SYNTHESES AND ABSORPTION SPECTRA OF 2-SUBSTITUTED-3-HYDROXY-5-PYRAZOLONES

4-*n*-HEXYL-5-PYRAZOLONES-4-C^{14} [1]

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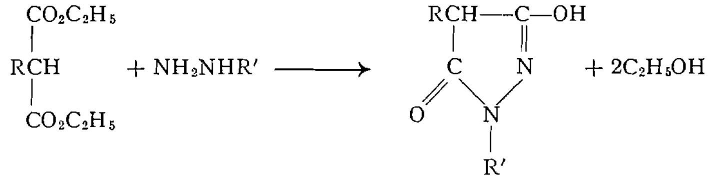
ABSTRACT

2-Monosubstituted-3-hydroxy-5-pyrazolones were prepared from diethyl malonate itself and diethyl malonates monosubstituted with methyl, ethyl, propyl, butyl, amyl, hexyl, heptyl, and benzyl groups by condensation of the esters with *o*-, *m*-, and *p*-chlorophenylhydrazines, and *n*-hexylhydrazine. By using diethyl *n*-hexyl malonate-2-C^{14} and *o*-, *m*-, and *p*-chlorophenylhydrazines, and *n*-hexylhydrazine as starting materials the corresponding pyrazolones labelled with C^{14} were obtained. Their specific activities were 7.0, 8.8, 9.0, and 8.8 μc./gm. respectively. Ultraviolet absorption spectra were determined in neutral and alkaline solution and the infrared spectra were also obtained. From the data it was possible to ascribe the tautomeric structures best suited for the compounds.

INTRODUCTION

The condensation of diethylmalonates (I) with hydrazine and hydrazine derivatives in the presence of sodium ethylate produces pyrazolones (II) and ethanol according to the following equation:



I II

The first pyrazolone of this type was isolated by Michaelis and Burmeister (10) as a product of the reaction between ethylchloromalonate and phenylhydrazine. It was erroneously concluded that it was a hydrazinedihydroindoxyl because of its acidic character and its facility to form salts.

Other authors (11, 12) assigned the correct formula to the pyrazolone (III), and it was again prepared from diethylmalonate and phenylhydrazine by Conrad and Zart (3).

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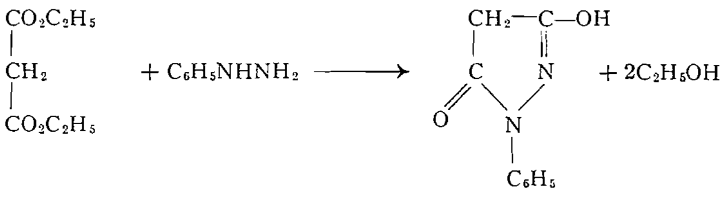


III

In 1950, Gagnon, Boivin, and Boivin (4) prepared several 3-hydroxy- and 3-oxopyrazolones by reacting phenylhydrazine with mono- and disubstituted malonates. It was shown by these authors that the monosubstituted pyrazolones existed as monobasic acids.

In the present investigations other new 4-monosubstituted-3-hydroxy-5-pyrazolones were prepared from diethyl malonate itself and diethyl malonates monosubstituted with methyl, ethyl, propyl, butyl, amyl, hexyl, heptyl, and benzyl groups by condensation of these esters with *o*-, *m*-, and *p*-chlorophenylhydrazines and *n*-hexylhydrazine. When diethyl *n*-hexyl malonate-2-C^{14} was used as starting material, the corresponding pyrazolones labelled with C^{14} were obtained and their specific activities determined.

The structure of the pyrazolones were studied with the aid of ultraviolet and infrared absorption spectra; it is well known that such pyrazolones may exist in many tautomeric forms. Pyrazolones bearing N-chlorophenyl and N-hexyl substituents were prepared to study the effect of N-aromatic and N-aliphatic substituents on the pyrazolone ring.

The starting esters were obtained by condensing alkyl halides with diethyl malonate in the presence of sodium ethylate. *o*-, *m*-, and *p*-Chlorophenylhydrazines were prepared by diazotization of their respective anilines followed by reduction with sodium sulphite. *n*-Hexylhydrazine was produced from *n*-hexylbromide and hydrazine hydrate in ethanol.

In the presence of sodium ethylate, diethylmalonates substituted with methyl, ethyl, and propyl radicals did not yield the corresponding pyrazolones when treated with the hydrazines. Fusion of the esters with the hydrazines at 165°C., and heating for a period of three hours was necessary.

The individual properties and analyses of all the pyrazolones prepared are given in Tables I, II, III, and IV.

Ultraviolet Absorption Spectra

The ultraviolet absorption spectra of all pyrazolones were determined in neutral and alkaline solutions. The results obtained are given in Tables I, II, III, and IV and shown graphically in Figs. 1, 2, 3, and 4.

The spectra of the *o*-, *m*-, and *p*-chlorophenylhydrazines are quite similar in their characteristics. In neutral solution these pyrazolones exhibit two maxima, one of high intensity at short wave length and one of low intensity at longer wave length. The spectra given by the *n*-hexyl pyrazolones do not exhibit definite maxima in many cases. In neutral solution a broad absorption band of low intensity is seen at short wave length. The ethyl, propyl, and butyl

