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REGIOSELECTIVE SYNTHESIS OF 3- AND 5-FUNCTIONAL DERIVATIVES OF PYRAZOLIDINE. 1. SYNTHESIS OF KETONES OF THE PYRAZOLIDINE SERIES

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When 5-hydroxypyrazolidines reacted with ketones on the surface of basic adsorbents the 3-regioisomers were obtained in addition to the expected 5-oxoalkylpyrazolidines. The conditions for the regiodirection of the process have been found.

Keywords: ketones, 3- and 5-oxoalkylpyrazolidines, diastereoselectivity, isomerization, mass spectroscopic analysis of isomers, reactions on the surface of adsorbents.

We have shown earlier [1] that 5-hydroxypyrazolidines **1a,b** react with CH-acids on the surface of alumina without solvent at 60°C to give the corresponding 5-functional derivatives of the pyrazolidine series; in particular, compound **1a** reacted with a number of ketones. The hydroxypyrazolidine **1b**, which has a *trans*-methyl group in position 3, does not react with ketones for steric reasons – replacement of the hydroxy group in compound **1b** requires more vigorous conditions than for compound **1a** [1]. We recently reported [2] that hydroxypyrazolidines **1a,b** reacted with acetophenone on a potassium fluoride surface deposited on aluminum oxide (at 80°C) or barium hydroxide (at room temperature) to form mixtures of the regioisomers **3a,b** and **5a,b** (Table 1).

It may be assumed that the reason for the formation of the regioisomers **3** is participation in the reaction of the linear tautomer of hydroxypyrazolidine **1** which readily undergoes "retro-Michael" decomposition to the hydrazide and crotonic aldehyde with subsequent "reverse" addition of the hydrazide to the double bond under conditions of basic catalysis.

The regioisomeric hydrazino aldehyde **1b'** evidently exists in the linear form only (likes its analog prepared from hydrazobenzene [3]) and reacts directly with acetophenone. In a model experiment on a KF/Al_2O_3 surface 1-acetyl-2-phenylhydrazine, crotonic aldehyde, and acetophenone were deposited on the surface and subjected to the conditions used for the reacion with hydroxypyrazolidine [2]. As a result the regioisomers **3** and **5** were obtained in close to the same ratio as in the normal reaction which serves as additional support in favor of the proposed scheme for the process.

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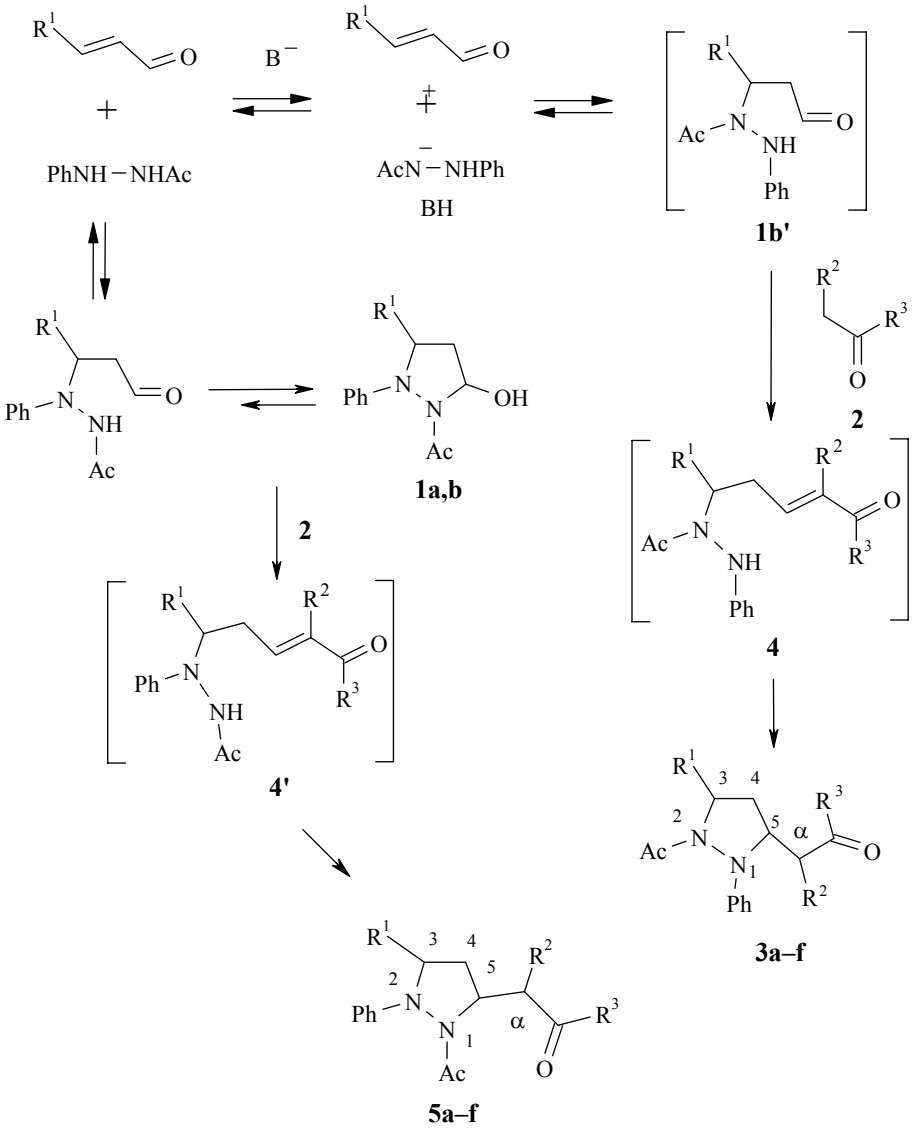


