Pyridazines. LXV. Reactions of Some 1-Phenacylazolopyridazinium Halides with 2,3-Diphenylcyclopropenone, -thione, or Hydrazine

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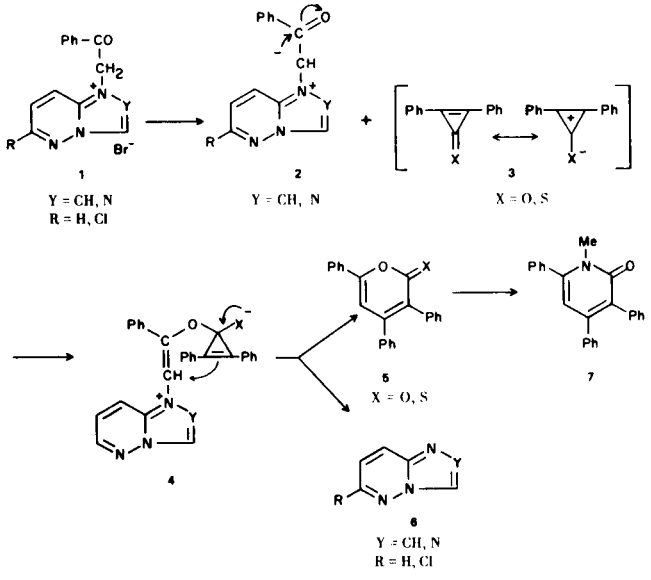
1-Phenacylazolopyridazinium bromides reacted with 2,3-diphenylcyclopropenone or -thione in the presence of triethylamine to give 3,4,6-triphenyl-2-pyrone or -2-thiopyrone and the corresponding azolopyridazine. Quaternized azolopyridazines reacted with hydrazine to give either 3,6-diphenylpyridazine and the corresponding azoloazine or by ring opening of the azine part to give 1-methyl-2-(pyrazolyl-5′)imidazole.

Cyclopropenone or its analogs, as representatives of strained rings, undergo cycloaddition reactions with a variety of heterocyclic systems (1-7). The presence of two reactive sites in the cyclopropenone molecule makes difficult the prediction of the mechanism involved in these reactions. The products can be formed either by addition on the carbon-carbon or carbon-oxygen double bond (8). Moreover, it has been shown that the reaction of enamines with cyclopropenones may proceed by C,N-insertion, C,C-insertion, condensation or addition (9-11).

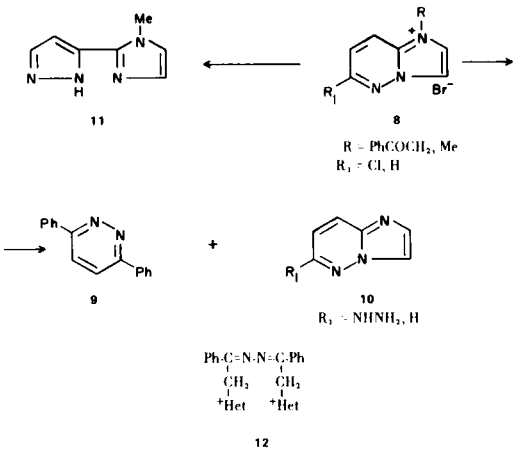
1-Phenancylimidazo[1,2-*b*]pyridazinium bromide (12) or its analogs and 1-phenacyl-*s*-triazolo[4,3-*b*]pyridazinium bromide (**1**) reacted with 2,3-diphenylcyclopropenone or -thione (**3**) in the presence of triethylamine to give products which were identified as 3,4,6-triphenyl-2-pyrone or -2-thiopyrone (**5**) and the corresponding azolopyridazine (**6**). It is most probable that the reaction proceeds *via* an ylid (**4**), formed under the influence of the base as outlined in the flow sheet. This is comparable to the formation of 2-pyrones from carbonylpyridinium ylids and diarylcyclopropylidene compounds or diarylcyclopropenones (13,14).



Another possibility, the formation of the corresponding 4-pyrones, must be also taken into consideration. Namely, it has been observed that pyridinium ylids react with diphenylthiirene dioxide to give 1,4-oxathiin dioxides which can be regarded as analogs of 4-pyrones (15). A reaction course which would lead to the formation of 4-pyrones (by addition to the C,C-double bond of the cyclopropenone) is excluded in our case on the basis of the following observations.

It has been observed that mass spectral fragmentation of phenyl-substituted 4-pyrones results in the formation of phenylacetylene and CO by the retro-Diels-Alder reaction (16) of the parent ion (17,18). These observations are said to be useful for mass-spectrometric differentiation between 4-pyrones and 2-pyrones. In the mass spectra of 3,4,6-triphenyl-2-pyrones or -2-thiopyrones, we could observe among the most abundant species the M-133 or M-149 peak corresponding to the loss of PhCCOX or PhCOCX unit, resulting from two possible pathways of fragmentation. Moreover, the 3,4,6-triphenyl-2-pyrone (**5**, X = O) obtained could be converted into 1-methyl-3,4,6-triphenyl-2(1*H*)pyridone (**7**) (19) for the purpose of identification.