TABLE I

2-*o*-CHLOROPHENYL-3-HYDROXY-4-MONOSUBSTITUTED-5-PYRAZOLONES, $RC_9H_7O_2N_2Cl$

R	M.p., °C.	Yield, %	Formula	Analysis						Ultraviolet absorption maxima			
				Calculated			Found			Neutral		Alkaline	
				C	H	N	C	H	N	Å	E_m	Å	E_m
H	181–182	38	$C_9H_8O_2N_2Cl$	51.17	3.79	13.20	51.70	3.39	13.82	2860	3.41	2820	3.92
CH_3	181–183	25	$C_{10}H_{10}O_2N_2Cl$	53.21	4.43	12.41	52.79	4.55	11.77	2340 2880	4.10 3.39	2380 2840	3.88 3.56
C_2H_5	160–162	28	$C_{11}H_{12}O_2N_2Cl$	55.22	5.01	11.69	55.70	5.42	11.20	2360 2860	4.13 3.48	2400 2820	3.65 4.08
C_3H_7	161–163	29	$C_{12}H_{14}O_2N_2Cl$	56.80	5.52	11.04	56.55	5.79	11.38	2360 2880	4.20 4.40	2380 2780	3.98 3.99
C_4H_9	169–170	52	$C_{13}H_{16}O_2N_2Cl$	58.32	5.97	10.37	58.80	5.97	9.72	2400 2840	4.08 3.49	2380 2820	3.89 4.15
C_5H_{11}	150–151	56	$C_{14}H_{18}O_2N_2Cl$	59.68	6.38	9.97	58.96	6.51	9.91	2360 2860	4.19 3.35	2360	4.03
C_6H_{13}	154–155	62	$C_{15}H_{20}O_2N_2Cl$	60.91	6.81	9.49	61.30	6.67	9.16	2440 2860	3.77 3.27	2540 2860	3.78 3.42
C_7H_{15}	131–133	51	$C_{16}H_{22}O_2N_2Cl$	62.02	7.15	9.06	61.15	6.82	8.64	2360 2460	3.99 3.73	2500 2600	3.51 3.69
$C_6H_5CH_2$	197–199	45	$C_{16}H_{14}O_2N_2Cl$	63.68	4.64	9.28	63.55	4.46	9.11	2480	3.59	2560	3.69

TABLE II

2-*m*-CHLOROPHENYL-3-HYDROXY-4-MONOSUBSTITUTED-5-PYRAZOLONES, $RC_9H_7O_2N_2Cl$

R	M.p., °C.	Yield, %	Formula	Analysis						Ultraviolet absorption spectra			
				Calculated			Found			Neutral		Alkaline	
				C	H	N	C	H	N	Å	E_m	Å	E_m
H	174–175	74	$C_9H_8O_2N_2Cl$	51.17	3.79	13.20	51.81	3.63	13.55	2740 2520	3.86 4.03	2840 2600	4.00 4.12
CH_3	210–211	32	$C_{10}H_{10}O_2N_2Cl$	53.21	4.43	12.41	52.73	4.30	12.10	2900 2440	3.41 4.09	2840 2540	3.86 3.81
C_2H_5	196–198	23	$C_{11}H_{12}O_2N_2Cl$	55.22	5.01	11.69	55.38	5.49	11.66	2980 2540	3.39 3.85	2840 2440	3.93 4.31
C_3H_7	239–240	26	$C_{12}H_{14}O_2N_2Cl$	56.80	5.52	11.04	56.06	5.47	11.28	2880 2420	3.38 4.20	2860 2480	3.82 3.86
C_4H_9	155–156	57	$C_{13}H_{16}O_2N_2Cl$	58.32	5.97	10.37	57.78	5.68	10.08	2820 2420	3.69 4.10	3000 2440	3.68 4.19
C_5H_{11}	132–134	62	$C_{14}H_{18}O_2N_2Cl$	59.68	6.38	9.97	58.92	6.34	9.87	2880 2400	3.41 4.08	2840 2460	3.89 3.88
C_6H_{13}	110–111	62	$C_{15}H_{20}O_2N_2Cl$	60.91	6.81	9.49	60.72	6.49	9.67	2780 2440	3.92 4.08	2840 2540	4.06 4.07
C_7H_{15}	106–108	60	$C_{16}H_{22}O_2N_2Cl$	62.02	7.15	9.06	62.13	7.13	9.16	2760 2460	3.94 4.05	2880 2560	3.96 4.04
$C_6H_5CH_2$	187–189	64	$C_{16}H_{14}O_2N_2Cl$	63.68	4.64	9.28	63.27	4.50	9.33	2780 2460	3.86 4.12	2860 2380	2.84 3.29

