SYNTHESES AND ABSORPTION SPECTRA OF 1-CHLOROPHENYL-3-PHENYL-4-ALKYL-5-PYRAZOLONES AND PYRAZOLONES-4-C^{14} [1]

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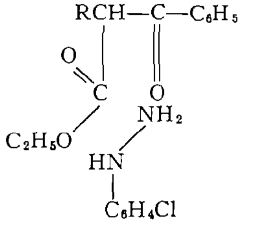
ABSTRACT

Monosubstituted benzoylacetic esters $C_6H_5COCH(R)CO_2C_2H_5$ (R = H, C_nH_{2n+1} (n = 1 to 9), and $C_6H_5CH_2$) obtained by the condensation of n-alkyl halides with ethyl benzoylacetate were reacted with *o*-, *m*-, and *p*-chlorophenylhydrazines to give 1-chlorophenyl-3-phenyl-4-alkyl-5-pyrazolones. Pyrazolones-4-C^{14} were prepared by the action of the same hydrazines on ethyl benzoylacetate-α-C^{14} obtained from benzoyl chloride and ethyl malonate-2-C^{14}. Their activities were 801, 894, and 847 c./min. respectively. The ultraviolet and infrared absorption spectra of all the pyrazolones were determined and the most probable structures ascribed to the compounds.

INTRODUCTION

The condensation of hydrazine and its monosubstituted derivatives with β-keto esters (I) gives by elimination of water a hydrazone (II) which, by elimination of another molecule of water, produces an alkoxypyrazole (III) or a pyrazolone (IV) by elimination of alcohol.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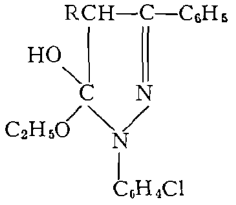
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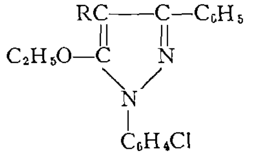
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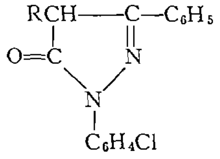
IV

The main product is an ethoxypyrazole when the reagents are heated in acid media and a pyrazolone when they are heated alone.

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TABLE I
1-*o*-CHLOROPHENYL-3-PHENYL-4-MONOALKYL-5-PYRAZOLONES $RC_{15}H_{10}ON_2Cl$

R	M.p.,°C.	Yield, %	Formula	Analysis: Calculated, % C	H	N	Found, % C	H	N	Ultraviolet absorption maxima Å	log E_m
H	170–171	86	$C_{15}H_{11}ON_2Cl$	66.54	4.09	10.34	66.35	4.18	10.47	3200 2540	3.798 4.292
CH_3	171–172	70	$C_{16}H_{13}ON_2Cl$	67.48	4.60	9.83	67.33	4.52	9.76	3050 2620	3.896 4.341
C_2H_5	121–122	67	$C_{17}H_{15}ON_2Cl$	68.33	5.06	9.37	68.27	5.07	9.36	3100 2580	3.633 4.376
C_3H_7	137–138	53	$C_{18}H_{17}ON_2Cl$	69.26	5.47	8.95	69.13	5.45	9.16	3100 2600	3.473 4.343
C_4H_9	130–131	74	$C_{19}H_{19}ON_2Cl$	69.82	5.85	8.57	69.80	5.90	8.81	3100 2600	3.718 4.349
C_5H_{11}	120–121	55	$C_{20}H_{21}ON_2Cl$	70.47	6.21	8.21	70.65	6.07	8.17	3100 2480	3.729 4.208
C_6H_{13}	122–123	51	$C_{21}H_{23}ON_2Cl$	71.07	6.53	7.89	70.94	6.47	8.07	3000 2600	3.873 4.172
C_7H_{15}	109–110	45	$C_{22}H_{25}ON_2Cl$	71.62	6.80	7.59	71.88	6.72	7.80	3050 2560	3.808 4.232
C_8H_{17}	103–104	56	$C_{23}H_{27}ON_2Cl$	72.13	7.10	7.31	72.18	7.04	7.60	2980 2600	3.751 4.246
C_9H_{19}	103–104	45	$C_{24}H_{29}ON_2Cl$	72.21	7.36	7.05	72.38	7.29	7.19	3100 2560	3.760 4.168
$C_6H_5CH_2$	157–158	78	$C_{22}H_{17}ON_2Cl$	73.22	4.75	7.76	73.17	4.71	7.64	3000 2620	3.398 4.283

