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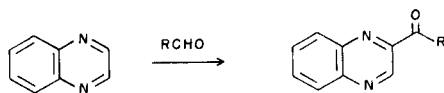
Homolytic acylation of pyrazine and alkylpyrazines by aldehydes, as a source of an acyl radical, gives mainly monoacylation products. The reactions proceed in reasonable yields and provide a new route to pyrazine ketones.

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The Friedel-Crafts acylation is a very useful method for the preparation of ketones in the benzenoid series. However, it is of no value for diazaaromatic compounds. Pyrazines are particularly unsuited to direct substitution by electrophilic reagents due to the inductive effect of the ring nitrogen atoms and to resonating structures causing a positive charge on the ring carbon atoms [1]. Therefore, most of the reported synthetic routes to acylpyrazines involve an oxidation of the α -carbon atom of the corresponding alkylpyrazine [2,3]. In other methods, chlorocarbonylpyrazines or cyanopyrazines and organometallic reagents were used [4,5].

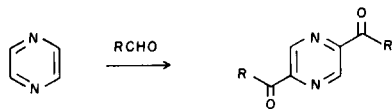
A direct acylation of heteroaromatic bases was first reported by Caronna *et al.*, [6]. Acylation was achieved by reacting an aldehyde with *t*-butyl hydroperoxide in the presence of ferrous sulphate to generate an acyl radical which in turn reacted with a protonated species of the heteroaromatic substrate. The reaction of quinoxaline with a variety of aldehydes gave the corresponding monoacylquinoxalines as shown in Scheme 1 [7].

Scheme 1



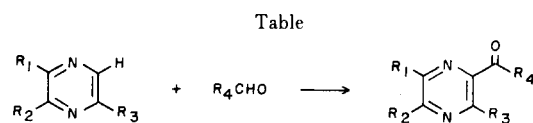
While 2,3-diacylation was not observed in quinoxaline, it was established that introduction of an acyl group activates the heteroaromatic ring towards further acylation so that diacylation occurs if another active position on the heteroaromatic ring is available [8,9]. Indeed, the reaction of pyrazine with an excess of aldehydes, such as acetaldehyde, propionaldehyde and a few aromatic aldehydes gave the corresponding 2,5-diacylpyrazines as shown in Scheme 2 [8]. In each reaction only a small amount of the corresponding monoacyl analogue was detected. It was suggested that steric and polar factors contribute to the introduction of the second acyl group at position-5 [8].

Scheme 2



We report a method for monoacylation of pyrazines using a slightly modified literature procedure. In their general procedure for acylating pyrazines which leads to diacylation products, Caronna *et al.* [8] treated a mixture of pyrazine and aldehyde in water containing acetic acid and sulfuric acid with a mixture of *t*-butyl hydroperoxide and ferrous sulphate in water. We used similar reaction conditions but eliminated acetic acid from the reaction mixture. While the difference between the two methods appears to be insignificant, it resulted in a major change in product distribution, making the monoacylpyrazine the major product in all of the cases studied. The general reaction and a summary of the results obtained for a large number of pyrazines and aldehydes are presented in the Table. It should be emphasized that in all of the above experiments the major product is the monoacylpyrazine, even when the yield is very low. In each of the cases studied a small amount of the corresponding diacyl product was also detected together with small amounts of the corresponding alkylation product. The latter is obtained by decarbonylation of the acyl radical to give the alkyl radical which in turn adds to the pyrazine ring.

The results shown in the Table indicate that reasonable yields are generally obtained. Thus, our method provides a useful one step route to acylpyrazines, some of which would be very difficult to synthesize by alternate methods. It is most interesting that the presence or absence of acetic acid from the reaction medium affect so strongly the products ratio. When acetic acid is used, the reaction mixture is homogeneous. However, in the absence of acetic acid a heterogeneous medium is obtained. Under these conditions it is likely that the monoacylation product is separated into the organic layer where it is more soluble and is, therefore, protected from further acylation. It should also be noted that the introduction of an acyl group on the pyrazine ring decreases significantly the basic character of both nitrogen atoms and thus hydrolytic equilibrium likewise helps partition the product into the organic layer. A similar observation was made [8] with 4-cyanopyridine, even in homogeneous medium, where the weakly basic monoacyl derivative precipitates as the un-