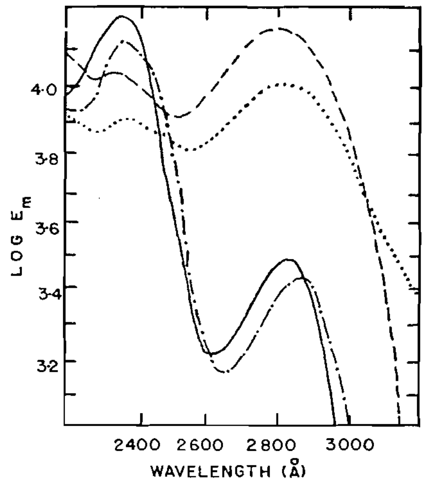
TABLE III

2-*p*-CHLOROPHENYL-3-HYDROXY-4-MONOSUBSTITUTED-5-PYRAZOLONES, $RC_9H_7O_2N_2Cl$

R	M.p., °C.	Yield, %	Formula	Analysis						Ultraviolet absorption maxima			
				Calculated			Found			Neutral		Alkaline	
				C	H	N	C	H	N	Å	E_m	Å	E_m
H	207–209	32	$C_9H_8O_2N_2Cl$	51.17	3.79	13.20	51.51	3.61	13.41	2760	3.94		
										2460	4.13	2640	4.14
CH_3	220–222	30	$C_{10}H_{10}O_2N_2Cl$	53.21	4.43	12.41	53.22	4.50	11.94	2840	3.79	3000	3.71
										2440	4.19	2560	4.10
C_2H_5	202–203	28	$C_{11}H_{12}O_2N_2Cl$	55.22	5.01	11.69	54.24	5.40	11.34	2880	3.75	3000	3.75
										2460	4.14	2580i	4.20
C_3H_7	193–195	28	$C_{12}H_{14}O_2N_2Cl$	56.80	5.52	11.04	56.66	5.42	11.18	2840	3.24	2920	3.82
										2460	4.12	2520	4.19
C_4H_9	193–195	63	$C_{13}H_{16}O_2N_2Cl$	58.32	5.97	10.37	58.31	5.49	10.08	2860	3.81	3000	3.68
										2460	4.25	2560	4.13
C_5H_{11}	174–175	60	$C_{14}H_{18}O_2N_2Cl$	59.68	6.38	9.97	59.68	6.38	9.60	2840	3.79	3000	3.74
										2460	4.14	2540	4.17
C_6H_{13}	147–148	69	$C_{15}H_{20}O_2N_2Cl$	60.91	6.81	9.49	61.05	6.95	9.61	2780	3.86	2860	3.95
										2440	4.13	2520	4.12
C_7H_{15}	160–162	38	$C_{16}H_{22}O_2N_2Cl$	62.02	7.15	9.06	61.51	7.28	9.03	2920	3.17	2920	2.97
										2420	4.23	2440	3.56
$C_6H_5CH_2$	181–182	31	$C_{16}H_{14}O_2N_2Cl$	63.68	4.64	9.28	63.89	4.13	8.93	2760	3.94	2840	4.29
										2480	4.15	2480i	4.06

TABLE IV
2-HEXYL-3-HYDROXY-4-MONOSUBSTITUTED-5-PYRAZOLONES, $RC_9H_{15}O_2N_2$

R	M.p., °C.	Yield, %	Formula	Analysis						Ultraviolet absorption maxima			
				Calculated			Found			Neutral		Alkaline	
				C	H	N	C	H	N	Å	E_m	Å	E_m
H	250–251	80	$C_9H_{16}O_2N_2$	58.70	8.68	15.22	58.01	8.48	15.20	2660	3.81	2750	4.06
CH_3			$C_{10}H_{18}O_2N_2$	60.60	9.09	14.14	59.73	8.62	14.71	2440	3.24	2800i 2540i	3.10 3.21
C_2H_5			$C_{11}H_{20}O_2N_2$	62.26	9.43	13.20	62.64	9.77	12.84	2800i 2520i	3.34 3.32	2800 2520	3.44 3.29
C_3H_7	83–84	38	$C_{12}H_{22}O_2N_2$	63.71	9.73	12.53	63.38	9.65	12.41	2560	3.53	2800 2560	3.50 3.64
C_4H_9	94–95	69	$C_{13}H_{24}O_2N_2$	65.54	10.00	11.66	65.47	9.95	11.69	2780 2520	3.34 3.29	2780 2560	3.48 3.47
C_5H_{11}	93–95	95	$C_{14}H_{26}O_2N_2$	66.14	10.23	10.98	65.11	10.25	10.68	2540	3.57	2780i 2560	3.49 3.61
C_6H_{13}	91–92	60	$C_{15}H_{28}O_2N_2$	67.16	10.44	10.41	66.80	10.17	10.31	2580	3.46	2880i 2580	3.43 3.47
C_7H_{15}	81–83	38	$C_{16}H_{30}O_2N_2$	68.09	10.64	9.93	68.09	10.64	9.81	2560	3.46	2760i 2540	3.48 3.51
$C_6H_5CH_2$	155–156	79	$C_{16}H_{22}O_2N_2$	70.03	8.08	10.21	70.00	8.03	10.12	2520	3.50	2840i 2500	3.36 3.79



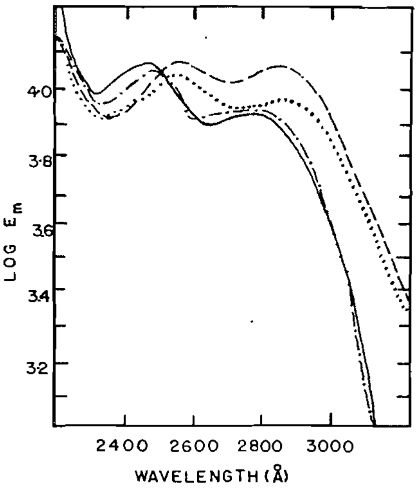
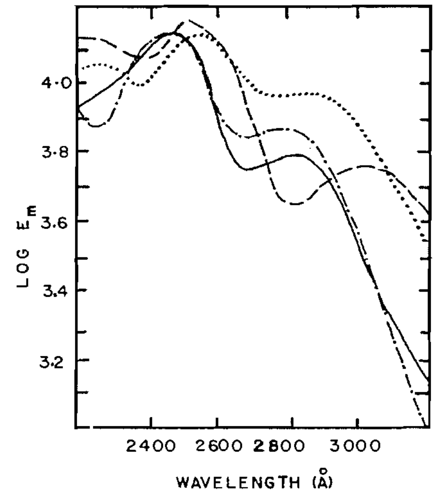


FIG. 1. (Left) Ultraviolet absorption spectrum of: 2-*o*-chlorophenyl-3-hydroxy-4-*n*-propyl-5-pyrazolone; ———————— in neutral solution - - - - - - in alkaline solution; 2-*o*-chlorophenyl-3-hydroxy-4-*n*-butyl-5-pyrazolone; —·—·—·— in neutral solution · · · · · · in alkaline solution.

FIG. 2. (Right) Ultraviolet absorption spectrum of: 2-*m*-chlorophenyl-3-hydroxy-4-*n*-hexyl-5-pyrazolone; ———————— in neutral solution - - - - - - in alkaline solution; 2-*m*-chlorophenyl-3-hydroxy-4-*n*-heptyl-5-pyrazolone; —·—·—· in neutral solution. · · · · · in alkaline solution.



