Chemistry of Heterocyclic Compounds, Vol. 34, No. 2, 1998

CONDENSED IMIDAZO-1,2,4-AZINES.
28.* SYNTHESIS AND TRANSFORMATIONS OF 2-AROYLMETHYL-6,7-DIPHENYLIMIDAZO-[1,2-*b*]-1,2,4-TRIAZIN-4H-3-ONES

V. P. Kruglenko, N. A. Klyuev, M. V. Povstyanoi,
and A. A. Timoshin

*The reaction of 1,2-diamino-4,5-diphenylimidazole with 3-aroyl-2-propanonoic acid yields 2-aroylmethyl-6,7-diphenylimidazo[1,2-*b*]-1,2,4-triazin-4H-3-one. The cyclization pathways of these imidazotriazines leading to condensed furo[2,3-*e*]-, thieno[2,3-*e*]-, pyrrolo[2,3-*e*]-, and furo[3,2-*e*]imidazo[1,2-*b*]-1,2,4-triazines were studied. A mass spectrometric study was carried out on the decomposition of these products upon electron impact.*

In previous work [2], we showed that the reaction of 1,2-diamino-4-phenylimidazole with 3-aroyl-2-propanonoic acids proceeds with involvement of the hydrazinic amine group and $C_{(5)}$ of the heterocycle, leading to substituted imidazo-[1,5-*b*]pyridazines.

In the present work, we studied the analogous reaction but using 1,2-diamino-4,5-diphenylimidazole (I), in which $C_{(5)}$ is blocked by a phenyl substituent. The structure of diamine I prevents reaction by the scheme given above and dictates a different direction. The pathway for the reaction of diamine I with 3-aroyl-2-propanonoic acids was found to depend on the reaction conditions. Salt II was isolated upon heating I with 3-benzoyl-2-propanonoic acid in methanol at reflux. The reaction of diamine I with 3-aroyl-2-propanonoic acids in acetic acid at reflux proceeds further and involves cyclization to give 2-aroylmethyl-6,7-diphenylimidazo[1,2-*b*]-1,2,4-triazin-4H-3-ones IIIa-IIId. Heating salt II in acetic acid at reflux also leads to imidazotriazin-4H-3-one IIIa. The IR spectrum of II shows bands close to those for diamine I and 3-benzoyl-2-propanonoic acid (ν_{CO_2} 1670, 1360 cm^{-1}, $\nu_{NH_3^+}$ 2500, $\delta_{NH_3^+}$ 1580 cm^{-1}) [3]. In contrast to salt II, IIIa shows IR bands for imine and carbonyl groups of a lactide fragment at 3435 and 1620 cm^{-1}, respectively, and for a ketonic C=O group at 1690 cm^{-1}.

The mass spectrum of imidazotriazinone IIIa shows a molecular ion peak with *m/z* 406. The initial steps in the decomposition of M^+ illustrate the structure and position of the benzoylmethyl substituent. Elimination of the $N{\equiv}C{-}CH_2{-}C(O)C_6H_5$ fragment from M^+ (ion Φ, *m/z* 252) is characteristic for all previously studied 1,2,4-triazine systems fused through the bridging nitrogen atom with another heterocycle [4]. Migration of a hydrogen atom of the methylene group to the carbonyl at the adjacent position also takes place. The benzoylmethyl substituent itself was indicated by the ions with *m/z* 119 $[CH_2C(O)C_6H_5]^+$ and *m/z* 105 $[C(O)C_6H_5]^+$.

Ketone IIIa cyclizes upon heating with P_2S_5 in pyridine at reflux to give 2,6,7-triphenylthieno-[2,3-*e*]imidazo-[1,2-*b*]-1,2,4-triazine (IV), while heating this compound with aniline and a catalytic amount of hydrochloric acid gives Schiff base V. The direction of heterocyclization of V depends on the nature of the cyclizing agent. Thus, heating V in $POCl_3$ at reflux gives 1,2,6,7-tetraphenylpyrrolo[2,3-*e*]imidazo[1,2-*b*]-1,2,4-triazine (VI), while heating V in polyphosphoric acid leads to furoimidazotriazine VIIa in 32% yield.