Compound No.	R ₁	R ₂	R ₃	R ₄	Yield % [a]
1	H	H	H	Ethyl	29
2	H	H	H	Propyl	25
3	H	H	H	<i>i</i> -Propyl	24
4	H	H	H	<i>i</i> -Butyl	12
5	H	H	H	<i>t</i> -Butyl	11
6	H	H	H	<i>p</i> -Methoxyphenyl	1.5
7	H	H	<i>i</i> -Butyl	Ethyl	29 [b]
8	methyl	methyl	H	Ethyl	25
9	methyl	methyl	H	<i>i</i> -Butyl	16
10	Cyclohexa		H	Methyl	22
11	Cyclohexa		H	Cyclohexyl	6
12	Cyclohexa		H	Phenyl	6
13	Cyclohepta		H	Ethyl	37
14	methyl	H	methyl	<i>i</i> -Butyl	17
15	H	methyl	methyl	Ethyl	39
16	methyl	methyl	methyl	Ethyl	48

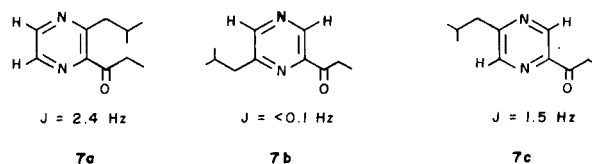
[a] Isolated yields. [b] A mixture of 2,3-, 2,6- and 2,5- isomers in a 3:4:3 ratio.

protonated product and thus selective monoacylation is achieved even though the substrate has an additional reactive position.

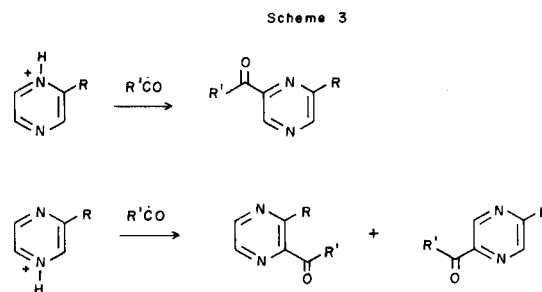
In some cases we added benzene to the reaction mixture. This resulted in a slight increase in yields of the monoacyl products and decrease of the diacylation product, again suggesting that selective monoacylation is due to the increased solubility of the product in the organic phase. However, the results in the Table indicate that aromatic and higher alkylaldehydes generally give lower yields. This is probably due to their relatively low solubility in the aqueous phase. Therefore, under heterogeneous conditions the water solubility of the aldehyde is also an important factor affecting the yield of the reaction. This is further supported by the observation that in the presence of benzene the yield with higher aldehydes becomes even lower. For example, the reaction of pyrazine with trimethylacetaldehyde using the general procedure gave 15% (by gc) of product **5**. In the presence of benzene, however, the yield was only 4%.

The reaction of isobutylpyrazine with propionaldehyde gave the three isomers **7a**, **7b** and **7c** in a 3:4:3 ratio respectively. The coupling constants of the pyrazine ring protons enable us to assign the substitution pattern for each of these isomers (see **7a**, **7b** and **7c**). The coupling constants for a series of monosubstituted pyrazines have been reported [10]: $J_{ortho} = 2.4\text{--}2.8$ Hz, $J_{meta} = 0.01\text{--}0.05$ Hz and $J_{para} = 1.3\text{--}1.5$ Hz. Our observed coupling constants agree very well with the literature values.

Unlike an acyl group which directs a second acylation into the *para*-position to give only the 2,5-disubstituted



pyrazine [8], an alkylpyrazine undergoes a non-selective acylation to give all three possible isomers in similar amounts [11]. Since the reaction proceeds by a nucleophilic addition of the acyl radical to the protonated pyrazine species, it is very likely that in alkylpyrazines both possible protonated species undergo this reaction (Scheme 3).



Experimental

The nmr spectra were recorded with a Bruker WP80 spectrometer and the chemical shifts are given in δ units downfield from internal TMS. Mass spectra were recorded with a MAT 112S spectrometer. Elemental analyses were performed by Galbraith Laboratories Inc., Knoxville, Tennessee. Both analytical and preparative tlc were carried out on silica gel GF plates using methylene chloride as the eluent. Gas chromatography analyses and preparative separations were done on a $\frac{1}{4}$ ' x 15' carbowax 20M - TPA column.