1 a R^1 = H, **b** R^1 = Me; **2 a** R^2 = H, R^3 = Ph; **b** R^2 = H, R^3 = C_6H_4OMe-*p*; **c** R^2 = H, R^3 = C_6H_4Br-*p*; **d** R^2 = H, R^3 = Me; **e** $R^2 + R^3 = (CH_2)_4$; **3-5 a** R^1 = Me, R^2 = H, R^3 = Ph; **b** $R^1 = R^2$ = H, R^3 = Ph; **c** R^1 = Me, R^2 = H, R^3 = C_6H_4OMe-*p*; **d** R^1 = Me, R^2 = H, R^3 = C_6H_4Br-*p*; **e** $R^1 = R^3$ = Me, R^2 = H; **f** R^1 = Me, $R^2 + R^3 = (CH_2)_4$

The reaction of the hydroxypyrazolidine **1b** with other ketones – *p*-bromoacetophenone, *p*-methoxyacetophenone, acetone and cyclohexanone – under these conditions also gave mixtures of the 3- and 5-isomers of the corresponding ketones. The ratio of the isomers in the reaction mixtures was determined by the nature of the ketone starting material and the base used (Table 1).

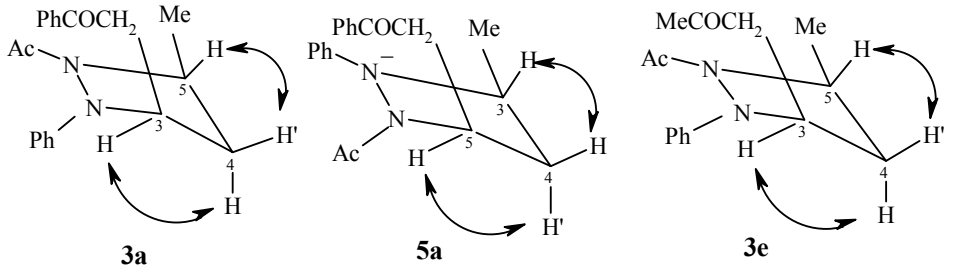
The reaction of ketones with pyrazolidine **1b** on a KF/Al_2O_3 surface does not depend much on the nature of the ketone and leads predominantly to the 3-functional derivatives, which is probably explained not only by the nature of the adsorbent but also by the higher reaction temperature (80°C) which increases the proportion of the linear tautomer of **1b** and accelerates its decomposition. The ratio of the isomers on a barium hydroxide surface at room temperature is different – the derivatives **5** predominate and the nature of the ketone has a considerable effect. For example, the reaction pyrazolidine **1b** with *p*-bromoacetophenone on barium hydroxide slowed the process leading to isomer **5d**, the content of the linear form of the pyrazolidine starting material and increased the amount of isomer **3d**.

