CONDENSATION OF PROTIC SALTS OF N-ALKYL-SUBSTITUTED C-AMINO-sym-TRIAZOLES WITH β-DIKETONES AND β-CHLOROVINYL KETONES

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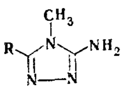
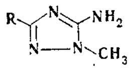
Condensation of protic salts of C-amino-sym-triazoles with β-diketones and β-chlorovinyl ketones leads to the corresponding sym-triazolopyrimidinium compounds. The structure of the condensation products was confirmed by the PMR spectra.

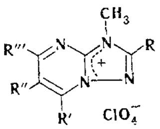
N-Unsubstituted 3-amino-sym-triazoles react with β-diketones in the presence of basic catalysts to give sym-triazolo[1,5-a]pyrimidines [1, 2]. The protic salts of condensed amino-sym-triazoles react with β-diketones, β-chlorovinyl ketones, and 1,1,3,3-tetraethoxypropane to give the corresponding pyrimidinium salts [3]. In the present research we have investigated the analogous condensation of the protic salts of 3-amino-4-methyl-sym-triazoles (Ia, b), 5-amino-1-methyl-sym-triazoles (IIa, b), and 3-amino-1-benzyl-sym-triazole (V).



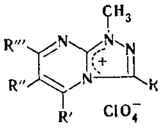
Ia,b



IIa, b



III



IV

I,II a R = H; b R = CH_3

One reaction path to give a pyrimidine ring is possible for I and II. The condensation products are the isomeric sym-triazolo[1,5-a]pyrimidinium (III) and sym-triazolo[4,3-a]pyrimidinium (IV) salts (Table 1).

The PMR spectra (Table 2) confirm structures III and IV and make it possible to determine the structure of the products of condensation with unsymmetrical carbonyl components. The N–CH_3 chemical shifts for III and IV attest to higher electron density on $N_{(3)}$ in III than in IV. Replacement of H by CH_3 in the triazole ring (R) shifts all of the signals a little too strong field except for the signal of the 5-CH_3 group in IVf, which is somewhat deshielded sterically by the 3-CH_3 group. In correspondence with the partial localization of the bonds in III and IV, when R'' = H the R' = CH_3 peak is always lower and broader than the R''' = CH_3 peak because of coupling with R'' = H (J = 0.8-1 Hz).

Perchlorates IIa, b react with benzoylacetone to give IVe and IVh. The phenyl signals in the PMR spectra of these compounds are not split; this is in keeping with their location in the 5 position [4]. In addition, δ 3-CH_3 in the spectrum of IVh is 1.82 ppm, as against 2.65 ppm in the spectrum of IVf; this is explained by the shielding by the phenyl group [5]. The phenyl group in IVh apparently deviates more from the plane of the molecule than in IVe. All of the signals of IVh, including the peak of the phenyl group itself, are shifted a little to strong field as compared with IVe as a consequence of the lesser conjugation of the phenyl group with the heterocyclic system. However, in IVe, the phenyl group also deviates from the plane of the heteroring, inasmuch as the 3-H chemical shift here is the same as in IVa, while the remaining signals are shifted to weak-field, i.e., 3-H is shielded by the phenyl group, which is possible when it is not coplanar.

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TABLE 1. Triazolopyrimidinium Perchlorates (III, IV, VII)