General Procedure for Monoacylation of Pyrazine. Preparation of 1-(2-Pyrazinyl)-1-propanone (**1**).

To a stirring mixture of freshly distilled propionaldehyde (3.48 g, 0.06 mole) and pyrazine (0.8 g, 0.01 mole) in 5 ml of 3.4 *M* sulfuric acid, at 3-5°, was added concurrently 70% *t*-butyl hydroperoxide (5.4 g, 0.042 mole) and a solution of ferrous sulfate (16.7 g, 0.06 mole) in water (50 ml) over a 15 minute period. The resulting heterogeneous mixture was stirred an additional 1 hour, during which time the temperature was raised to 15°. Solid sodium sulfite was then added until test with starch-iodide paper was negative. The aqueous layer was extracted with methylene chloride (3 x 100 ml). The combined organic layers were washed with water, dried (magnesium sulfate) and evaporated under reduced pressure to give 2.5 g of crude oil. Sublimation (1 mm Hg at 55°) gave 0.39 g of pure **1**, mp 46-47°. An analytically pure sample was obtained by preparative gc; ir (nujol): 3050, 1700, 1050, 1020, 980 cm⁻¹; ¹H nmr (deuteriochloroform): δ 1.25 (3H, t, J = 7 Hz, CH₃), 3.25 (2H, q, J = 7 Hz, CH₂), 8.63 (1H, m, pyrazine), 8.74 (1H, d, J = 2 Hz, pyrazine), 9.23 (1H, d, J = 2 Hz, pyrazine); ms: (m/e) 136 (M⁺, 22), 135 (18), 108 (74), 107 (35), 81 (15), 80 (50), 79 (81), 57 (100).

Anal. Calcd. for C₈H₁₀N₂O: C, 61.75; H, 5.92; N, 20.58. Found: C, 61.55; H, 5.81; N, 20.41.

Also isolated by gc were trace amounts of 2,5-dipropionylpyrazine and ethylpyrazine, the structures of which were verified by nmr.

1-(2-Pyrazinyl)-1-butanone (**2**).

The reaction of pyrazine and butyraldehyde was conducted as described for the case of **1**. The crude product was purified by tlc to give 25% yield of pure **2** as a liquid. An analytically pure sample was obtained by preparative gc; ir (neat): 3050, 1698, 1165, 1050, 1020, 1005 cm⁻¹; ¹H nmr (deuteriomethylene chloride): δ 0.93 (3H, doublet of t, J = 7 Hz and 0.5 Hz, CH₃), 1.70 (2H, sextet of doublets, J = 7 Hz and 0.5 Hz, CH₂), 3.12 (2H, t, J = 7 Hz, CH₂), 8.67 (1H, m, pyrazine), 8.78 (1H, d, J = 2 Hz, pyrazine), 9.22 (1H, d, J = 2 Hz, pyrazine); ms: (m/e) 150 (M⁺, 14), 135 (14), 122 (35), 108 (27), 107 (32), 94 (20), 80 (81), 43 (100).

Anal. Calcd. for C₈H₁₀N₂O: C, 63.98; H, 6.72; N, 18.65. Found: C, 63.69; H, 6.86; N, 18.87.

1-(2-Pyrazinyl)-2-methyl-1-propanone (**3**).

The reaction of pyrazine and isobutyraldehyde was carried out as described for the case of **1**. Preparative tlc gave 24% yield of pure **3** as an oil. An analytically pure sample was obtained by gc; ir (neat): 3050, 1700, 1380, 1365, 1245, 1055, 1020, 990 cm⁻¹; ¹H nmr (deuteriomethylene chloride): δ 1.17 (6H, d, J = 7 Hz, 2 CH₃), 4.00 (1H, septet, J = 7 Hz, CH), 8.67 (1H, m, pyrazine), 8.75 (1H, d, J = 2 Hz, pyrazine), 9.16 (1H, d, J = 2 Hz, pyrazine); ms: (m/e): 150 (M⁺, 22), 149 (33), 135 (5), 122 (18), 108 (14), 107 (26), 80 (64), 79 (54), 43 (100).

Anal. Calcd. for C₈H₁₀N₂O: C, 63.98; H, 6.72; N, 18.65. Found: C, 64.07; H, 6.61; N, 18.42.