TABLE 1. Ratios of the Regioisomers in the Reactions of Ketones with Hydroxypyrazolidines on the Surface of Basic Adsorbents

Isomers **3** and **5**	KF (A)		$Ba(OH)_2$ (B)		
	3 : **5**	Reaction time, h	**3** : **5**	Reaction time, days	Conversion of **1a**,**b**, %
a	2 : 1	4	1 : 2.5	4	60
b	1 : 2	2	—	—	—
c	2 : 1	4	1 : 4	4	80
d	2 : 1	4	10 : 11	9	40
e	2.5 : 1	3	1 : 2.5	4	—
f	3 : 1	3	1 : 5.5	3	70

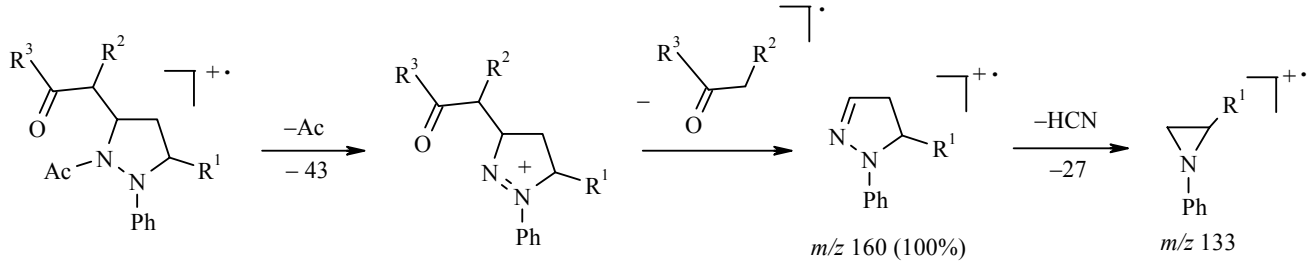
The IR and ^{1}H NMR spectra of the 3- and 5-isomers were not inconsistent with the expected structures but, despite the differences noted, did not permit the unambiguous identification of the products. The structures of compounds **3a,e** and **5a** were studied additionally by ^{1}H NMR spectroscopy with the use of the nuclear Overhauser effect. According to the NOE data, all these compounds are *trans* isomers (H' is a weak field signal):

3a $\eta_{H\text{-}3}$ (H-4) = 4.1, $\eta_{H\text{-}5}$ (H'-4) = 3.65%;
5a $\eta_{H\text{-}4}$ (H-3) = 6.3, $\eta_{H'\text{-}4}$ (H-5) = 8.8%;
3e $\eta_{H\text{-}4}$ (H-3) = 9.1, $\eta_{H'\text{-}4}$ (H-5) = 3.1, $\eta_{H\text{-}3}$ (H-4) = 8.0, $\eta_{H\text{-}5}$ (H'-4) = 6.9%.



This precludes the proposal that the isomers **3** and **5** have the *cis* structure.

A reliable indicator of the structures of the regioisomers is obtained from their mass spectra. Both the 3- and 5-functional derivatives have characteristic basic fragmentations for the respective series (Table 2). The splitting of a ketone fragment as a free radical is observed for compounds **5**:

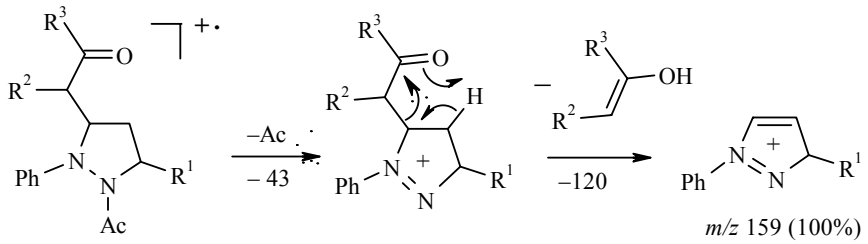


The pyrazolinium ion-radical with *m/z* 160 formed in this way is either the base peak or is very intense in the spectra of all the isomers of this series, which is explained by its stabilization by the phenyl substituent on atom N-2. This pattern of fragmentation is typical of all 1-acetyl-2-phenyl-5-substituted pyrazolidines [4].