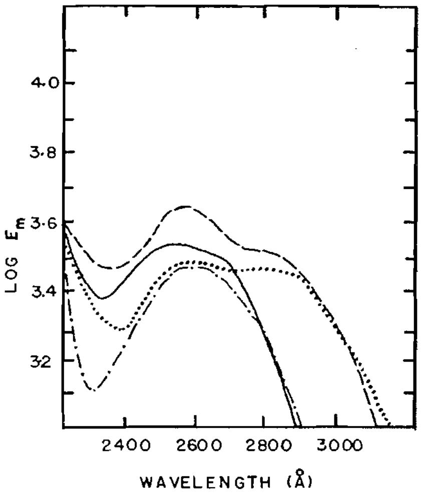
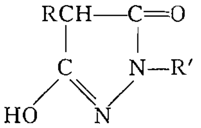


FIG. 3. (Left) Ultraviolet absorption spectrum of: 2-*p*-chlorophenyl-3-hydroxy-4-*n*-amyl-5-pyrazolone; ———————— in neutral solution - - - - - - in alkaline solution; 2-*p*-chlorophenyl-3-hydroxy-4-*n*-hexyl-5-pyrazolone; —·—·—· in neutral solution · · · · · · in alkaline solution.

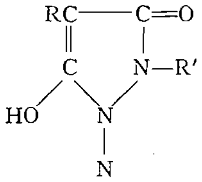
FIG. 4. (Right) Ultraviolet absorption spectrum of: 2-*n*-hexyl-3-hydroxy-4-*n*-propyl-5-pyrazolone; ———————— in neutral solution - - - - - - in alkaline solution; 2-*n*-hexyl-3-hydroxy-4-*n*-hexyl-5-pyrazolone; —·—·— in neutral solution · · · · · · in alkaline solution.

monosubstituted hexyl pyrazolones show a second maximum of equal intensity at long wave length. In alkaline solution a number of the *n*-hexyl pyrazolones exhibit two maxima, one at short and one at long wave lengths but of equal intensity.

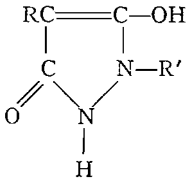
Several structures may be postulated for 4-monosubstituted-3-hydroxy-5-pyrazolones. The following are theoretically possible (IV–VIII) owing to tautomeric displacement.



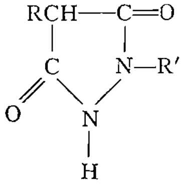
IV



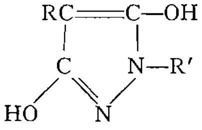
V



VI



VII



VIII

It is possible to disqualify a few of the above structures by examining the chemical and physical properties of the compounds actually obtained. An examination of the ultraviolet absorption spectra has been very useful as a means of postulating the structures of many pyrazolones.

Biquard and Grammaticakis (2) showed that 1-phenyl-2,3,4-trimethyl-5-pyrazolone and 1-phenyl-3,4,4-trimethyl-5-pyrazolone which differ in the position in which the double bond is fixed in the ring gave different ultraviolet spectra.

The spectra exhibited by many pyrazolones have been studied intensively by Gagnon and co-workers (4, 5, 6, 8). These authors related the position of the double bond in the pyrazolone ring to the wave length and the intensity of the absorption. It was found that a high intensity maximum at short wave length corresponded to a double bond between the two carbon atoms 3 and 4, while a low intensity maximum at long wave length was indicative of a single bond between these two carbon atoms. A compound giving two maxima was shown to exist in two tautomeric forms (9).

In 1950, Gagnon, Boivin, and Boivin (4) studied the properties of several 4-monosubstituted-3-hydroxy-5-pyrazolones. They found that the pyrazolones exhibited two maxima in neutral and alkaline solutions and that they were best represented by structures V and VI. A pK_a value of 4 to 5 revealed that the compounds were monobasic acids thereby eliminating the diketo and dienol forms VII and VIII theoretically possible.

The results of the present work compares favorably with that of Gagnon, Boivin, and Boivin (4). Two maxima, indicative of two structures are found in neutral and alkaline solutions in the case of the chlorophenyl pyrazolones. An absorption band of high intensity at short wave length, indicative of an ethylenic double bond may be represented by structures V and VI, while another maximum at low intensity at long wave length satisfy the requirements of structure IV.

The *n*-hexyl-3-hydroxy-5-pyrazolones do not exhibit absorption spectra identical to those 2-chlorophenyl-3-hydroxy-5-pyrazolones. An attempt to explain their structure will be dealt with in the section on infrared absorption spectra.

Infrared Absorption Spectra

The infrared absorption spectra of the pyrazolones were determined with a Perkin-Elmer spectrophotometer. The results obtained are given in Tables V, VI, VII, and VIII and some of the data are plotted in Figs. 5, 6, 7, and 8.