TABLE II

1-*m*-CHLOROPHENYL-3-PHENYL-4-MONOALKYL-5-PYRAZOLONES $RC_{15}H_{10}ON_2Cl$

R	M.p.,°C.	Yield, %	Formula	Analysis						Ultraviolet absorption maxima	
				Calculated, %			Found, %				
				C	H	N	C	H	N	Å	log E_m
H	108–109	81	$C_{15}H_{11}ON_2Cl$	66.54	4.09	10.34	66.56	4.13	10.32	3000 2600	3.970 4.394
CH_3	160–161	57	$C_{16}H_{13}ON_2Cl$	67.48	4.60	9.83	67.51	4.49	9.85	3050 2560	3.867 4.017
C_2H_5	105–106	64	$C_{17}H_{15}ON_2Cl$	68.33	5.06	9.37	68.17	5.06	9.39	3100 2520	3.438 4.394
C_3H_7	109–110	57	$C_{18}H_{17}ON_2Cl$	69.26	5.47	8.95	69.37	5.54	9.17	3000 2540	3.862 4.268
C_4H_9	119–120	69	$C_{19}H_{19}ON_2Cl$	69.82	5.85	8.57	69.97	6.05	8.61	2980 2540	3.403 4.119
C_5H_{11}	120–121	57	$C_{20}H_{21}ON_2Cl$	70.47	6.21	8.21	70.40	6.14	8.33	2980 2480	3.804 4.222
C_6H_{13}	140–141	49	$C_{21}H_{23}ON_2Cl$	71.07	6.53	7.89	71.05	6.57	8.10	3150 2500	3.559 4.366
C_7H_{15}	102–103	46	$C_{22}H_{25}ON_2Cl$	71.62	6.80	7.59	71.73	6.87	7.68	3100 2520	3.585 4.328
C_8H_{17}	111–112	52	$C_{23}H_{27}ON_2Cl$	72.13	7.10	7.31	71.85	7.03	7.45	2980 2480	3.457 4.322
C_9H_{19}	118–119	49	$C_{24}H_{29}ON_2Cl$	72.61	7.36	7.05	72.65	7.54	7.15	3100 2600	3.326 4.134
$C_6H_5CH_2$	161–162	62	$C_{22}H_{17}ON_2Cl$	73.22	4.75	7.76	73.31	4.71	7.81	2980 2520	3.642 4.108