TABLE 2. Mass Spectra of β-Oxoalkylpyrazolidines

Com-pound	*m/z* (I_{rel}, %)
5a	322 $[M]^+$ (29.7), 279 (94.1), 160 **(**100**),** 159 (21), 145 (24.8), 133 (5), 118 (32.7)
3a	322 $[M]^+$ (15.9), 279 (7), 159 (100**),** 118 (32.7), 105 (72.3)
5b	308 $[M]^+$ (4.2), 265 (52.8), 146 (62.0), 145 (21.1), 105 (100)
3b	308 $[M]^+$ (4.2), 265 (12.0), 145 (100), 105 (31.7)
5c	400, 402 $[M]^+$ (5.6), 357, 359 (29.7), 182 (49), 184 (34.3), 160 (100), 159 (28.7), 133 (4.9)
3c	400, 402 $[M]^+$ (5.6), 357, 359 (6.3), 182, 184 (13.3), 159 (100)
5e	260 $[M]^+$ (40.6), 217 (100), 160 (35.6), 159 (20.8), 145 (16.3), 133 (7.4)
3e	260 $[M]^+$ (21.3), 217 (22.3), 159 (100)
5f[1]	300 $[M]^+$ (14.0), 257 (100), 160 (37.1), 159 (11.2), 133 (9.1), 118 (49.0)
3f	300 $[M]^+$ (14.0), 257 (21.0), 159 (100), 118 (12.6)

In the case of derivatives of **3** the enolic form of the ketone is lost as a result of a MacLafferty rearrangement to give a stable pyrazolium ion with *m/z* =159 which is the base peak in all the spectra. Neither loss of a ketone radical with formation of an ion with *m/z* 160 nor elimination of HCN molecules was observed in the mass spectra of 3-functional compounds. We have observed this regularity in derivatives of pyrazolidine **1a** – the ketones **3b** and **5b**.



In the derivatives of cyclohexanone **3f** and **5f**, in consequence of the existence of another center of asymmetry (the methyne group of the cyclohexanone unit), both regioisomers occur as two diastereomers. In the reaction on potassium fluoride the ratio of the diastereomers **5f**[1] and **5f** [2] is 2:1 , while for the 3-functional derivatives **3f**[1] and **3f**[2] it is 1.5:1. The diastereomers of the 5-functional derivative were separated chromatographically and isolated in pure form.

EXPERIMENTAL

IR spectra were recorded as nujol mulls or films on a UR-20 instrument. ^1H and ^{13}C NMR spectra of $CDCl_3$ solutions with TMS as internal standard were recorded with a Varian VXR-400 instrument (400 and 100 MHz respectively). Mass spectra (EI, 70eV, direct injection) were recorded on a Finnigan SSQ-7000 instrument. Purity of the compounds synthesized was monitored by TLC on Silufol plates with 1:1 petroleum ether–ethyl acetate as eluent using iodine vapor and $FeCl_3$ in ethanol for development. Chromatographic purification of the compounds synthesized was by flash chromatography in a dry column with silicagel L5/40 according to [5].

β-Oxoalkylpyrazolidines 3 and 5 (General Methods). All experiments were carried out under an inert atmosphere up to the extraction of the reaction mixture from adsorbent.

A. Potassium fluoride (2.2 g) adsorbed on aluminum oxide [6] was placed in an ampule and a solution of a hydroxypyrazolidine (1 mmol) and a ketone (1 mmol) in benzene was added, the solvent was removed in vacuum without heating and the mixture was stirred. The ampule was evacuated, sealed, and heated for 4 h at 80°C. The ampul was opened and the mixture extracted with ether. The extract was evaporated and the residue was separated by flash chromatography on a dry column with SiO_2. The mixture was eluted with petroleum ether (40-70°C)–ethyl acetate in a gradient from 10:1 to 1:1. The compounds isolated were recrystallized from ether.

B. Anhydrous barium hydroxide (8.8 g) was placed in an ampule and a solution of a hydroxypyrazolidine (2 mmol) and a ketone (3 mmol) in benzene (2 ml) was added. The solvent was removed in vacuum without heating, stirred, and the ampule was evacuated. The ampul was shaken twice in a day (for duration of the experiment see Table 1). After opening the ampule, the mixture was extracted with ether. Further treatment was as for method A.