1-(2-Pyrazinyl)-3-methyl-1-butanone (**4**).

The reaction of pyrazine and isovaleraldehyde was carried out as described for the case of **1**. Preparative tlc gave 12% yield of pure **4** as a liquid. An analytically pure sample was obtained by gc; ir (neat): 3050, 1700, 1060, 1020, 1015 cm⁻¹; ¹H nmr (deuteriochloroform): δ 1.00 (6H, d, J = 7 Hz, 2 CH₃), 2.32 (1H, septet, J = 7 Hz, CH), 3.08 (2H, d, J = 7 Hz, CH₂), 8.70 (1H, m, pyrazine), 8.83 (1H, d, J = 2 Hz, pyrazine), 9.30 (1H, d, J = 2 Hz, pyrazine); ms: (m/e): 164 (M⁺, 12), 149 (6), 136 (8), 122 (6), 121 (6), 108 (40), 107 (15), 80 (100), 57 (46), 41 (29).

Anal. Calcd. for C₉H₁₂N₂O: C, 65.83; H, 7.37; N, 17.06. Found: C, 65.61; H, 7.22; N, 16.82.

1-(2-Pyrazinyl)-2,2-dimethyl-1-propanone (**5**).

The reaction of pyrazine with trimethylacetaldehyde was carried out as described for the case of **1**. Preparative tlc gave 11% of pure **5** as a liquid; ir (neat): 3050, 1685, 1060, 1020, 970 cm⁻¹; ¹H nmr (deuteriomethylene chloride): δ 1.40 (9H, s, 3 CH₃), 8.65 (1H, m, pyrazine), 8.75 (1H, d, J = 2 Hz, pyrazine), 9.12 (1H, d, J = 2 Hz, pyrazine); ms: (m/e): 164 (M⁺, 8),

136 (7), 109 (10), 108 (29), 80 (65), 79 (10), 57 (100).

Anal. Calcd. for C₉H₁₂N₂O: C, 65.83; H, 7.37; N, 17.06. Found: C, 65.80; H, 7.50; N, 16.87.

2-Pyrazinyl *p*-Methoxyphenyl ketone (**6**).

The reaction of pyrazine with *p*-methoxybenzaldehyde was carried out as described in the case of **1**. Successive preparative tlc gave only 1.5% of pure **6** as an oil; ¹H nmr (deuteriochloroform): δ 3.88 (3H, s, OCH₃), 6.99 and 8.15 (4H, AA', BB', q, phenyl), 8.68 (1H, double d, pyrazine), 8.78 (1H, d, pyrazine), 9.24 (1H, d, pyrazine); ms: (m/e) 214 (M⁺, 16), 186 (2), 135 (100), 107 (14), 92 (9), 77 (19).

Reaction of Isobutylpyrazine with Propionaldehyde.

The reaction of isobutylpyrazine and freshly distilled propionaldehyde was carried out as described in the case of **1**. Preparative tlc afforded 29% yield of the mixture of the three isomers. Separation of isomers was done by gc. The 2,3-, 2,6- and 2,5-isomer ratio was found to be 3:4:3 respectively. Pure 1-[3-(2-methyl-1-propyl)-2-pyrazinyl]-1-propanone (**7a**) was obtained as a liquid; ir (neat): 3035, 1700, 1460, 1400, 1160, 1095, 960 cm⁻¹; ¹H nmr (deuteriomethylene chloride): δ 0.90 (6H, d, J = 7 Hz, 2 CH₃), 1.15 (3H, t, J = 7 Hz, CH₃), 2.11 (1H, septet, J = 7 Hz, CH), 3.00 and 3.14 (4H overlapping, 2 CH₂), 8.43 (1H, d, J = 2.4 Hz, pyrazine), 8.59 (1H, d, J = 2.4 Hz, pyrazine); ms: (m/e) 192 (M⁺, 48), 177 (40), 150 (100), 149 (30), 135 (89), 122 (88), 120 (28), 94 (66), 93 (32), 57 (76), 43 (43), 41 (90).

Anal. Calcd. for C₁₁H₁₆N₂O: C, 68.72; H, 8.39; N, 14.57. Found: C, 68.80; H, 8.38; N, 14.55.