TABLE III

1-*p*-Chlorophenyl-3-phenyl-4-monoalkyl-5-pyrazolones $RC_{15}H_{10}ON_2Cl$

R	M.p.,°C.	Yield, %	Formula	Analysis						Ultraviolet absorption maxima	
				Calculated, %			Found, %				
				C	H	N	C	H	N	Å	log E_m
H	161–162	64	$C_{15}H_{11}ON_2Cl$	66.54	4.09	10.34	66.56	4.23	10.56	3050 2520	3.723 4.197
CH_3	160–161	70	$C_{16}H_{13}ON_2Cl$	67.48	4.60	9.83	67.20	4.64	9.93	3150 2540	3.854 4.280
C_2H_5	117–118	67	$C_{17}H_{15}ON_2Cl$	68.33	5.06	9.37	68.15	5.18	9.50	3000 2480	3.842 4.131
C_3H_7	182–183	65	$C_{18}H_{17}ON_2Cl$	69.26	5.47	8.95	69.04	5.34	9.03	3000 2500	3.395 4.177
C_4H_9	125–126	49	$C_{19}H_{19}ON_2Cl$	69.82	5.85	8.57	69.70	5.74	8.77	3050 2560	3.778 4.220
C_5H_{11}	167–168	56	$C_{20}H_{21}ON_2Cl$	70.47	6.21	8.21	70.48	5.93	8.45	3150 2600	3.738 4.257
C_6H_{13}	152–153	45	$C_{21}H_{23}ON_2Cl$	71.07	6.53	7.89	71.32	6.44	8.12	3100 2520	3.740 4.249
C_7H_{15}	112–113	42	$C_{22}H_{25}ON_2Cl$	71.62	6.80	7.59	71.65	6.84	7.62	3150 2500	3.760 4.312
C_8H_{17}	117–118	49	$C_{23}H_{27}ON_2Cl$	72.13	7.10	7.31	72.11	7.15	7.34	3050 2580	3.454 4.297
C_9H_{19}	113–114	39	$C_{24}H_{29}ON_2Cl$	72.61	7.36	7.05	72.48	7.19	7.28	2960 2520	3.686 4.237
$C_6H_5CH_2$	165–166	50	$C_{22}H_{17}ON_2Cl$	73.22	4.75	7.76	73.25	4.88	7.89	2980 2480	3.469 4.332

One of the objects of the present investigation was to synthesize and to determine the structure of 1-chlorophenyl-3-phenyl-4-alkyl-5-pyrazolones. Another object was to prepare pyrazolones-4-C^{14}.

The starting esters used in the present work, the ethyl-α-monosubstituted-α-benzoylacetates, were prepared (9) by alkylation of ethyl benzoylacetate. The *o*-, *m*-, and *p*-chlorophenylhydrazines were prepared by diazotation of their respective anilines followed by reduction with sodium sulphite. The ethyl benzoylacetate-α-C^{14} was obtained by the condensation of benzoyl chloride with ethyl malonate-2-C^{14} and decarboxylation (1, 8).

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

Ultraviolet Absorption Spectra

The ultraviolet absorption spectra of all pyrazolones were determined in alcohol solution. The results obtained are given in Tables I, II, and III and shown graphically in Figs. 1, 2, and 3.

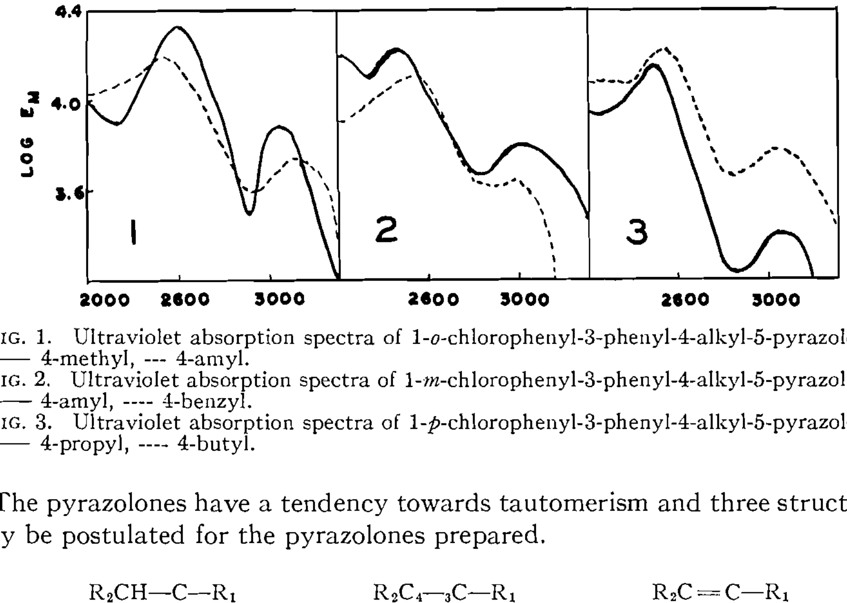
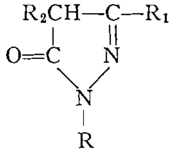


FIG. 1. Ultraviolet absorption spectra of 1-*o*-chlorophenyl-3-phenyl-4-alkyl-5-pyrazolones; ——— 4-methyl, --- 4-amyl.
FIG. 2. Ultraviolet absorption spectra of 1-*m*-chlorophenyl-3-phenyl-4-alkyl-5-pyrazolones; ——— 4-amyl, ---- 4-benzyl.
FIG. 3. Ultraviolet absorption spectra of 1-*p*-chlorophenyl-3-phenyl-4-alkyl-5-pyrazolones; ——— 4-propyl, ---- 4-butyl.