Compound	R	R′	R″	R‴	Reaction conditions		mp, °C	Empirical formula	Cl, %		Yield, %
					temp., °C	time, min			found	calc.	
IIIa	H	CH_3	H	CH_3	170—175	120	215—217	$C_8H_{11}ClN_4O_4$	13,1	13,5	32
IIIb	H	CH_3	CH_3	CH_3	170—175	60	170—172	$C_9H_{13}ClN_4O_4$	13,1	12,8	28
IIIc, d*	H	CH_3(H)	H	H(CH_3)				$C_7H_9ClN_4O_4$	13,9	14,3	64
IIIe	H	C_6H_5	H	CH_3	170—175	180	217—219	$C_{13}H_{13}ClN_4O_4$	10,6	10,6	25
IIIf	CH_3	CH_3	H	CH_3	175—180	180	246—247	$C_9H_{13}ClN_4O_4$	13,0	12,8	99
IIIg	CH_3	CH_3	CH_3	CH_3	175—180	180	171—173	$C_{10}H_{15}ClN_4O_4$	12,0	12,2	48
IIIh†	CH_3	CH_3	H	C_6H_5	175—180	120	274—275	$C_{14}H_{15}IN_4$ ‡	—	—	40
IVa	H	CH_3	H	CH_3	125—130	150	177—179	$C_8H_{11}ClN_4O_4$	13,6	13,5	100
IVb	H	CH_3	CH_3	CH_3	185—190	240	115—116	$C_9H_{13}ClN_4O_4$	12,6	12,8	19
IVc	H	CH_3	H	H	—	—	181—182	$C_7H_9ClN_4O_4$	14,3	14,3	48
IVe	H	C_6H_5	H	CH_3	150—155	240	233—234	$C_{13}H_{13}ClN_4O_4$	10,9	10,6	77
IVf	CH_3	CH_3	H	CH_3	150—155	180	195—197	$C_9H_{13}ClN_4O_4$	12,9	12,8	89
IVg	CH_3	CH_3	CH_3	CH_3	185—190	120	191—193	$C_{10}H_{15}ClN_4O_4$	12,4	12,2	35
IVh	CH_3	C_6H_5	H	CH_3	175—180	120	190—193	$C_{14}H_{15}ClN_4O_4$	10,5	10,5	65
VIIa	—	CH_3	H	CH_3	145—150	150	121—123	$C_{14}H_{15}ClN_4O_4$	10,6	10,5	89
VIIb	—	CH_3	C_2H_5	CH_3	145—150	90	146—147	$C_{16}H_{19}ClN_4O_4$	10,1	9,7	82
VIIc	—	CH_3	H	C_6H_5	135—140	90	216—218	$C_{19}H_{17}ClN_4O_4$	8,9	8,9	95
VIId	—	C_6H_5	H	C_6H_5	185—190	150	248—249	$C_{24}H_{19}ClN_4O_4$	8,1	7,7	80

*A mixture of isomers (1 : 4).

†Iodide.

‡ Found: N 15.3%. Calculated: N 15.3%.

Methyl β-chlorovinyl ketone reacts with $IIa \cdot HClO_4$ to give a mixture of isomeric IVc and IVd in a ratio of 1.5 : 1, from which pure IVc was isolated by crystallization. In contrast to the 7-CH_3 signal, the 5-CH_3 signal is split by coupling with 6-H (J = 1 Hz). In addition, J(5-H, 6-H) > J(7-H, 6-H), as was observed in [6, 7].

Benzoylacetone reacts with Ia to give a mixture of IIIe and its isomer in a ratio of 3 : 1, from which pure IIIe was isolated. The 7-C_6H_5 signal in the PMR spectrum of IIIe is split into two groups of bands with an intensity ratio of 2 : 3 (the lower at weak field) and a difference of 0.37 ppm between the centers of these bands; this is characteristic for such molecular fragments [4, 8], in which the phenyl group is at a certain angle to the plane of the heteroring and shifts the 6-H signal to weak field by 0.23 ppm as compared with IIIa. The product of the reaction of Ib with benzoylacetone is IIIh, in the PMR spectrum of which the phenyl signal is split similarly but with a greater difference between the centers of the bands (0.66 ppm); this is characteristic for a phenyl group in the 5-position [9]. In the case of IIIh, the plane of the phenyl group makes a considerably smaller angle with the plane of the heteroring, inasmuch as it shifts the 6-H signal considerably more strongly to weak-field (by 0.56 ppm as compared with IIIf).

Methyl β-chlorovinyl ketone reacts with Ia to give a mixture of isomeric IIIc and IIId with predominance of the latter (1 : 4, from the PMR spectrum). The structure of IIIa was also confirmed by alternative synthesis by methylation of the appropriate sym-triazolo[1,5-a]pyrimidine derivative [10].

Salts III and IV, which contain methyl groups in the 5- and 7- positions, give polymethine dyes. The 7-CH_3 group is more active in IIIa, as attested to by the structure of the dye – a monostyryl from IIIa and p-dimethylaminobenzaldehyde. The signal of the 7-CH_3 group is absent in the PMR spectrum of this dye, but the 5-CH_3 signal remains.

In contrast to I and II, the formation of a 1-substituted sym-triazolo[1,5-a]pyrimidinium salt (VI) or 2-substituted sym-triazolo[4,3-a]pyrimidinium salt (VI) or 2-substituted sym-triazolo[4,3-a]-pyrimidinium salts (VII) is possible for V on reaction with β-diketones. The formation of VI is less favorable, inasmuch as the positive charge in it would be distributed between two adjacent nitrogen atoms. It is apparently for this same reason that 3-substituted derivatives (III), in which the positive charge is distributed between two amidine nitrogen atoms, rather than the 1-substituted derivatives (VI) are also formed in the alkylation of sym-