1-Acetyl-5-benzoylmethyl-3-methyl-2-phenylpyrazolidine (5a) was obtained from the reaction of pyrazolidine **1b** (2.2 g, 10 mmol) with acetophenone (2.4 ml, 15 mmol), yield 0.8 g [25% (A) and 5% (B)]; mp 98-99°C. IR spectrum, ν, cm^{-1}: 1650 (CO amide), 1690 (CO ketone). ^1H NMR spectrum, δ, ppm (*J*, Hz): 1.21 (3H, d, *J* = 6.8, 3-CH_3); 2.02 (3H, s, CH_3CO); 1.85 (1H, m, H-4); 2.25 (1H, m, H-4); 2.83 (1H, dd, $J_{\alpha\alpha}$ = 16.2, $J_{\alpha5}$ = 10.6, H-α); 4.10 (1H, dd, $J_{\alpha\alpha}$ = 16.0, $J_{\alpha5}$ = 3.5, H-α); 4.15 (1H, m, H-3); 4.76 (1H, m, H-5); 6.95-7.27 (5H, m, N–C_6H_5); 7.40-7.90 (5H, m, O–C_6H_5). ^{13}C NMR spectrum, δ, ppm: 19.5 (CH_3); 21.3 (CH_3); 38.2 (C-4); 44.6 (C-α); 53.7 (C-3); 61.7 (C-5); 115.0 (*o*-C_6H_5N); 121.7 (*p*-C_6H_5N); 128.1 (*m*-C_6H_5N); 128.5 (*m*-C_6H_5CO); 129.2 (*o*-C_6H_5CO); 133.2 (*p*-C_6H_5CO); 136.3 (*i*-C_6H_5CO); 150.4 (*i*-C_6H_5N); 174.6 ($\underline{C}OCH_3$); 197.8 (COC_6H_5). Found, %: C 74.78; H 6.78; N 8.60. $C_{20}H_{22}N_2O_2$. Calculated, %: C 74.53; H 6.83; N 8.70.

1-Acetyl-3-benzoylmethyl-5-methyl-2-phenylpyrazolidine (3a) was obtained from the reaction of pyrazolidine **1b** (2.2 g, 10 mmol) with acetophenone (2.4 ml, 15 mmol), yield 0.5 g [16%(B) and 7%(A)]; mp 124-125°C. IR spectrum, ν, cm^{-1}: 1650, 1690. ^1H NMR spectrum, δ, ppm (*J*, Hz): 1.50 (3H, d, *J* =6.4, 5-CH_3); 1.83 (3H, s, CH_3CO); 1.95 (1H, m, H-4); 2.10 (1H, m, H-4); 2.83 (1H, dd, $J_{\alpha\alpha}$ = 17.1, $J_{\alpha3}$ = 5.0, H-α); 3.38 (1H, dd, $J_{\alpha\alpha}$ = 17.0, $J_{\alpha3}$ = 9.0, H-α); 4.40 (1H, m, H-5); 4.70 (1H, m, H-3); 6.95-7.55 (10H, m, Ar). ^{13}C NMR spectrum, δ, ppm: 21.18 (CH_3); 21.25 (CH_3); 38.2 (C-4); 40.1 (C-α); 52.6 (C-3); 62.9 (C-5); 115.6 (*o*-C_6H_5N); 121.9 (*p*-C_6H_5N); 127.9 (*m*-C_6H_5N); 128.6 (*m*-C_6H_5CO); 128.9 (*o*-C_6H_5CO); 133.3 (*p*-C_6H_5CO); 136.6 (*i*-C_6H_5CO); 150.2 (*i*-C_6H_5N); 173.8 ($\underline{C}OCH_3$); 197.6 (COC_6H_5). Found, %: C 75.29; H 6.99; N 8.83. $C_{20}H_{22}N_2O_2$. Calculated, %: C 74.53; H 6.83; N 8.70.

1-Acetyl-5-benzoylmethyl-2-phenylpyrazolidine (5b) was prepared by the reaction of pyrazolidine **1a** (0.41 g, 2 mmol) with acetophenone (0,36 ml, 3 mmol) by method B, yield 0.03 g (5%); mp 102-103°C (an oil according to [1]). ^1H NMR spectrum, δ, ppm (*J*, Hz): 2.10 (3H, s, CH_3CO); 1.70 (1H, m, H-4); 2.88 (1H, dd, $J_{\alpha\alpha}$ = 16.4, $J_{\alpha3}$ = 10.6, H-α); 4.12 (1H, d, *J* = 15.3, H-α); 3.35 (1H, m, H-3); 4.75 (1H, m, H-5); 7.0-7.5 (10H, m, C_6H_5).

