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Note

Structure of Some *s*-Triazoloquinazolinones*

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Reaction between 3-amino-1,2,4-triazole and 2-carbethoxycyclohexanone can theoretically afford the tricyclic product of the types IV—VII. It was established that the product has structure V and similarly for other cyclization products structures are proposed.

The solution of the structural problem relating condensation products between 3-amino-1,2,4-triazoles and 1,3-dicarbonyl compounds, which may form either *s*-triazolo(4,3-*a*)pyrimidines (I) or *s*-triazolo(2,3-*a*)-pyrimidines (II), has been tried to be solved by chemical methods[1,2], but it appears that only derivatives of (I) have been prepared by unequivocal synthesis[3]. In addition, the structural problem is complicated by the fact that under the influence of bases, acids or temperature, compounds of the type (I) may isomerize into those of the type II (Dimroth rearrangement).

We should like to report on structural investigations of compounds which are formed by reaction between 3-amino-1,2,4-triazole and 2-carbethoxycyclohexanone or related β-keto esters. The reaction with 2-carbethoxycyclohexanone, which leads to the corresponding tetrahydro-*s*-triazoloquinazolines, may, theoretically, take several different courses, depending on the reaction site in the triazole part and upon the initial condensation step with the cyclic β-keto ester. If the first step involves a condensation between the keto group (or its enolized form) to give the intermediate III, the subsequent cyclization step may involve attack either at N_4 of the triazole ring to give the *s*-triazolo (3,4-*b*)-quinazoline system (IV) or on N_2 which then produces the isomeric *s*-triazolo(3,2-*b*)quinazoline system (V).

On the other hand, if we anticipate that the first reaction step would involve the formation of an intermediate amide (reaction between the carbethoxy and amino group) then the following cyclization may again either involve the N_4 atom of the triazole ring to give the *s*-triazolo(4,3-*a*)quinazoline analog VI or with participation of N_2 the *s*-triazolo(2,3-*a*)quinazoline ring system VII may be formed. Although very unlikely, these last mentioned isomeric systems may be generated also by assuming the keto group (in the enolized form) to react with either the 2-NH or the 4-NH group of the triazole. Thus, although the synthesis has been described[4], and only one compound formed, the structure of the condensation product has been left unsettled.

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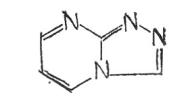
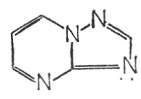
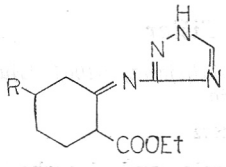
* Heterocycles, Part XCVI.

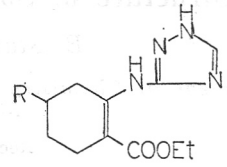




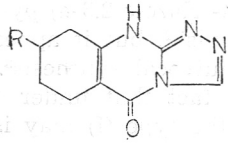
II



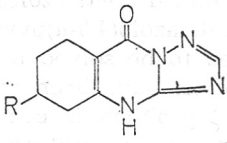
IIIa



IIIb

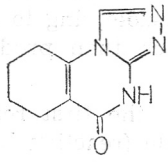


IV

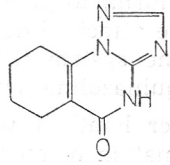


V

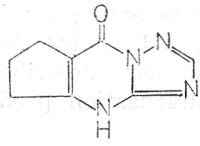
It is conceivable that an intermediate condensation product might give some insight into the reaction path. Although we were not able to isolate a pure intermediate during the preparation of the tricycle, the reaction could be followed in a NMR probe at 26° in CD_3OD solution. Since no ethanol was liberated during this conversion, the structures VI and VII can be eliminated. The NMR spectrum of the intermediate is consistent with its formulation



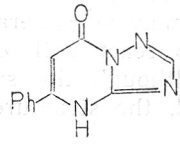
VI



VII



VIII



IX

as IIIb since no signal for the methine hydrogen could be observed. A distinction between the possible cyclic products, IV or V, could be made again on hand of the NMR spectrum. The signal for the proton in the triazole part appeared at $\tau = 2.15$ which excludes the form IV and favours the structure of the tricyclic product as 5,6,7,8-tetrahydro-*s*-triazolo(3,2-*b*)quinazolin-9(4H)one (V). The signal for H_3 in the isomeric system IV would be expected to be about one τ unit lower, as established in the case of isomeric *s*-triazolopyrimidines[5,6] or *s*-triazolo(4,3-*a*)-1,3,5-triazin-5(6H)ones[7].

The same observation could be made in the case of the condensation products with 2-carbethoxycyclopentanone or ethyl benzoylacetate for which structures as 5H-6,7-dihydrocyclopenta/*d*/-*s*-triazolo(2,3-*a*)-pyrimidin-8(4H)one (VIII) and 5-phenyl-*s*-triazolo(2,3-*a*)pyrimidin-7(4H)one (IX) appear to be most adequate.

Finally, it should be mentioned that a rearrangement of the type II → I can be regarded as improbable in the case of V to IV under the employed reaction conditions since it would represent a retro-Dimroth rearrangement of which, so far, only one case is known[8] and this takes place in concentrated sulfuric acid.

EXPERIMENTAL

Melting points were taken on a Kofler micro hot stage. NMR spectra were recorded on a JEOL JNM-C-60HL spectrometer, with TMS as internal standard, and mass spectra were taken on a CEC 21-110C instrument using direct sample insertion into the ion source.