The pyrazolones have a tendency towards tautomerism and three structures may be postulated for the pyrazolones prepared.



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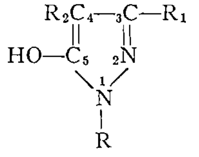

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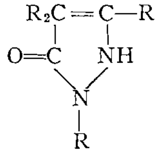

III

The 4,4-dialkyl-pyrazolones as well as the pyrazolone dyes are derived from formula I. Formula II is invoked to explain the formation of alkoxypyrazoles and the formation of sodium salt. Formula III explains the easy methylation of the nitrogen atom 2.

The spectra exhibited by many pyrazolones have been studied intensively by many workers (2, 3, 4, 5, 6). These authors related the wavelength of the absorption band and its intensity to the position of the double bond in the ring. It was found that a high intensity maximum at short wavelength was indicative of a double bond between two carbon atoms while a low intensity maximum at longer wavelength corresponded to a double bond between the nitrogen atom 2 and the carbon atom 3. The presence of two maxima for the same compound was attributed to the presence of two tautomeric forms (7).

The spectra of the *o*-, *m*-, and *p*-chlorophenylpyrazolones prepared are quite similar in their characteristics. In neutral solution these pyrazolones exhibit two maxima, one of high intensity at short wavelength and one of low intensity at longer wavelength. These results indicate that during the spectra determination in alcoholic solution the pyrazolones existed in at least two tautomeric forms; one with a carbon nitrogen double bond, formula I or II, and the other with the carbon carbon double bond as shown in formulas II and III.

Infrared Absorption Spectra

The infrared absorption spectra of the pyrazolones were determined with a Perkin-Elmer spectrometer. The results obtained are given in Tables IV, V, and VI and some data are plotted in Figs. 4, 5, and 6.

Because of the three tautomeric structures theoretically possible for the 1,3,4-trisubstituted pyrazolones, they may be expected to give rise to very complicated infrared spectra. The problem of interpretation of those spectra

TABLE IV

INFRARED ABSORPTION MAXIMA OF
1-*o*-CHLOROPHENYL-3-PHENYL-4-MONOALKYL-5-PYRAZOLONES

R	Absorption bands, cm.$^{-1}$					
H	1640	1565	1515	1345	1260	1165
CH_3	1645	1575	1535	1315	1265	1120
C_2H_5	1630	1580		1310	1255	1120
C_3H_7	1635	1590	1570	1315	1230	1115
C_4H_9	1630	1575		1325	1250	1125
C_5H_{11}	1640	1610	1580	1310	1250	1120
C_6H_{13}	1630	1575		1315	1240	1170
C_7H_{15}	1640	1610	1575	1325	1255	1125
C_8H_{17}	1640	1615	1580	1315	1250	1125
C_9H_{19}	1640	1610	1585	1320	1250	1120
$C_6H_5CH_2$	1630	1575	1310	1255	1215	1110

TABLE V

INFRARED ABSORPTION MAXIMA OF
1-*m*-CHLOROPHENYL-3-PHENYL-4-MONOALKYL-5-PYRAZOLONES

R	Absorption bands, cm.$^{-1}$					
H	1710	1590	1490	1320	1290	1120
CH_3	1650	1590	1500	1325	1245	
C_2H_5	1650	1590	1480	1330	1230	1120
C_3H_7	1640	1585	1480	1315	1230	1125
C_4H_9	1660	1590	1480	1310	1210	1120
C_5H_{11}	1700	1590	1500	1300		1130
C_6H_{13}	1675	1575	1420	1375	1230	1120
C_7H_{15}	1680	1580	1420	1320	1250	1125
C_8H_{17}	1640	1580	1415	1325	1250	1120
C_9H_{19}	1640	1580	1420	1320	1250	1120
$C_6H_5CH_2$	1640	1575	1490	1310	1230	1110