---

*For Communication 27, see [1].

Kherson Industrial Institute, 325008 Kherson, Ukraine. A. N. Severtsov Institute of Ecology and Evolution, Russian Academy of Sciences, 117071 Moscow. Translated from Khimiya Geterotsiklicheskikh Soedinenii, No. 2, pp. 258-262, February, 1998. Original article submitted May 20, 1995; revision submitted May 30, 1997.

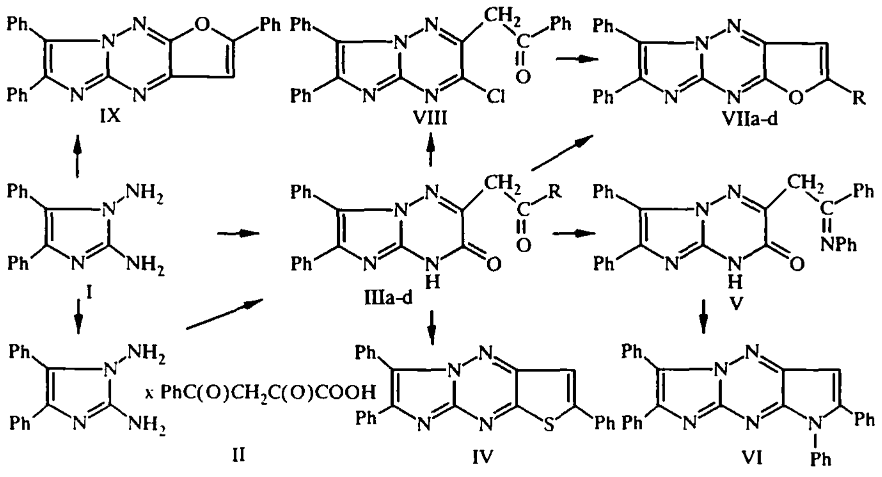
0009-3122/98/3402-0232$20.00

The formation of VIIa-VIId using imidazotriazinones IIIa-IIId proceeds much more smoothly. Heating IIIa-IIId in polyphosphoric acid at 80°C or in $POCl_3$ or with thionyl chloride in chloroform at reflux in the presence of catalytic amounts of dimethylformamide substantially increases the yields of VIIa-VIId (Table 2). The greatest yields for VIIa-VIId are achieved using $POCl_3$ or a mixture of chloroform with $SOCl_2$ as the cyclizing agent. These discrepancies may be attributed to differences in the cyclization pathways for 2-aryltrimethylimidazotriazines IIIa-IIId. Prior enolization of ketones IIIa-IIId occurs upon the action of water-absorbing agents followed by intramolecular dehydration, while substitution of the lactide hydroxyl group in IIIa-IIId by chlorine is observed upon the action of chlorinating agents with subsequent intramolecular dehydrochlorination.

The second reaction direction was supported experimentally. Thus, 2-benzoyl-3-chloro-6,7-diphenylimidazo-[1,2-*b*]-1,2,4-triazine (VIII) was isolated upon brief heating of imidazotriazin-4H-3-one IIIa in $POCl_3$ at reflux. The mass spectrum of VIII showed an M^+ peak with *m/z* 424:426 in 3:1 ratio, which is in accord with the calculated molecular mass for the proposed structure and indicates the presence of one chlorine atom in the molecule. The presence of a benzoylmethyl group in VIII was indicated by ions with *m/z* 279 assigned to $[M - C_6H_5C(O)CH_2CN]^+$, 105 assigned to $[C_6H_5CO]^+$, and 77 assigned to $[C_6H_5]^+$. Chlorine derivative VIII is extremely labile. Brief heating of this compound at 70°C in anhydrous 2-propanol or heating at reflux in $POCl_3$ for 10 min leads to a quantitative yield of furoimidazotriazine VIIa.