1-Acetyl-3-benzoylmethyl-2-phenylpyrazolidine (3b) was prepared by the reaction of pyrazolidine **1a** (0.41 g, 2 mmol) with acetophenone (0,36 ml, 3 mmol) by method B, yield 0.02 g (3%), oil. ^1H NMR spectrum, δ, ppm (*J*, Hz): 1.85 (3H, s, CH_3CO); 1.90 (1H, m, H-4); 2.25 (1H, m, H-4); 2.82 (1H, dd, $J_{\alpha\alpha}$ = 16.9, $J_{\alpha3}$ = 5.0, H-α); 3.40 (1H, dd, $J_{\alpha\alpha}$ = 16.8, $J_{\alpha3}$ = 9.2, H-α); 3.46 (1H, m, H-5); 4.10 (1H, m, H-5); 4.62 (1H, m, H-3); 7.00-7.45 (10H, m, C_6H_5). Found, %: C 74.20; H 6.65; N 8.87. $C_{19}H_{20}N_2O_2$. Calculated, %: C 74.03; H 6.49; N 9.09.

1-Acetyl-5-*p*-bromobenzoylmethyl-3-methyl-2-phenylpyrazolidine (5c) was made by reaction of pyrazolidine **1b** (0.22g, 1 mmol) with *p*-bromoacetophenone (0.2 g, 1 mmol), yield 0.053 g (12%, A); mp 108-109°C. IR spectrum, ν, cm^{-1}: 1650, 1690. ^1H NMR spectrum, δ, ppm (*J*, Hz): 1.20 (3H, d, *J* = 6.8, 3-CH_3); 1.79 (1H, m, H-4); 2.05 (3H, s, CH_3CO); 2.20 (1H, m, H-4); 2.80 (1H, dd, $J_{\alpha\alpha}$ = 16.0, $J_{\alpha5}$ = 10.5, H-α); 3.95 (1H, dd, $J_{\alpha\alpha}$ = 16.1, $J_{\alpha5}$ = 3.4, H-α); 4.10 (1H, m, H-3); 4.50 (1H, m, H-5); 6.95-7.28 (5H, m, C_6H_5); 7.65, 7.80 (4H, 2 d, *J* = 8.6, *p*-BrC_6H_4CO). Found, %: C 60.01; H 5.40; N 6.95. $C_{20}H_{21}BrN_2O_2$. Calculated, %: C 59.85; N 5.24; N 6.98.

1-Acetyl-3-*p*-bromobenzoylmethyl-5-methyl-2-phenylpyrazolidine (3c) was made by reaction of pyrazolidine **1b** (0.22g, 1 mmol) with *p*-bromoacetophenone (0.2 g, 1 mmol), yield 0.13 g (32%, B); mp 149-150°C. IR spectrum, ν, cm^{-1}: 1650, 1690. ^1H NMR spectrum, δ, ppm (*J*, Hz): 1.47 (3H, d, *J* = 6.4, 5-CH_3); 1.84 (3H, s, CH_3CO); 1.98 (1H, m, H-4); 2.12 (1H, m, H-4); 2.80 (1H, dd, $J_{\alpha\alpha}$ = 17.3, $J_{\alpha3}$ = 4.8, H-α); 3.35 (1H, dd, $J_{\alpha\alpha}$ = 17.0, $J_{\alpha3}$ = 8.9, H-α); 4.50 (1H, m, H-5); 4.75 (1H, m, H-3); 7.0-7.3 (5H, m, N–C_6H_5); 7.60, 7.83 (4H, 2d, *J* = 8.6, ArCO). Found, %: C 60.14; H 5.29; N. 7.21. $C_{20}H_{21}BrN_2O_2$. Calculated, %: C 59.85; N 5.24; N 6.98.