Also obtained was pure 1-[6-(2-methyl-1-propyl)-2-pyrazinyl]-1-propanone (**7b**) as a liquid; ir (neat): 3030, 1700, 1585, 1415, 1015, 990 cm⁻¹; ¹H nmr (deuteriomethylene chloride): δ 0.95 (6H, d, J = 7 Hz, 2 CH₃), 1.18 (3H, t, J = 7 Hz, CH₃), 2.18 (1H, septet, J = 7 Hz, CH), 2.74 (2H, d, J = 7 Hz, CH₂), 3.19 (2H, q, J = 7 Hz, COCH₂), 8.56 (1H, s, pyrazine), 8.96 (1H, s, pyrazine); ms: (m/e) 192 (M⁺, 16), 177 (16), 150 (100), 132 (9), 94 (12), 66 (12), 57 (26), 43 (23), 41 (27).

Anal. Calcd. for C₁₁H₁₆N₂O: C, 68.72; H, 8.39; N, 14.57. Found: C, 68.49; H, 8.36; N, 14.75.

Also obtained was pure 1-[5-(2-methyl-1-propyl)-2-pyrazinyl]-1-propanone (**7c**) as a liquid; ir (neat): 3065, 3030, 1700, 1585, 1185, 1040, 1020, 960 cm⁻¹; ¹H nmr (deuteriomethylene chloride): δ 0.94 (6H, d, J = 7 Hz, 2 CH₃), 1.18 (3H, t, J = 7 Hz, CH₃), 2.18 (1H, septet, J = 7 Hz, CH), 2.76 (2H, d, J = 7 Hz, CH₂), 3.17 (2H, q, J = 7 Hz, COCH₂), 8.44 (1H, d, J = 1.5 Hz, pyrazine), 9.08 (1H, d, J = 1.5 Hz, pyrazine); ms: (m/e) 192 (M⁺, 16), 177 (19), 150 (100), 135 (11), 121 (63), 94 (13), 66 (11), 57 (22), 53 (14), 43 (27), 41 (32).

Anal. Calcd. for C₁₁H₁₆N₂O: C, 68.72; H, 8.39; N, 14.57. Found: C, 68.47; H, 8.52; N, 14.50.

1-(2,3-Dimethyl-5-pyrazinyl)-1-propanone (**8**).

The reaction of 2,3-dimethylpyrazine with freshly distilled propionaldehyde was carried out as described for the case of **1**. Preparative tlc gave 25% yield of pure **8** as a liquid. An analytically pure sample was obtained by gc; ir (neat): 3050, 1700, 1165, 960, 920 cm⁻¹; ¹H nmr (deuteriomethylene chloride): δ 1.16 (3H, t, J = 7 Hz, CH₃), 2.57 (6H, s, 2 CH₃), 3.14 (2H, q, J = 7 Hz, CH₂), 8.83 (1H, s, pyrazine); ms: (m/e) 164 (M⁺, 23), 163 (7), 137 (6), 135 (25), 108 (60), 107 (100).

Anal. Calcd. for C₈H₁₂N₂O: C, 65.83; H, 7.37; N, 17.06. Found: C, 65.75; H, 7.50; N, 17.20.

1-(2,3-Dimethyl-5-pyrazinyl)-3-methyl-1-butanone (**9**).

The reaction of 2,3-dimethylpyrazine with isovaleraldehyde was carried out as described for the case of **1**. Purification by tlc gave 16% of pure **9** as an oil; ir (neat): 1695, 1560, 1540, 1465, 1445, 1395, 1310, 1190, 1170 cm⁻¹; ¹H nmr (deuteriomethylene chloride): δ 0.98 (6H, d, J = 7 Hz, 2 CH₃), 2.00-2.55 (1H, m, CH), 2.60 (6H, s, 2 CH₃), 3.02 (2H, d, J = 7 Hz, CH₂), 8.84 (1H, s, pyrazine); ms: (m/e) 192 (M⁺, 13), 177 (8), 164 (9), 122 (20), 108 (100), 107 (47), 66 (17), 58 (24), 53 (30), 43 (23), 41 (25).

Anal. Calcd. for $C_{11}H_{16}N_2O$: C, 68.84; H, 8.45; N, 14.67. Found: C, 68.72; H, 8.39; N, 14.57.

2-Acetyl-5,6,7,8-tetrahydrocyclohexa[b]pyrazine (**10**).