The reaction of diaminoimidazole I with 5-phenylfuran-2,3-dione was studied. This dione was used for the purpose of synthesizing isomeric furo[3,2-*e*]imidazo[1,2-*b*]-1,2,4-triazine IX. The condensation of these compounds proceeds smoothly for 12 h in sulfuric acid and leads to the formation of IX (Scheme 1).

Scheme 1



III, VII a R = Ph, b R = C_6H_4Me-4, c R = C_6H_4OMe-4, d R = C_6H_4Cl-4

A mass spectrometric study of IV, VIIa-VIId, and IX indicated the structures of these compounds and suggested a scheme for the fragmentation of furo- and thienoimidazo-1,2-triazines. A feature of the mass spectra of these compounds (Table 1) is the finding of an $[M]^+$ peak with 100% intensity and high resistance to electron impact (18.0, 25.5, and 20.6% for IV, VIIa, and IX, respectively) and a peak for a doubly charged molecular ion $[M^{2+}]$. These features are characteristic for aromatic heterocycles with diphenyl structure [5]. The mass spectrum of such compounds is extremely selective and is observed for IV, VIIa-VIId, and IX. The fragmentation of IV and VIIa-VIId may be represented by the following scheme for the case of tricyclic VIIa:

Scheme 2

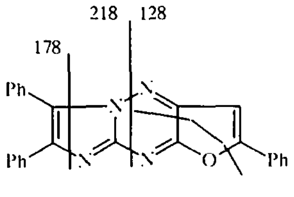


TABLE 1. Mass Spectra of Tricyclics IV, VIIa-d, IX

Ions	I_{rel} (%)*					
	IV	VIIa	VIIb	VIIc	VIId	IX
$[M + 1]^+$	405(30)	389(26)	403(33)	419(3)	423(35)	389(30)
$[M]^+$	404(100)	388(100)	402(100)	418(100)	422(100)	388(100)
$[M-H]^+$	403(18)	387(11)	401(23)	417(36)	421(22)	387(7)
$[M-H-CO]^+$	—	—	—	—	—	359(7)
$[M-RCCHCN]^+$	276(20)	260(16)	260(22)	260(18)	260(30)	—
$[(M-H)-RCCHCN]^+$	275(10)	259(8)	—	—	259(15)	—
$[C_{15}H_{10}N_2]^+$	218(7)	218(5)	218(3)	218(4)	218(6)	218(5)
$[M]^{2+}$	202(5)	194(5)	201(10)	209(9)	—	194(4)
$[C_6H_5CCC_6H_5]^+$	178(5)	178(5)	178(10)	178(5)	178(5)	178(5)
$[C_{13}H_9]^+$	165(13)	165(11)	165(12)	165(30)	165(21)	165(8)
$[RCCHCN]^+$	128(10)	128(22)	142(85)	158(88)	162(23)	—
$[R\ C\ X]^+$	121(12)	105(18)	119(22)	135(3)	139(17)	105(6)
$[R\ CCH]^+$	102(6)	102(27)	116(3)	132(23)	136(6)	102(25)
$[C_6H_5]^+$	77(12)	77(21)	77(35)	77(86)	77(15)	77(25)

---

*Peaks are given for ions with intensity >3%; X = O, S.