TABLE 2. Chemical Shifts of the Protons of III, IV, and VII (δ, ppm)*

Compound	R	R′	R″	R‴	N-CH_3 or N-$CH_2C_6H_5$
IIIa	8,53	2,0 (0,8)	7,14	2,51	3,78
IIIc	—	2,64	—	8,49 (5)	3,80
IIId	8,46	8,58 (7)	7,22 (7)	2,55	3,76
IIIe	8,60	7,30and7,67	7,37	2,58	3,82
IIIf	2,74	2,49	7,04	2,44	3,65
IIIh	2,65	2,47	7,60	7,20 and 7,86	3,58
IVa	8,65	2,58	6,93	2,50	3,93
IVc	8,85	2,67 (1)	7,17 (5)	8,77 (5)	4,02
IVd	8,75	8,53 (7)	7,17 (7)	2,55	3,92
IVe	8,65	7,40	7,17	2,58	4,04
IVe	2,65	2,65	6,82	2,43	3,82
IVh	1,82	7,32	6,97	2,53	3,92
VIIa	9,54†	2,49	6,92	2,49	5,43 and 7,10
VIIc	9,57†	2,70	—	7,25 and 7,71	5,45 and 7,12
VIId	9,53†	7,25	7,43	7,22 and 7,67	5,38 and 6,99

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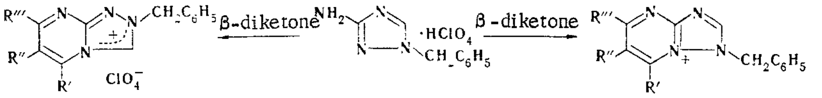
*The J constants in hertz are indicated in parentheses.

†For δ 3-H.

triazolo[1,5-a]pyrimidine. Amidine delocalization of charge is also possible in VII, which are also formed as a result of condensation of V•$HClO_4$ with β-diketones (Table 1).



VII V VI

In conformity with this structure, δ_{CH_2} in the PMR spectrum of the product of condensation with dibenzoylmethane (VIId) does not differ substantially from δ_{CH_2} of the remaining derivatives, in which there is no phenyl group in the 5-position, while in the case of structure VI this group should be shielded by the phenyl group in the 5-position [7, 11]. In addition, in conformity with formula VII, 5-C_6H_5 has precisely the same effect on 3-H as 5-C_6H_5 has on 3-H in IV. There is no reason to doubt that the condensation proceeds in the same manner with dibenzoylmethane as with other β-diketones. Confirmation for this is provided by the closeness of the 3-H chemical shifts of VIIa, c, d, the signals of which are found in the region of 5-H absorption of 1,4-disubstituted sym-triazolium salts [12].

Condensation of V • $HClO_4$ with benzoylacetone gives one isomer (VIIc, R‴ = C_6H_5). The phenyl signal in the PMR spectrum of VIIc is split into two groups of bands with an intensity ratio of 2 : 3 and a difference between their centers of 0.45 ppm. The 7-C_6H_5 signal of VIId has the same character, while 5-C_6H_5 gives an unsplit peak.

EXPERIMENTAL

The amino-sym-triazoles were obtained by the methods in [13, 14]. The PMR spectra of trifluoroacetic acid solutions were determined with a ZKR-60 spectrometer with hexamethyldisiloxane (HMDS) as the internal standard.

Condensation of Aminotriazoles I, II, and V with β-Diketones. A mixture of 0.01 mole of the aminotriazole perchlorate and 0.13 mole of the β-diketone was heated at 120-190° for 1-4 h (Table 1). The mixture was then cooled, and the product was triturated with ether or ether and acetone. The mixture was filtered, and the solid was crystallized from alcohol or water.

Condensation of Perchlorates Ia and IIa with Methyl β-Chlorovinyl Ketone. A 0.02-mole sample of the ketone was added to a solution of 0.01 mole of salt Ia or IIa in the minimum amount of alcohol. The resulting solution warmed up and darkened, and IIIc, d or IVc, d (Table 1) precipitated from the hot solution. The precipitates were separated and crystallized from alcohol.

1,5-Dimethyl-7-(p-dimethylaminostyryl)-sym-triazolo[1,5-a]pyrimidinium Perchlorate. A 0.26-g (1 mmole) sample of IIIa and 0.35 g (2.3 mmole) of p-dimethylaminobenzaldehyde was refluxed in 2 ml of acetic anhydride for 30 min. The resulting precipitate was washed with boiling alcohol and water. Workup gave 0.21 g (54%) of a product with mp 258° and λ_{max} (in alcohol) 506 nm (log ε 4.95). PMR spectrum, δ, ppm: 3.80 (N−CH_3), 3.14 [$N(CH_3)_2$], 2.58 (5-CH_3). Found: Cl 9.3%. $C_{17}H_{20}ClN_5O_4$. Calculated: Cl 9.0%.

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