The formation of 3,6-diphenylpyridazine (**9**) from 2-phenacylimidazo[1,2-*b*]pyridazinium bromide (**8**, R = $PhCOCH_2$, R_1 = H) and hydrazine can be envisaged as proceeding through an intermediate ketazine (**12**) as proposed recently for a related conversion of some pyridinium salts (20). However, it is also possible that



first an azomethine ylid (**2**, Y = CH, R = H) is formed (21) under the action of hydrazine as a base. From the ylid, 1,2-dibenzoylethylene may be generated which in turn is transformed by hydrazine into 3,6-diphenylpyridazine.

On the other hand, 1-methylimidazo[1,2-*b*]pyridazinium bromide (**8**, R = Me, R_1 = H) was transformed with hydrazine into 1-methyl-2-(pyrazolyl-5')imidazole (**11**). The reaction proceeds by an attack of the base at position 6 of the bicycle, followed by ring opening and recyclization as already observed previously (22,23).

EXPERIMENTAL (25)

1-Phenacylimidazo[1,2-*b*]pyridazinium Bromide (**1**, Y = CH, R = H).

A solution of imidazo[1,2-*b*]pyridazine (11.9 g.) in ethanol (200 ml.) was treated with phenacyl bromide (19.9 g.), and the solution was heated under reflux for 1 hour. The solvent was evaporated *in vacuo* to half of its volume and the residue was left on ice. The separated product was filtered off and crystallized from ethanol, m.p. 260° (67% yield); nmr (DMSO-d_6): τ = 1.53 (d, H_2), 1.30 (dd, H_3), 1.00 (dd, H_6), 2.10 (dd, H_7), 1.20 (ddd, H_8), 3.55 (s, CH_2), 2.50 and 2.10 (m, Ph), $J_{2,3}$ = 1.5, $J_{3,8}$ = 0.6, $J_{6,7}$ = 4.7, $J_{6,8}$ = 1.3, $J_{7,8}$ = 9.7 Hz.

Anal. Calcd. for $C_{14}H_{12}BrN_3O$: C, 52.84; H, 3.80; N, 13.20. Found: C, 52.83; H, 3.93; N, 13.48.

In the same manner the following compounds were prepared.

1-Phenacyl-6-chloroimidazo[1,2-*b*]pyridazinium Bromide (**1**, Y = CH, R = Cl).

This compound was obtained in 62% yield, m.p. 264° (from ethanol); nmr (DMSO-d_6): τ = 1.55 (d, H_2), 1.28 (dd, H_3), 2.00 (d, H_7), 1.10 (dd, H_8), 3.57 (s, CH_2), 2.50 and 2.10 (m, Ph), $J_{2,3}$ = 1.5, $J_{3,8}$ = 0.6, $J_{7,8}$ = 9.7 Hz.

Anal. Calcd. for $C_{14}H_{11}BrClN_3O$: C, 47.68; H, 3.14; N, 11.91. Found: C, 47.45; H, 3.22; N, 12.39.

1-Phenacyl-*s*-triazolo[4,3-*b*]pyridazinium Bromide (**1**, Y = N, R = H).

This compound was prepared in 53% yield, m.p. 210° (from ethanol); nmr (DMSO-d_6): τ = -0.35 (s, H_3), 0.85 (dd, H_6), 1.75 (dd, H_7), 0.95 (dd, H_8), 3.28 (s, CH_2), 2.40 and 1.90 (m, Ph), $J_{6,7}$ = 4.5, $J_{7,8}$ = 9.2, $J_{6,8}$ = 1.5 Hz.

Anal. Calcd. for $C_{13}H_{11}BrN_4O$: C, 48.91; H, 3.47; N, 17.55. Found: C, 48.92; H, 3.77; N, 17.35.

Reaction Between 1-Phenacylimidazo[1,2-*b*]pyridazinium Bromide and 2,3-Diphenylcyclopropenone.

A mixture of **1**, (Y = CH, R = H) (1.6 g.), 2,3-diphenylcyclopropenone (26) (**3**, X = O) (1.0 g.), methanol (20 ml.), and triethylamine (1 ml.) was heated under reflux for 20 minutes. The yellow product was filtered off and crystallized from methanol and *N,N*-dymethylformamide (10:1) to give the pure 3,4,6-triphenyl-2-pyrone (**5**, X = O) (0.93 g., 58%), m.p. 183-185° (lit. (19) gives m.p. 183-184°); mass spectrum: M^+ 324; nmr (DMSO-d_6): τ = 3.07 (s, H_5), 2.20 and 2.57 (m, 6-Ph), 2.90 and 2.94 (s, 3- and 4-Ph). In the filtrate imidazo[1,2-*b*]pyridazine (**6**, Y = CH, R = H) was identified.