TABLE 2. Physical Indices of II-IX

Compound	Chemical formula	Found, % / Calculated, %				mp, °C	R_f	Yield, %
		C	H	N	Cl			
II	$C_{25}H_{22}N_4O_4$	67,75 67,84	5,01 5,01	12,73 12,67	—	168 dec.	0,12	61
IIIa	$C_{25}H_{18}N_4O_2$	73,95 73,86	4,51 4,47	13,69 13,79	—	285...286	0,49	84
IIIb	$C_{26}H_{20}N_4O_2$	74,35 74,25	4,70 4,79	13,40 13,33	—	289...290	0,37	71
IIIc	$C_{26}H_{20}N_4O_3$	71,48 71,53	4,63 4,62	12,80 12,84	—	292...293	0,44	64
IIId	$C_{25}H_{17}N_4O_2Cl$	68,11 68,06	4,01 4,04	12,71 12,78	8,10 8,04	298...299	0,35	66
IV	$C_{25}H_{16}N_4S$	74,15 74,22	4,03 3,99	13,89 13,86	—	251...253	0,86	84
V	$C_{31}H_{23}N_5O$	77,28 77,30	4,90 4,82	14,61 14,55	—	301...302	0,69	71
VI	$C_{31}H_{21}N_5$	80,39 80,31	4,63 4,57	15,07 15,12	—	>350	0,31	98
VIIa	$C_{25}H_{16}N_4O$	77,35 77,29	4,21 4,15	14,38 14,44	—	294...295	0,71	82
VIIb	$C_{26}H_{18}N_4O$	77,55 77,58	4,68 4,70	14,00 13,93	—	313...314	0,7	81
VIIc	$C_{26}H_{18}N_4O_2$	74,71 74,61	4,41 4,34	13,43 13,40	—	296...297	0,72	83
VIId	$C_{25}H_{15}N_4OCl$	71,04 70,98	3,65 3,58	13,18 13,26	8,32 8,39	286...288	0,68	60
VIII	$C_{25}H_{17}N_4OCl$	70,73 70,66	4,09 4,04	13,15 13,20	8,37 8,35	190...191	0,65	62
IX	$C_{25}H_{16}N_4O$	77,32 77,28	4,20 4,15	14,36 14,43	—	352...353	0,54	89

The nature of the fragmentation of isomeric furo[3,2-*e*]imidazo[1,2-*b*]-1,2,4-triazine IX differs from the above scheme. There are no peaks for ions $[M - C_6H_5CCHCN]^+$ and $[C_6H_5CCHCN]^+$, while the ejection of CO from $[M - H]^+$ is a new process. This specific decomposition permits us to distinguish between isomers VIIa and IX.

A study of the capacity of these products to generate laser emission showed that imidazotriazines IIIa-IIId, V, VIII, and condensed heterocycles IV, VI, and VIIa-VIId do not have such properties. An exception is found for furoimidazotriazine IX, which generates at 604-612 nm (3% efficiency).

EXPERIMENTAL

The IR spectra were taken on an IKS-22 spectrometer in KBr pellets. The mass spectra were obtained on a Varian MAT 311A mass spectrometer under standard operational conditions. The purity of the compounds was monitored chromatographically on Silufol-254 plates using 2:1 toluene–2-propanol as the eluent.

1,2-Diamino-4,5-diphenylimidazole 3-Benzoyl-2-propanonate (II). A sample of 1.03 g (5 mmoles) 3-benzoylpropanonoic acid was added to a solution of 1.2 g (5 mmoles) diamine I in 30 ml methanol and heated at reflux for 1 h. The reaction mixture was cooled. The white precipitate was filtered off, washed with ether, and dried in the air.

2-Aroylmethyl-6,7-diphenylimidazo[1,2-*b*]-1,2,4-triazin-4H-3-ones (IIIa-IIId). A mixture of 1.2 g (5 mmoles) diaminoimidazole I and 5 mmoles corresponding 3-aroyl-2-propanoloic acid in 15 ml acetic acid was heated at reflux for 4 h. The reaction mixture was evaporated in vacuum. The oil formed was dissolved in 20 ml acetone and poured onto ice. The precipitate formed was filtered off, suspended in 50 ml 10% aq. Na_2CO_3, and filtered after 12 h. The product was crystallized from dimethylformamide.

Mass spectrum of IIIa, *m/z* (I_{rel}, %): 406(3) $[M]^+$, 405(7) $[M-H]^+$, 251(5) Φ, 218(4), 178(5), 145(3), 106(8), 105(100), 77(37), 43(90).

2,6,7-Triphenylthieno[2,3-*e*]imidazo[1,2-*b*]-1,2,4-triazine (IV). A suspension of 0.4 g (1 mmole) imidazotriazinone IIIa and 0.44 g (2 mmoles) phosphorus pentasulfide in 10 ml pyridine was heated at reflux for 3 h. After cooling, the reaction mixture was poured onto ice. The violet precipitate formed was filtered off and washed with water. The product was crystallized from aqueous DMF.

