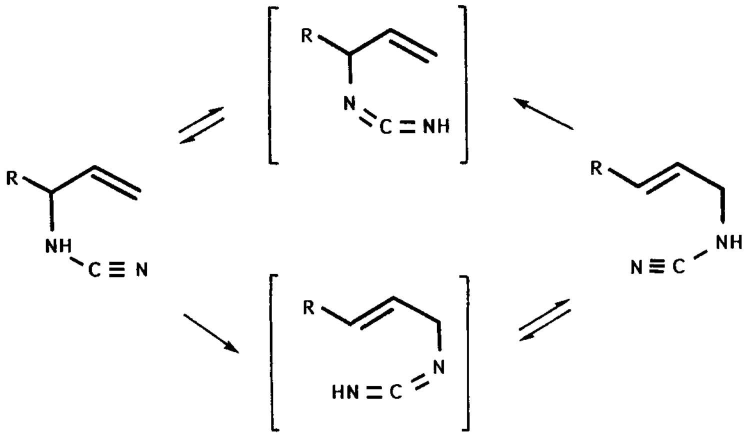

TABLE. Thermal rearrangement of allylic cyanamides and cyaniaziridines

Substrate	Solvent	Temp, °C	Time, h	Products (Yield %)
1[15]	p-Xylene	125	110	2[16](95)
3[17]	Decalin	190	2	4[18](45)
5[19]	p-Xylene	138	0.8	6[20](100)
7[21]	Decalin	190	3.5	8[22](37),7 (37)
9[23]	p-Xylene	138	57	10[24](92)
11[25]	p-Xylene	138	72	6[20](80)

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15. Compound (**1**): oil; IRν_{max} ($CHCl_3$) 3380, 2220 cm^{-1}; ^{1}HNMR (200 MHz, $CDCl_3$) δ 4.1 (1H, m, NHCN), 4.81 (1H, m, 1-H), 5.34 and 5.36 (2H, J 0.8, 10.2, 17.0 Hz, 3-H_2), 5.99 (1H, ddd, 2-H), 7.3 (5H, m, Ar); MS m/z 158.0818 (M^+, 21%), 117 (100).

16. Compound (**2**): m.p. 50 °C (EtOAc-n-Hexane); IR ν_{max} 3390, 2220 cm^{-1}; ^{1}HNMR δ 3.59 (1H, m, NHCN), 3.84 [2H, t (after D_2O, d, J 6.4 Hz), 3-H_2], 6.20 (1H, td, J 15.7, 6.4 Hz, 2-H), 6.62 (1H, d, J 15.8 Hz, 1-H), 7.2-7.4 (5H, m, Ar); MS m/z 158 (M^+, 90), 117 (100).

17. Compound (**3**): oil; IRν_{max} 3390, 3220, 3095, 2210, 995, 930 cm^{-1}; ^{1}HNMR δ 1.3 (3H, s, 3-Me), 1.63, 1.55 (6H, s, 7-Me_2), 1.95 (2H, m, 5-H_2), 4.21 (1H, m, NHCN), 5.03 (1H, m, 6-H), 5.75, 5.18, 5.15 (3H, ABX, J 1.0, 10.75, 17.34 Hz, 2-H, 1-H_2); MS m/z 178 (M^+, 0.5).

18. Compound (**4**): oil;50:50 mixture of **Z** and **E** isomers; IRν_{max} 3395, 3250, 2210 cm^{-1}; ^{1}HNMR δ 3.61 (2H, apparent t, 1-H_2), 5.25, 5.04 (2H, m, 6-H, 2-H), 1.57, 1.65 (6H, s, 7-Me_2), 1.73 (3H, s, 3-Me, Z isomer), 1.65 (3H, s, 3-Me, E isomer); MS m/z 178 (M^+, 0.6).

19. Compound (**5**): m.p. 138-140 °C (n-Hexane); IRν_{max} 3390, 3370, 2210 cm^{-1}; ^{1}HNMR δ 0.63 (3H, s, 13-Me), 0.83 (6H, d, J 6.8 Hz, 25-Me_2), 0.87 (3H, d, J 7.5 Hz, 20-Me), 0.94 (3H, s, 10-Me), 3.63 (1H, m, NHCN), 5.51 (1H, m, 4-H), 5.89 (1H, m, 3-H); MS m/z 410.3645 (M^+, 13), 368 (100).