TABLE V

INFRARED MAXIMA OF *o*-CHLOROPHENYL-3-HYDROXY-4-MONOSUBSTITUTED-5-PYRAZOLONES

R	Absorption bands, cm.$^{-1}$											
H	3300	1700	1698	1645	1600	1565	1490	1322	1300	1235	1203	1155
CH_3	3300	1710	1670	1650	1600	1526	1490	1310	1287	1270	1148	1135
C_2H_5	3300	1710	1680	1650	1600	1535	1490	1320	1305	1235	1205	1155
C_3H_7	3300	1705	1680	1638	1600	1538	1490	1365	1305	1270	1163	1135
C_4H_9	3300	1750	1680	1680	1590	1530	1490	1421	1310	1270	1178	1148
C_5H_{11}	3320	1750	1700	1680	1590	1530	1490	1422	1312	1270	1210	1135
C_6H_{13}	3310	1710	1690	1610	1590	1535	1485	1420	1365	1230	1210	1136
C_7H_{15}	3240	1745	1655	1600	1585	1484		1335	1325	1270	1205	1142
$C_6H_5CH_2$	3328	1738	1700		1590		1490	1358	1320	1290	1205	1148

TABLE VI

INFRARED MAXIMA OF *m*-CHLOROPHENYL-3-HYDROXY-4-MONOSUBSTITUTED-5-PYRAZOLONES

R	Absorption bands, cm.$^{-1}$										
H	3120	1730	1683	1596	1490	1405	1345	1295	1723	1165	1136
CH_3	3300	1710	1670	1602	1490		1340	1310	1220	1165	1139
C_2H_5	3310	1750	1700	1600	1490	1425	1355	1295	1242	1192	1137
C_3H_7	3260	1675		1605	1492	1407	1349	1285	1232	1157	1142
C_4H_9	3320	1745	1695	1590	1492	1418	1304	1290	1224	1182	1138
C_5H_{11}	3260	1735	1670	1605	1490	1423	1330	1273	1205	1165	1145
C_6H_{13}	3120	1735	1675	1600	1495	1420	1330	1305	1216	1162	1100
C_7H_{15}	3310	1731	1680	1600	1490	1415	1326	1303	1220	1161	
$C_6H_5CH_2$	3120	1745	1690	1600	1490	1418	1355	1295	1270	1170	

TABLE VII

INFRARED MAXIMA OF *p*-CHLOROPHENYL-3-HYDROXY-4-MONOSUBSTITUTED-5-PYRAZOLONES

R	Absorption bands, cm.$^{-1}$										
H	3310	1770	1695	1600	1500	1420	1360	1300	1230	1190	1152
CH_3	3320	1750	1690	1600	1545	1418	1335	1300	1240	1185	1145
C_2H_5	3320	1750	1700	1600	1505	1425	1345	1300	1236	1186	1133
C_3H_7	3331	1745	1690	1600	1464	1425	1345	1292	1235	1185	1136
C_4H_9	3320	1745	1690	1600	1500	1425	1340	1295	1228	1175	
C_5H_{11}	3320	1750	1700	1605	1500	1430	1345	1292	1236	1186	
C_6H_{13}	3320	1740	1680	1605	1505	1418	1335	1290	1225	1190	1138
C_7H_{15}	3310	1720	1620	1590	1500	1405		1285	1225	1195	1124
$C_6H_5CH_2$	3315	1750	1675	1590	1490	1415	1330	1305	1225	1182	1137

TABLE VIII

INFRARED MAXIMA OF *n*-HEXYL-3-HYDROXY-4-MONOSUBSTITUTED-5-PYRAZOLONES

R	Absorption bands, cm.$^{-1}$							
H	3210	1705	1610	1550	1361	1300	1190	1115
CH_3	3110	1745	1660	1490	1340	1298	1185	1140
C_2H_5	3100	1740	1650	1490	1351	1271	1172	1122
C_3H_7	3110	1730	1665	1490	1342	1305	1186	1122
C_4H_9	3310	1745	1670	1490	1310	1260	1160	1125
C_5H_{11}	3150	1750	1670	1505	1340	1300	1187	1140
C_6H_{12}	3300	1760	1665	1495	1342	1265	1168	1132
C_7H_{15}	3270	1750	1680		1325			1142
$C_6H_5CH_2$	3230	1752	1685	1500	1305		1180	1132

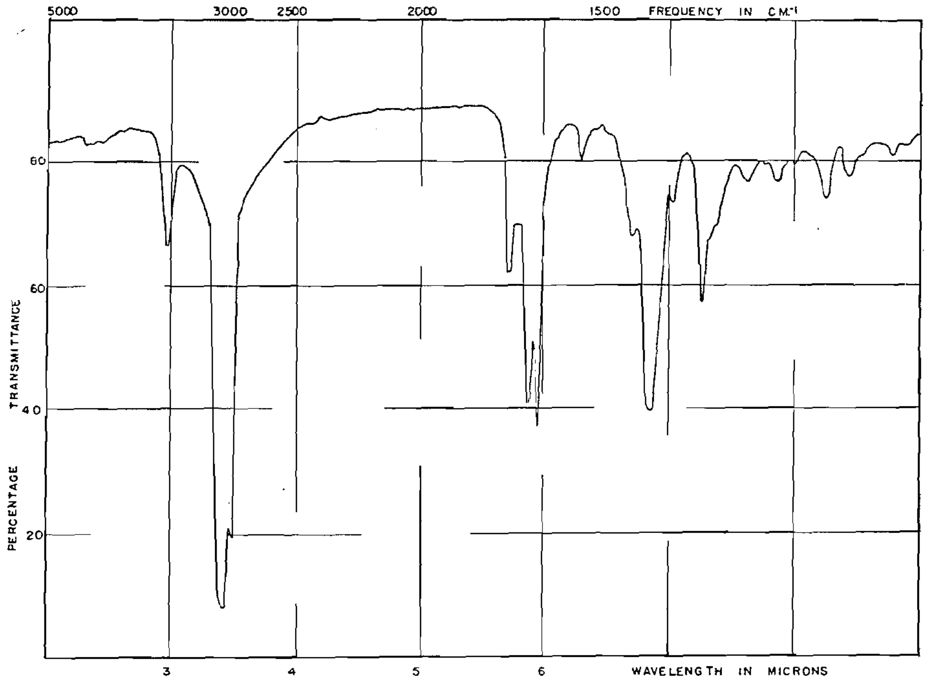


FIG. 5. Infrared absorption spectrum of 2-*o*-chlorophenyl-3-hydroxy-4-*n*-butyl-5-pyrazolone.