For identification, 3,4,6-triphenyl-2-pyrone was transformed with aqueous methylamine into the known (19) 1-methyl-3,4,6-triphenyl-2(1*H*)pyridone (**7**); nmr (DMSO-d_6): τ = 3.90 (s, H_5), 6.70 (s, 1-Me), 2.50 (broad s, 2-Ph), 2.93 (broad s, 3- and 4-Ph).

The same conversion into 3,4,6-triphenyl-2-pyrone could be observed with 1-phenacyl-6-chloroimidazo[1,2-*b*]pyridazinium bromide (**1**, Y = CH, R = Cl) or 1-phenacyl-*s*-triazolo[4,3-*b*]pyridazinium bromide (**1**, Y = N, R = H). In the last case besides the pyrone, *s*-triazolo[4,3-*b*]pyridazine (**6**, Y = N, R = H) was formed and detected in the filtrate.

Reaction Between 1-Phenacylimidazo[1,2-*b*]pyridazinium Bromide and 2,3-Diphenylcyclopropenethione.

A mixture of 1-phenacylimidazo[1,2-*b*]pyridazinium bromide (**1**, Y = CH, R = H) (0.3 g.), 2,3-diphenylcyclopropenethione (27) (**3**, X = S) (0.2 g.), methanol (5 ml.) and triethylamine (0.5 g.) was heated under reflux for 30 minutes. The red precipitate was filtered off and in the filtrate imidazo[1,2-*b*]pyridazine (**6**, Y = CH, R = H) was detected by tlc. The precipitate was identified as 3,4,6-triphenyl-2-thiopyrone (**5**, X = S), m.p. 165° (from ethanol and *N,N*-dimethylformamide, 2:1) (lit. (19) gives m.p. 165-166°); mass spectrum: M^+ = 340; nmr (DMSO-d_6): τ = 2.58 (s, H_5), 2.05 and 2.55 (m, 6-Ph), 2.88 and 2.92 (s, 3-Ph, 4-Ph).

The same reaction could be observed with 1-phenacyl-6-chloroimidazo[1,2-*b*]pyridazinium bromide (**1**, Y = CH, R = Cl) and 1-phenacyl-*s*-triazolo[4,3-*b*]pyridazinium bromide (**1**, Y = N, R = H).

3,6-Diphenylpyridazine (**9**).

A mixture of 1-phenacyl-6-chloroimidazo[1,2-*b*]pyridazinium bromide (**8**, R = $PhCOCH_2$, R_1 = Cl) (1.76 g.) and hydrazine hydrate (5 ml. of 80%) was heated under reflux for 30 minutes. Upon cooling the product which separated was collected and washed with water. It was crystallized from ethanol (0.52, 78% yield), m.p. 225° (lit. (28) gives m.p. 221-222°); mass spectrum: M^+ 232; nmr (TFAA): τ = 1.30 (s, H_4, H_5), 2.40 and 2.10 (m, Ph).

The filtrate, after the diphenyl compound was separated, was evaporated to dryness, cold water (5 ml.) was added and the residue filtered off. It consisted of 3,6-diphenylpyridazine (10%) and 6-hydrazinoimidazo[1,2-*b*]pyridazine (**10**, R_1 = $NHNH_2$), identical with an authentic specimen.

In the same manner, 1-phenacylimidazo[1,2-*b*]pyridazinium bromide (**8**, R = $PhCOCH_2$, R_1 = H) reacted to give 3,6-diphenylpyridazine and imidazo[1,2-*b*]pyridazine (**10**, R_1 = H).

1-Methyl-2-(pyrazolyl-5')imidazole (**11**).

A mixture of 1-methylimidazo[1,2-*b*]pyridazinium iodide (**8**,

R = Me, R_1 = H) (0.65 g.) and hydrazine hydrate (3 ml. of 80%) was heated under reflux until the evolution of ammonia ceased. Excess hydrazine was distilled off *in vacuo* and the residue was crystallized from ethanol, m.p. of the hydroiodide 214°; mass spectrum: $M^+ - HJ = 148$; nmr (DMSO-d_6): τ = 2.15 (d, H_5), 1.82 (d, H_4), 6.20 (s, Me), 1.57 (d, H_3), 3.08 (d, H_4), $J_{4,5}$ = 2.4, $J_{3',4'}$ = 2.4 Hz.

Anal. Calcd. for $C_7H_9IN_4$: C, 30.45; H, 3.29; N, 20.29. Found: C, 30.46; H, 3.33; N, 20.34.

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