20. Compound (**6**): m.p. 137-139 °C (n-Pentane);$[\alpha]_D$ +84° ($CHCl_3$); IR ν_{max} 3380, 2210 cm^{-1}; ^{1}HNMR δ 0.64 (3H, s, 13-Me), 0.82 (6H, d, J 6.7 Hz, 25-Me_2), 0.86 (3H, d, J 7.4 Hz, 20-Me), 0.96 (3H, s, 10-Me), 3.34 (1H, m, NHCN), 3.66 (1H, m, 3β-H), 5.29 (1H, d, J 4.7 Hz, 4-H); MS m/z 410.3672 (M^+, 26), 368 (100).

21. Compound (**7**): m.p. 152 °C (n-Hexane); $[\alpha]_D$ -14° ($CHCl_3$); IRν_{max} 3395, 2210 cm^{-1}; ^{1}HNMR δ 0.64 (3H, s, 13-Me), 0.79 (3H, s, 10-Me), 0.84 (6H, d, J 6.7 Hz, 25-Me_2), 0.87 (3H, d, J 7Hz, 20-Me), 3.47 (1H, m, NHCN), 3.69 (1H, m, 3β-H), 5.5 (1H, dd, J 4.5, 10 Hz, 2-H), 6.16 (1H, d, J 10 Hz, 1-H); MS m/z 410.3504 (M^+, 50), 368 (100).

22. Compound (**8**): Amorphous; IRν_{max} 3390, 2210 cm^{-1}; ^{1}HNMR δ 0.67 (3H, s, 13-Me), 0.79 (3H, s, 10-Me), 0.86 (6H, d, J 7 Hz, 25-Me_2), 0.90 (3H, d, J 7 Hz, 20-Me), 3.24 (1H, m, NHCN), 3.38 (1H, m, 1β-H), 5.77 (1H, m, 2-H), 5.94 (1H, m, 3-H); MS m/z 410.3560 (M^+, 4).

23. Compound (**9**): m.p. 178-182 °C (MeOH); $[\alpha]_D$ -46° ($CHCl_3$); IRν_{max} 2190, 1720 cm^{-1}; ^{1}HNMR δ 0.56 (3H, s, 13-Me), 0.82 (6H, d, J 6.5 Hz, 25-Me_2), 0.85 (3H, d, J 7 Hz, 20-Me), 1.05 (3H, s, 10-Me), 1.99 (3H, s, OAc), 2.74 (1H, d, J 5.0 Hz, 6β-H), 4.97 (1H, m, 3α-H); MS m/z 468.3682 (M^+, 33).

24. Compound (**10**): m.p. 176-177 °C (Acetona-n-Hexane); $[\alpha]_D$ -157°($CHCl_3$); IR 3390, 2205, 1720 cm^{-1}; ^{1}HNMR δ 0.68 (3H, s, 13-Me), 0.86 (6H, d, J 6.5 Hz, 25-Me_2), 0.93 (3H, d, J 6.3 Hz, 20-Me), 1.02 (3H, s, 10-Me), 2.03 (3H, s, OAc), 3.42 (2H, m, NHCN, 7β-H), 4.64 (1H, m, 3α-H), 5.58 (1H, d, J 4.75 Hz, 6-H); MS m/z 408 (M^+-AcOH, 10).

25. Compound (**11**): m.p. 130-132 °C (MeOH); $[\alpha]_D$ +71°($CHCl_3$); IRν_{max} 2190 cm^{-1}; ^{1}HNMR δ 0.65 (3H, s, 13-Me), 0.83 (3H, d, J 6.7 Hz, 25-Me_2), 0.87 (3H, d, J 6.8 Hz, 20-Me), 1.02 (3H, s, 10-Me), 2.74 (1H, dd, J 4.2, 1.2 Hz, 4β-H); MS m/z 410.3651 (M^+, 9).

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