The reaction of 5,6,7,8-tetrahydroquinoxaline and freshly distilled acetaldehyde was carried out as described for the case of **1**. Preparative tlc gave 22% yield of pure **10** as a solid, mp 42-45°; ir (melt): 3040, 1700, 1395 cm^{-1} ; 1H nmr (deuteriomethylene chloride): δ 1.95 (4H, m, 2 CH_2), 2.63 (3H, s, CH_3), 2.99 (4H, m, 2 CH_2), 8.85 (1H, s, pyrazine); ms: (m/e) 176 (M^+ , 77), 161 (9), 148 (38), 134 (87), 133 (100), 106 (26).

Anal. Calcd. for $C_{10}H_{12}N_2O$: C, 68.16; H, 6.86; N, 15.90. Found: C, 68.01; H, 6.90; N, 15.74.

2-Cyclohexanoyl-5,6,7,8-tetrahydrocyclohexa[b]pyrazine (**11**).

The reaction of 5,6,7,8-tetrahydroquinoxaline with cyclohexanecarboxaldehyde was carried out as described for the case of **1**. The product was purified by column chromatography (25 g silica gel, eluted with 5% acetone/hexane). Crystallization from methanol gave 6% yield of pure **11**, mp 64-65°; ir (nujol): 3040, 1690, 1555, 1455, 1435, 1395, 1375, 1275, 1205, 1160, 990 cm^{-1} ; 1H nmr (deuteriochloroform): δ 1.05-2.20 (14H, m, 7 CH_2), 3.00 (4H, m, 2 CH_2), 3.75 (1H, m, CH), 8.89 (1H, s, pyrazine); ms: (m/e) 244 (M^+ , 25), 216 (49), 161 (25), 148 (33), 135 (13), 134 (100), 133 (28), 79 (20), 77 (13), 67 (10), 55 (34), 53 (12), 41 (39).

Anal. Calcd. for $C_{15}H_{20}N_2O$: C, 73.73; H, 8.25; N, 11.47. Found: C, 73.94; H, 8.24; N, 11.45.

2-Benzoyl-5,6,7,8-tetrahydrocyclohexa[b]pyrazine (**12**).

The reaction of 5,6,7,8-tetrahydroquinoxaline and benzaldehyde was carried out as described for the case of **1**. Purification by high performance liquid chromatography (Whatman, Partisil M9, 10/20, 4% acetone/2,2,4-trimethylpentane as the eluent) gave 6% yield of pure **12** as a solid, mp 62-64°; ir (nujol): 3045, 1660, 1595, 1550, 1445, 1385, 1320, 1300, 970, 950, 880 cm^{-1} ; 1H nmr (deuteriochloroform): δ 1.75-2.25 (4H, m, 2 CH_2), 2.80-3.25 (4H, m, 2 CH_2), 7.35-7.80 (3H, m, phenyl), 7.95-8.20 (2H, m, phenyl), 8.92 (1H, s, pyrazine); ms: (m/e) 238 (M^+ , 46), 237 (22), 210 (37), 209 (14), 105 (100), 77 (69), 51 (15).

Anal. Calcd. for $C_{15}H_{14}N_2O$: C, 75.60; H, 5.92; N, 11.76. Found: C, 75.63; H, 6.08; N, 11.60.

2-Propionyl-5H-6,7,8,9-tetrahydrocyclohepta[b]pyrazine (**13**).

The reaction of 5H-6,7,8,9-tetrahydrocyclohepta[b]pyrazine with freshly distilled propionaldehyde was conducted as described for the case of **1**. The crude product was passed through a silica gel column (5% acetone/hexane) to yield 37% of pure **13** as a liquid. An analytical sample was obtained by gc, ir (neat): 3040, 1690, 1560, 1525, 1445, 1345, 1065, 1045, 1005, 950, 930 cm^{-1} ; 1H nmr (deuteriomethylene chloride): δ 1.19 (3H, t, J = 7 Hz, CH_3), 1.55-2.12 (6H, m, 3 CH_2), 2.98-3.25 (4H, m, 2 CH_2), 3.19 (2H, q, J = 7 Hz, CH_2), 8.81 (1H, s, pyrazine); ms: (m/e) 204 (M^+ , 53), 176 (100), 148 (82), 147 (54), 120 (14), 93 (15), 79 (16), 77 (14), 57 (18), 53 (17), 41 (18).