2-(β-Phenylamino)phenethyl-6,7-diphenylimidazo[1,2-*b*]-1,2,4-triazin-4H-3-one (V). Three drops of hydrochloric acid were added to a solution of 0.4 g (1 mmole) IIIa in 10 ml aniline and heated at reflux for 5 h. After cooling, the precipitate was filtered off and washed with water. The product was crystallized from 2-propanol.

1,2,6,7-Tetraphenylpyrrolo[2,3-*e*]imidazo[1,2-*b*]-1,2,4-triazine (VI). A suspension of 0.48 g (1 mmole) arylamine V in 10 ml $POCl_3$ was heated at reflux for 1.5 h. The reaction mixture was cooled and poured onto ice. The precipitate formed was filtered off, washed with water, and suspended in 10% aq. sodium carbonate. After 12 h, the precipitate was filtered off, washed with water until the wash water was neutral, and dried. The product was crystallized from aqueous DMF.

2-Aryl-6,7-diphenylfuro[2,3-*e*]imidazo[1,2-*b*]-1,2,4-triazines (VIIa-VIId). A suspension of 1 mmole imidazotriazinone IIIa-IIId in 20 ml $POCl_3$ or in 30 ml chloroform with 0.24 g (2 mmoles) thionyl chloride was heated at reflux for 1 h or heated in 7 ml polyphosphoric acid or 10 ml concentrated sulfuric acid at reflux for 24 h. The reaction mixture was cooled, poured into ice water, and neutralized by adding aqueous sodium carbonate. The precipitate formed was filtered off. The yield ranged from 50% in the acids to 80% in the mixture of chloroform and thionyl chloride. The product was crystallized from dimethylformamide.

2-Benzoylmethyl-3-chloro-6,7-diphenylimidazo[1,2-*b*]-1,2,4-triazine (VIII). A suspension of 0.4 g (1 mmole) imidazotriazine IIIa in 10 ml $POCl_3$ was heated for 10 min at 60°C. The precipitate formed was filtered off, washed with water, dried, and crystallized from 2-propanol. Mass spectrum of VIII: *m/z* (I_{rel}, %): 426(2), 424(9) $[M^+]$, 388(6), 279(5), 167(11), 150(5), 135(7), 106(8), 105(100), 103(7), 83(5), 77(3), 76(6), 71(9), 70(9), 69(6), 57(24), 56(7), 55(13), 51(5), 42(15).

2,6,7-Triphenylfuro[2,3-*e*]imidazo[1,2-*b*]-1,2,4-triazine (IX). A mixture of 0.25 g (1 mmole) diamine I and 0.16 g (1 mmole) 5-phenyl-2,3-furandione in 15 ml concentrated sulfuric acid was heated at 60°C for 10 h, cooled and poured onto ice. The precipitate formed was filtered off, washed with water, and dried. The product was crystallized from aqueous DMF.

REFERENCES

1. N. A. Klyuev, M. V. Povstyanoi, V. M. Orlov, V. P. Gnidets, and V. P. Kruglenko, Khim. Geterotsikl. Soedin., No. 7, 937 (1992).
2. V. P. Kruglenko, A. A. Timoshin, V. A. Idzikovskii, N. A. Klyuev, and M. V. Povstyanoi, Ukr. Khim. Zh., 5, No. 6, 612 (1988).
3. A. Gordon and R. Ford, Chemist's Handbook [Russian translation], Mir, Moscow (1976).

4. M. V. Povstyanoi, V. P. Kruglenko, A. A. Timoshin, N. A. Klyuev, I. I. Grandberg, and Yu. Yu. Stoilov, Izv. TSKhA, No. 5, 155 (1984).
5. N. A. Klyuev, A. K. Sheinkman, R. A. Khmel'nitskii, G. A. Mal'tseva, and N. R. Kal'nitskii, Zh. Org. Khim., **13**, No. 5, 1079 (1977).
6. V. P. Kruglenko, N. S. Patalakha, P. B. Kuranov, N. A. Klyuev, and V. A. Idzikovskii, Khim. Geterotsikl. Soedin., No. 5, 694 (1985).