1-Acetyl-5-*p*-methoxybenzoylmethyl-3-methyl-2-phenylpyrazolidine (5d) was prepared by the reaction of pyrazolidine **1b** (0.220 g, 1 mmol) with *p*-methoxyacetophenone (0.165 g, 1 mmol), yield 0.06 g (17%, A); mp 95-96°C. IR spectrum, ν, cm^{-1}: 1660, 1680. ^1H NMR spectrum, δ, ppm (*J*, Hz): 1.22 (3H, d, *J* = 7.0, 3-CH_3); 2.10 (3H, s, CH_3CO); 1.85 (1H, m, H-4); 2.22 (1H, m, H-4); 2.82 (1H, dd, $J_{\alpha\alpha}$ = 15.6, $J_{\alpha5}$ = 10.6, H-α); 3.88 (3H, s, OCH_3); 4.05 (1H, dd, $J_{\alpha\alpha}$ = 15.9, $J_{\alpha5}$ = 3.2, H-α); 4.15 (1H, m, H-3); 4.80 (1H, m, H-5); 6.85, 7.93 (4H, 2 d, *J* = 8.9, ArCO); 7.00-7.23 (5H, m, N–C_6H_5). Found, %: C 71.40; H 6.99; N 8.14. $C_{21}H_{24}N_2O_3$. Calculated, %: C 71.59; H 6.82; N 7.95.

1-Acetyl-3-*p*-methoxybenzoylmethyl-5-methyl-2-phenylpyrazolidine (3d) was prepared by the reaction of pyrazolidine **1b** (0.22 g, 1 mmol) with *p*-methoxyacetophenone (0.15 g, 1 mmol), yield 0.47 g (13%, B); mp 146-147°C. IR spectrum, ν, cm^{-1}: 1660, 1690. ^1H NMR spectrum, δ, ppm (*J*, Hz): 1.44 (3H, d, *J* = 6.3, 5-CH_3); 1.82 (1H, s, CH_3CO); 1.98 (1H, m, H-4); 2.12 (1H, m, H-4); 2.75 (1H, dd, $J_{\alpha\alpha}$ = 16.7, $J_{\alpha3}$ = 4.9, H-α); 3.37 (1H, dd, $J_{\alpha\alpha}$ = 16.6, $J_{\alpha3}$ = 9.0, H-α); 3.88 (3H, s, OCH_3); 4.45 (1H, m, H-5); 4.72 (1H, m, H-3); 6.95-7.95 (9H, m, Ar). Found, %: C 71.60; H 7.02; N 8.14. $C_{21}H_{24}N_2O_3$. Calculated, %: C 71.59; H 6.82; N 7.95.

5-Acetonyl-1-acetyl-3-methyl-2-phenylpyrazolidine (5e) was prepared by the reaction of pyrazolidine **1b** (2.2 g, 10 mmol) with acetone (6 ml, 100 mmol), yield [30% [A], 4% [B]; mp 69-70°C. IR spectrum, ν, cm^{-1}: 1650, 1720. ^1H NMR spectrum, δ, ppm (*J*, Hz): 1.22 (3H, d, *J* = 6.8, 3-CH_3); 1.85 (1H, m, H-4); 2.05 (3H, s, 1-CH_3CO); 2.15 (3H, s, 5-CH_3CO); 2.22 (1H, m, H-4); 2.44 (1H, dd, $J_{\alpha\alpha}$ = 17.2, $J_{\alpha5}$ = 10.2, H-α); 3.40 (1H, dd, $J_{\alpha\alpha}$ = 17.1, $J_{\alpha5}$ = 3.7, H-α); 4.12 (1H, m, H-3); 4.61 (1H, m, H-5); 6.96-7.26 (5H, m, C_6H_5). Found, %: C 69.00; H 7.85; N 10.90. $C_{15}H_{20}N_2O_2$. Calculated, %: C 69.23; H 7.69; N 10.77.