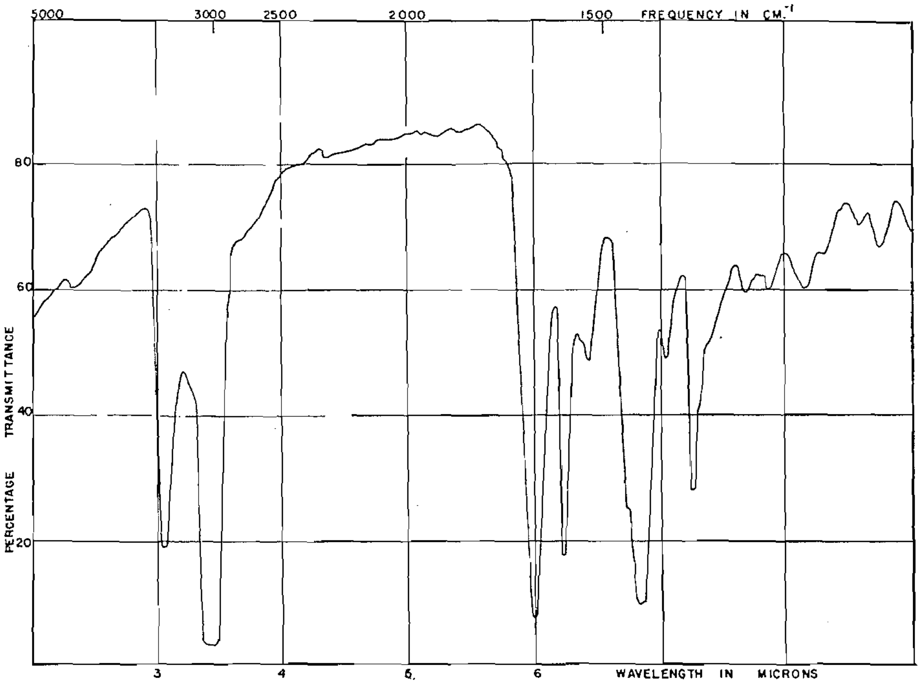


FIG. 6. Infrared absorption spectrum of 2-*m*-chlorophenyl-3-hydroxy-4-*n*-amyl-5-pyrazolone.

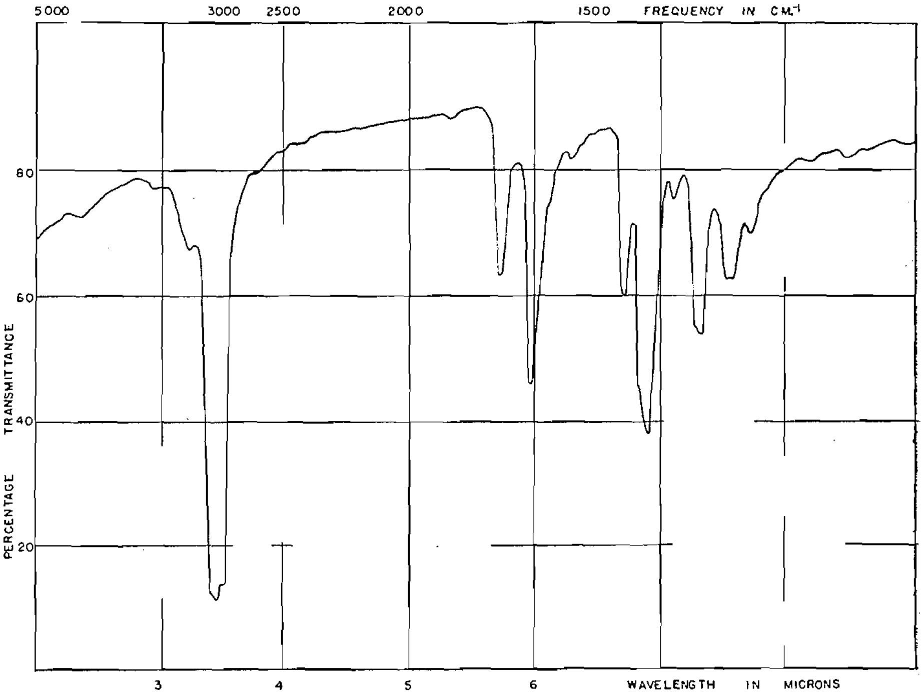


FIG. 7. Infrared absorption spectrum of 2-*p*-chlorophenyl-3-hydroxy-4-*n*-hexyl-5-pyrazolone.