5,6,7,8-Tetrahydro-s-*triazolo(3,2*-b*)quinazolin-9(4H)one* (V, R = H)

The compound was synthesized in an ethanolic solution as described previously[4]. M. p. 282° (from water) Lit.[4] gives m. p. 279—281°). Mass spectrum: $M^+ = 190$. IR (KBr): 1711 cm^{-1} (CO). NMR (DMSO-d_6): $\tau = 2.15$ (s, H_2), 7.5 (m, 4 H, 5-CH_2- and 8-CH_2-), 8.25 (m, 4 H, 6-CH_2- and 7-CH_2-).

Anal. $C_9H_{10}N_4O$ calc'd.: C 56.83; H 5.30; N 29.46%
found: C 56.61; H 5.33; N 29.32%

When condensation between 3-amino-1,2,4-triazole and 2-carbethoxycyclohexanone was conducted in a solution of CD_3OD at 26° the formation of the intermediate IIIb could be followed. At the beginning the NMR spectrum of the mixture of both reactants showed the following characteristics: 2-carbethoxycyclohexanone (as the enolic form): $\tau = 5.84$ (q, CH_2CH_3), 8.72 (t, CH_2CH_3), 7.80 (m, 4 H, 3-CH_2- and 6-CH_2-), 8.35 (m, 4 H, 4-CH_2- and 5-CH_2-), $J_{CH_2CH_3} = 7.2$ Hz; 3-amino-1,2,4-triazole: $\tau = 2.50$ (s, H_5). A broad signal at 4.9 accounts for NH, NH_2 and OH groups of both compounds. NMR of IIIb: $\tau = 5.87$ (q, CH_2CH_3), 8.75 (t, CH_2CH_3), 7.80 (m, 4 H, 3-CH_2-, 6-CH_2-), 8.30 (m, 4 H, 4-CH_2-, 5-CH_2-), 2.50 (s, triazole H_5), 4.9 (NH, broad), $J_{CH_2CH_3} = 7.2$ Hz.

6-Methyl-5,6,7,8-tetrahydro-s-*triazolo(3,2*-b*)quinazolin-9(4H)one* (V, R = Me)

A mixture of 3-amino-1,2,4-triazole (0.84 g.), 2-carbethoxy-5-methylcyclohexanone (1.84 g.) and glacial acetic acid (5 ml.) was heated under reflux for 5 hrs. Upon cooling the separated product was filtered off and crystallized from water. M. p. 226—228°. NMR (DMSO-d_6, 24°): $\tau = 1.99$ (s, H_2), 8.98 (d, 6-CH_3), 7.5 (m, 5 H, 5-CH_2-, 8-CH_2 and H_6), 8.2 (m, 2 H, 7-CH_2-).

Anal. $C_{10}H_{12}N_4O$ calc'd.: C 58.81; H 5.92; N 27.44%
found: C 58.90; H 5.82; N 27.13%

5H,6,7-Dihydrocyclopenta/d/-s-*triazolo(2,3*-a*)pyrimidin-8(4H)one* (VIII)

The compound was prepared according to the described procedure[4], but instead of ethanol as solvent glacial acetic acid could be used and the reaction is completed

in 3 hrs. M. p. 305—310° (d., from water) (lit.[4] gives m. p. 290°). Mass spectrum: $M^+ = 176$. IR (KBr): 1680 cm^{-1} (CO). NMR (DMSO-d_6, 101°): $\tau = 1.99$ (s, H_2), 3.20 (m, 4 H, 5-CH_2- and 7-CH_2-), 7.85 (m, 2 H, 6-CH_2-).

Anal. $C_8H_8N_4O$ calc'd.: C 54.54; H 4.58%
found: C 54.25; H 4.86%

5-Phenyl-s-triazolo(2,3-a)pyrimidin-7(4H)one (IX)

A mixture of 3-amino-1,2,4-triazole (4.2 g.), ethyl benzoylacetate (9.6 g.) and glacial acetic acid (25 ml.) was heated under reflux for 8 hrs. Upon standing overnight the separated product was filtered off and crystallized from glacial acetic acid (3.4 g.), m. p. 300—302°. NMR (DMSO-d_6, 21°): $\tau = 1.75$ (s, H_2), 3.83 (s, H_6), 2.3 and 2.6 (m, Ph).

Anal. $C_{11}H_8N_4O$ calc'd.: C 62.25; H 3.80; N 26.40%
found: C 62.02; H 3.98; N 26.52%

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REFERENCES

1. C. F. H. Allen, H. R. Beilfuss, D. M. Burness, G. A. Reynolds, J. F. Tinker, and J. A. VanAllan, *J. Org. Chem.* **24** (1959) 787.
2. C. F. H. Allen, H. R. Beilfuss, D. M. Burness, G. A. Reynolds, J. F. Tinker, and J. A. Van Allan, *J. Org. Chem.* **24** (1959) 796, and previous papers.
3. J. D. Bower and F. P. Doyle, *J. Chem. Soc.* (1957) 727.
4. J. W. Cook, R. P. Gentles, and S. H. Tucker, *Rec. trav. chim. Pays-Bas* **69** (1950) 343.
5. W. W. Paudler and L. S. Helmick, *J. Heterocyclic Chem.* **3** (1966) 269.
6. H. Reimlinger, R. Jacquier, and J. Daunis, *Chem. Ber.* **104** (1971) 2702.
7. J. Kobe, B. Stanovnik, and M. Tišler, *Tetrahedron* **26** (1970) 3357.
8. M. Mühlstädt, H. Krausmann, and G. Fischer, *J. prakt. Chem.* **312** (1970) 254.

IZVLEČEK

Struktura nekaterih *s*-triazolokinazolinov

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Teoretično lahko vodi reakcija med 3-amino-1,2,4-triazolom in etilnim estrom cikloheksanon-2-karboksilne kisline do tricikličnih produktov tipa IV—VII. Ugotovili smo, da ima produkt strukturo V in podobno smo ugotovili tudi strukture za nekatere druge produkte ciklizacije.

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