Anal. Calcd. for $C_{11}H_{16}N_2O$: C, 70.56; H, 7.90; N, 13.71. Found: C, 70.74; H, 7.92; N, 13.71.

1-(2,5-Dimethyl-3-pyrazinyl)-3-methyl-1-butanone (**14**).

The reaction of 2,5-dimethylpyrazine with isovaleraldehyde was carried out as described for the case of **1**. Purification by tlc gave 17% yield of pure **14** as a liquid; ir (neat): 3020, 1695, 1560, 1525, 1450, 1370, 1300, 1178, 1020, 960 cm^{-1} ; 1H nmr (deuteriomethylene chloride): δ 0.99 (6H, d, J = 7 Hz, 2 CH_3), 2.24 (1H, septet, J = 7 Hz, CH), 2.56 (3H, s, CH_3), 2.71 (3H, s, CH_3), 3.04 (2H, d, J = 7 Hz, CH_2), 8.42 (1H, s, pyrazine); ms: (m/e) 192 (M^+ , 17), 177 (19), 164 (37), 149 (11), 136 (30), 135 (15), 122 (81), 109 (30), 108 (100), 107 (87), 81 (10), 80 (22), 69 (14), 66 (16), 57 (55), 53 (10), 43 (20), 42 (60), 41 (39).

Anal. Calcd. for $C_{11}H_{16}N_2O$: C, 68.72; H, 8.39; N, 14.57. Found: C, 68.79; H, 8.47; N, 14.40.

1-(3,5-Dimethyl-2-pyrazinyl)-1-propanone (**15**).

The reaction of 2,6-dimethylpyrazine and freshly distilled propionaldehyde was carried out as described for the case of **1**. Purification by tlc gave 39% yield of pure **15** as a liquid; ir (neat): 3040, 1700, 1170, 925 cm^{-1} ; 1H nmr (deuteriomethylene chloride): δ 1.08 (3H, t, J = 7 Hz, CH_3), 2.50 (3H, s, CH_3), 2.67 (3H, s, CH_3), 3.08 (2H, q, J = 7 Hz, CH_2), 8.30 (1H, s, pyrazine); ms: (m/e) 164 (M^+ , 30), 149 (7), 136 (36), 135 (21), 108 (39), 107 (100), 80 (3).

Anal. Calcd. for $C_9H_{12}N_2O$: C, 65.83; H, 7.37; N, 17.06. Found: C, 65.59; H, 7.50; N, 16.88.

1-(2,3,5-Trimethyl-6-pyrazinyl)-1-propanone (**16**).

The reaction of trimethylpyrazine and freshly distilled propionaldehyde was carried out as described for the case of **1**. Preparative tlc gave 48% of pure **16** as a solid, mp 65-67°; ir (methylene chloride): 1695, 1140, 925 cm^{-1} ; 1H nmr (deuteriomethylene chloride): δ 1.10 (3H, t, J = 8 Hz, CH_3), 2.50 (6H, s, 2 CH_3), 2.67 (3H, s, CH_3), 3.13 (2H, q, J = 8 Hz, CH_2); ms: (m/e) 178 (M^+ , 33), 163 (7), 150 (43), 149 (18), 122 (46), 121 (100), 80 (43).

Anal. Calcd. for $C_{10}H_{14}N_2O$: C, 67.39; H, 7.92; N, 15.72. Found: C, 67.24; H, 8.13; N, 15.52.

Reaction in the Presence of Benzene.

Pyrazine was reacted with acetaldehyde under conditions described for the case of **1** to give 25% yield of acetylpyrazine as determined by gc. The ratio of acetylpyrazine to 2,5-diacetylpyrazine was also determined by gc to be 84/16. The same reaction was repeated in the presence of 40 ml of benzene. The yield of acetylpyrazine rose to 28% and the ratio of acetylpyrazine to 2,5-diacetylpyrazine was found to be 96/4.

The reaction of pyrazine with trimethylacetaldehyde gave 15% of **5** by gc. In the presence of 40 ml benzene the yield dropped to 4%. No diacylation product was detected in either case.

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- [11] The reaction of methylpyrazine with isobutyraldehyde also gave three isomers in a 5:4:2 ratio. The isomers could not be separated.