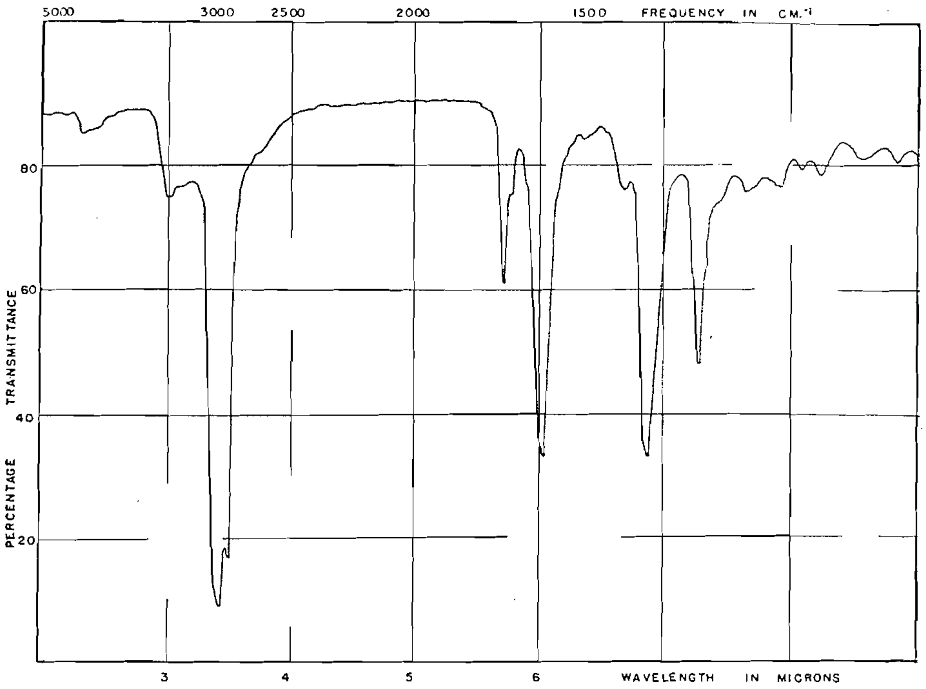


FIG. 8. Infrared absorption spectrum of 2-*n*-hexyl-3-hydroxy-4-*n*-hexyl-5-pyrazolone.

Because of the tautomeric structures theoretically possible for 3-hydroxypyrazolones, the pyrazolones may be expected to give rise to very complicated infrared spectra. The problem of interpretation is also difficult since very few reference spectra for pyrazolones are available. Randal and his co-workers (13) reported the absorption spectrum of 3-methyl-5-pyrazolone but only gave an assignment for a cyclic C = N band. The infrared spectra of several 4-monosubstituted-3-phenyl-5-pyrazolones and 4-monosubstituted-1,3-diphenyl-5-pyrazolones were given by Gagnon, Boivin, and Paquin (7). They assigned an absorption peak which appeared at 3300 cm.$^{-1}$ in the spectra of the 3-phenyl-5-pyrazolones to an OH group. This seemed plausible since no band for a carbonyl group was present, and pyrazolones may exist in the enolic form. Two or more peaks in the double bond region were interpreted as a sign of conjugation. The spectra of 1,3-diphenyl-5-pyrazolones were less complicated. Bond assignments were made tentatively for the C = O group at 1700 cm.$^{-1}$, and the C = N group at 1600 cm^{-1}.

In the present investigation, bond assignments have been made for several functional groups. The *o*-, *m*-, and *p*-2-chlorophenyl pyrazolones exhibit very complicated spectra, but the positions of the peaks are quite similar for the three homologous series. A band of medium to high intensity occurs in the spectra of the compounds at 3300 cm^{-1}. It is easy to assign this band to the absorption of a definite NH or OH group. It has already been mentioned that the pyrazolones prepared in this work are monobasic acids. With this chemical evidence in mind it is reasonable to attribute this band to an OH group.

An absorption band of high intensity occurs in the range 1675–1770 cm^{-1}. This is the region in which the C=O group absorbs. Randal and his co-workers have attributed the absorption in this range to the carbonyl group of lactams, therefore it is reasonable to do the same for pyrazolones.

A second band of very high intensity always occurs in the double bond region and absorbs in the range 1670–1700 cm^{-1}. This band is much too strong to be attributed to C=C absorption or vibrational ring influences, both of which could occur at this place. Randal studied the absorption spectra of many nitrogen compounds such as thiazolidines, imidazolines, pyridines, oxazolones, and 3-methyl-5-pyrazolone and found that the C=N group in these cyclic structures occurred in the region 1590–1680 cm^{-1}. Therefore we may ascribe this peak to that of a cyclic C=N.

A very constant absorption peak of low to medium intensity occurs at 1490 cm^{-1}. This band appears in both the 2-chlorophenyl and the 2-*n*-hexyl pyrazolones and therefore cannot be ascribed to the absorption of the phenyl ring. The absorption of the C=C group is in almost every case found in this region but usually at lower wave length. In the absorption spectrum of α-phenylazoacetoacetic acid ethyl ester, Randal assigns a peak at 1510 cm.$^{-1}$ to the influence of an enolic carbon double bond. Since this structure is possible in the compounds prepared we may assign the peak to a —C=C—OH enolic structure. Other peaks present at 1600 cm.$^{-1}$, 1640 cm.$^{-1}$, and 1530 cm.$^{-1}$ may be caused by the phenyl ring vibrations.

From a consideration of the infrared spectra and assignments made we must consider the following formulae to represent the 2-chlorophenyl pyrazolones. An enolic —C=C—OH bond and an OH absorption peak indicate the partial structure of a phenol —C=C—OH. Structures V and VI satisfy this postulation since they both have an enolic structure.

The infrared spectra also shows the presence of a C=N group. The only possibility for a bond of this nature is formula IV.

The spectra of the *n*-hexyl pyrazolones are not as complicated as those of the 2-chlorophenyl pyrazolones. A peak in the region of 3100–3300 cm.$^{-1}$ may be ascribed to the vibration of the OH group. An absorption band at 1735–1750 indicates the presence of a C=O group while an intense band at 1660–1685 cm.$^{-1}$ is ascribed to a cyclic C=N. A very constant absorption band which appears in all the pyrazolones at 1490 cm.$^{-1}$ indicates the presence of an enolic —C=C—OH grouping.

The *n*-hexyl pyrazolones can then be given the same structures as the 2-chlorophenyl pyrazolones.

EXPERIMENTAL PART*

2-o-Chlorophenyl-3-hydroxy-4-monosubstituted-5-pyrazolones

Diethyl malonates (0.05 mole) and *o*-chlorophenylhydrazine (0.05 mole) were condensed in two different ways. The malonates containing the substituents, butyl, amyl, hexyl, heptyl, and benzyl were condensed with *o*-chlorophenylhydrazine in the presence of sodium ethylate in absolute ethyl alcohol.

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*All melting points are uncorrected.