3-Acetonyl-1-acetyl-5-methyl-2-phenylpyrazolidine (3e) was prepared by the reaction of pyrazolidine **1b** (2.2 g, 10 mmol) with acetone (6 ml, 100 mmol), yield 0.74 g (28%, B); mp 95-96°C. IR spectrum, ν, cm^{-1}: 1650, 1710. ^1H NMR spectrum, δ, ppm (*J*, Hz): 1.45 (3H, d, *J* = 6.4, 5-CH_3); 1.90 (1H, m, H-4); 1.95 (3H, s, 1-CH_3CO); 2.00 (1H, m, H-4); 2.20 (3H, s, 3-CH_3CO); 2.40 (1H, dd, $J_{\alpha\alpha}$ = 17.7, $J_{\alpha3}$ = 4.9, H-α); 2.80 (1H, dd, $J_{\alpha\alpha}$ = 17.1, $J_{\alpha3}$ = 9.2, H-α); 4.40 (1H, m, H-5); 4.49 (1H, m, H-3); 6.98-7.13 (5H, m, C_6H_5). Found, %: C 69.23; H 8.52; N 11.19. $C_{15}H_{20}N_2O_2$. Calculated, %: C 69.23; H 7.69; N 10.77.

1-Acetyl-3-methyl-5-(2-oxocyclohexyl)-2-phenylpyrazolidine ($5f^1$) was prepared by the reaction of pyrazolidine **1b** (0.44 g, 2 mmol) with cyclohexanone (0.2 ml, 2 mmol), yield 0.248 g [40% (A) and 10%(B)]; mp 143-144°C. IR spectrum, ν, cm^{-1}: 1660, 1710. ^1H NMR spectrum, δ, ppm (*J*, Hz): 1.22 (3H, *J* = 6.4, 3-CH_3); 1.55, 1.70, 1.75, 1.88, 2.01, 2.20-2.32 (11H, m, 4-CH_2 + C_6H_9O); 2.10 (3H, s, CH_3CO); 4.15 (1H, m, H-3); 4.71 (1H, s, H-5); 6.95-7.28 (5H, m, C_6H_5). Found, %: C 71.83, H 7.88, N 9.12. $C_{18}H_{24}N_2O_2$. Calculated, %: C 72.00; H 8.00; N 9.33.

1-Acetyl-3-methyl-5-(2-oxocyclohexyl)-2-phenylpyrazolidine ($5f^2$) was prepared by the reaction of pyrazolidine **1b** (0.44 g, 2 mmol) with cyclohexanone (0.2 ml, 2 mmol), yield 0.248 g [40% (A) and 10%(B)], oil. IR spectrum, ν, cm^{-1}: 1660, 1710. ^1H NMR spectrum, δ, ppm (*J*, Hz): 1.20 (3H, d, *J* = 6.5, 3-CH_3); 1.50-2.40, 2.65, 2.87 (11H, m, H-4, H'-4, + C_6H_9O); 2.O5 (3H, s, CH_3CO); 4.20 (1H, m, H-3); 4.83 (1H, m, H-5); 6.90-7.30 (5H, m, C_6H_5).

1-Acetyl-5-methyl-3-(2-oxocyclohexyl)-2-phenylpyrazolidine ($3f^1$ and $3f^2$) were prepared by the reaction of pyrazolidine **1b** (0.55 g, 2.5 mmol) with cyclohexanone (1 ml, 10 mmol), yield 0.303 g (40%, B); mp 134-135°C. IR spectrum, ν, cm^{-1}: 1680, 1710. ^1H NMR spectrum, δ, ppm (*J*, Hz): 1.38, 1.43 (3H, 2 d,

$J(\mathbf{f}^1)$ = 6.5, $J(\mathbf{f}^2)$ = 6.2, 5-CH_3); 1.80 (1H, m, H-4); 1.93 (3H, s, CH_3CO); 2.08 (1H, m, H'-4); 1.72, 2.18, 2.38, 2.48 (9H, m, C_6H_9O); 4.33 (2H, m, H-3,5); 6.98-7.28 (5H, m, C_6H_5). Found, %: C 72.22, H 7.99, N 9.67. $C_{18}H_{24}N_2O_2$. Calculated, %: C 72.00; H 8.00; N 9.33.

Model Experiment. Potassium fluoride (4.4 g) deposited on aluminum oxide was placed in an ampule, a solution of acetylphenylhydrazine (0.32 g, 2 mmol) dissolved in benzene (3 ml) was added, the solvent was removed in vacuum, crotonic aldehyde (0.18 ml, 2 mmol) and acetophenone (0.36 ml, 3 mmol) were added, the mixture was moistened to 0.5 cm above the surface of the adsorbent with octane and then heated for 5 h (monitored by TLC). Further treatment was as in method A. Yields of compound **5a** 0.080 g (12%) and of **3a** 0.010 g (1.5%).

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