The reaction time varied from 18 to 20 hr. The excess alcohol was then removed and the remaining residues dissolved in water. The aqueous solutions were well extracted with ethyl ether and acidified with dilute acetic acid (33%), whereupon the pyrazolones were obtained usually as crystalline solids. The compounds were purified by crystallization from either xylene or petroleum ether.

The malonates bearing the substituents methyl, ethyl, and propyl and unsubstituted ethyl malonate did not yield pyrazolones when condensed with *o*-chlorophenylhydrazines in the above manner. Heating of the esters with *o*-chlorophenylhydrazine at 165°C. yielded the pyrazolones in small amounts. Heating was continued until no more ethanol was evolved from the reaction mixture. This usually required three hours. The mixture was then cooled and dissolved in sodium hydroxide solution (5%). Insoluble material was filtered off and the alkaline solution was extracted several times with ethyl ether. Upon acidification with acetic acid (33%), the pyrazolones were obtained. The pyrazolones are listed together with their melting points, analyses, and ultraviolet absorption maxima in Table I and the infrared data are given in Table V. Typical ultraviolet absorption curves are plotted in Fig. 1 while some infrared data are plotted in Fig. 5.

2-m-Chlorophenyl, 2-p-Chlorophenyl, and 2-n-Hexyl-3-hydroxy-4-monosubstituted-5-pyrazolones

Diethyl malonates and *m*-chloro, *p*-chloro, and *n*-hexylhydrazines were condensed in a manner similar to that used to obtain the 2-*o*-chlorophenyl pyrazolones. The melting points, analyses, and ultraviolet absorption maxima are given in Tables II, III, and IV. The infrared absorption bands are given in Tables VI, VII, and VIII.

Preparation of Diethyl-n-hexyl Malonate-2-C^{14}

To a solution of sodium metal (5.6 gm., 0.242 mole) in ethanol (400 ml.) was added diethyl malonate (20 gm., 0.125 mole) and 9.3 mgm. of diethyl malonate-2-C^{14} containing 0.1 mc. of activity. Hexyl bromide (21 gm., 0.125 mole) was added and the mixture was refluxed until acidic to wet litmus paper. The excess ethanol was then removed under reduced pressure and the inorganic salts dissolved in water. The oil which separated was extracted with ether and the extract was washed with water and dried over sodium sulphate. The ether was removed by distillation and the substituted ester distilled under reduced pressure: b.p. 154–156°C. at 10 mm. There was obtained 23 gm. of product, yield, 63.3%. A small sample of the product (18.4 mgm.) was taken and converted to carbon dioxide, absorbed in barium hydroxide, and counted as barium carbonate. The specific activity was calculated to be 12.4 μc. per gram of material.

Preparation of 2-Substituted-3-hydroxy-4-n-hexyl-5-pyrazolones-4-C^{14}

Diethyl *n*-hexyl malonate-2-C^{14} (4.0 gm., 0.017 mole) was reacted with *o*-, *m*-, and *p*-chlorophenylhydrazine (2.4 gm., 0.017 mole) and *n*-hexylhydrazine (2.0 gm., 0.017 mole) in the presence of sodium metal (2.4 gm., 0.11 mole) in absolute ethanol (200 ml.). After a reaction time of 18 hr. the excess alcohol was evaporated and the remaining residue dissolved in water. The aqueous solution was purified by extracting several times with ethyl ether. Acidification with dilute acetic acid (33%) gave the labelled pyrazolones. The chemical yields varied from 60 to 70%, after purification from petroleum ether. Their specific activities were determined by conversion of the compounds to carbon dioxide and counting as barium carbonate.

Combustion of C^{14} Products, Plating, and Counting

All the compounds were completely transformed to carbon dioxide by dry combustion. Samples weighing from 20 to 30 mgm. were burned in the presence of oxygen in a closed system. The carbon dioxide evolved was absorbed in two traps containing carbonate free barium hydroxide solution. When combustion was complete the absorbers were removed from the apparatus and the barium carbonate separated by centrifuging. A sample of the active barium carbonate and water was transferred to an aluminum counting plate and dried under an infrared lamp. Continuous agitation was necessary to ensure even distribution throughout the mount. Sufficient barium carbonate was added to each plate to ensure "infinite thickness". When dry the samples were counted using an end window Geiger-Mueller counter. The counting rates were corrected as suggested by Andrews and Mannet (1). The results obtained are given in Table IX.

TABLE IX
COUNTING DATA OF 2-SUBSTITUTED-3-HYDROXY-4-*n*-HEXYL-5-PYRAZOLONES-4-C^{14}

2-Substituent	Weight, mgm.	Total count	Time, min.	Count rate per min.	Specific activity, μc./gm.
o-Chlorophenyl	21.3	7,565	5	1491	7.0
m-Chlorophenyl	19.4	8,110	5	1600	8.8
p-Chlorophenyl	22.0	10,010	5	1980	9.0
n-Hexyl	24.7	10,450	5	2070	8.8

Ultraviolet Absorption Spectra

The ultraviolet absorption spectra of the pyrazolones were taken on a Beckman Spectrophotometer Model DU. The method has been previously described (6). The solvents used were ethanol (95%) and a solution of sodium hydroxide (0.01 *N*) in ethanol. The results are listed in Tables I, II, III, and IV and some of the data are plotted in Figs. 1, 2, 3, and 4.

Infrared Absorption Spectra

All the infrared absorption spectra of the pyrazolones were obtained with a Perkin-Elmer Model 21 double-beam null principle recording spectrophotometer. The method has been described in the literature (7).

The spectra covering the range from 5000 to 1100 cm.$^{-1}$ only are given in Figs. 5, 6, 7, and 8. The curves all show the four specific bands of Nujol. The other absorption bands are listed in Tables V, VI, VII, and VIII, and have been discussed in the theoretical part.

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