TABLE VI

INFRARED ABSORPTION MAXIMA OF
1-*p*-CHLOROPHENYL-3-PHENYL-4-MONOALKYL-5-PYRAZOLONES

R	Absorption bands, cm.$^{-1}$					
H	1700	1590	1432	1332	1177	1120
CH_3	1660	1590	1485	1330	1183	
C_2H_5	1700	1605	1562	1490	1162	1090
C_3H_7	1695	1580	1484	1320	1160	1130
C_4H_9	1630	1575	1410	1310	1212	1115
C_5H_{11}	1710	1590	1492	1320	1185	1100
C_6H_{13}	1640	1570		1310	1175	1120
C_7H_{15}	1650	1575		1315	1180	1115
C_8H_{17}	1660	1580	1410	1310	1250	1120
C_9H_{19}	1635	1580	1405	1318	1250	1120
$C_6H_5CH_2$	1640	1575		1310	1250	1105

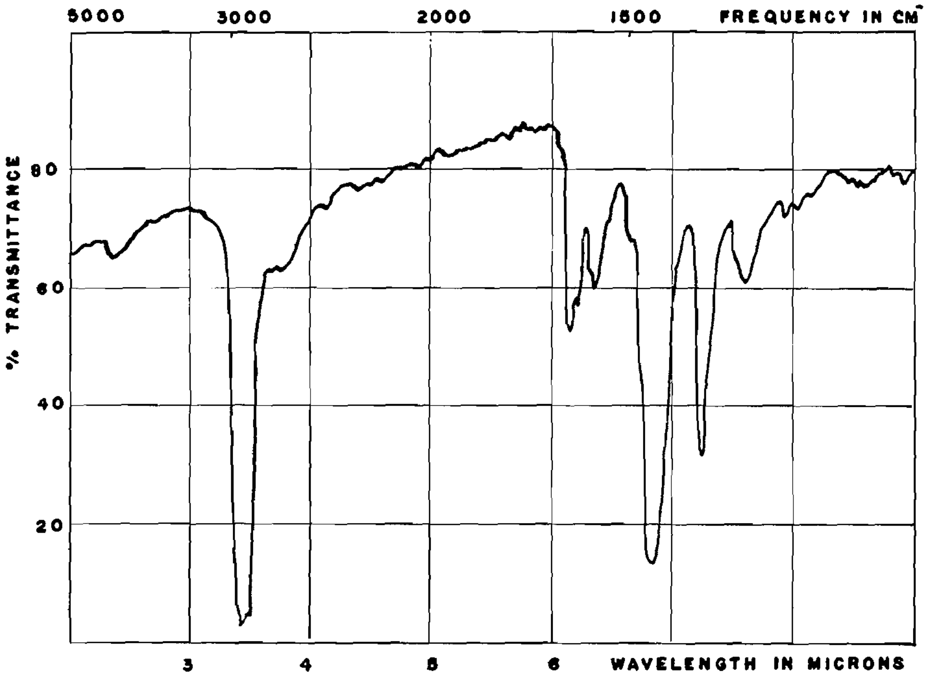

FIG. 4. Infrared absorption spectrum of 1-*o*-chlorophenyl-3-phenyl-4-methyl-5-pyrazolone.

is difficult since few reference spectra for pyrazolones are available in the literature. The absorption spectrum of the 3-methyl-5-pyrazolone has been reported by Randall and his co-workers (10) and he only gave an assignment for a cyclic C=N band. The infrared spectra of several 4-monosubstituted-1,3-diphenyl-5-pyrazolones were determined by Gagnon, Boivin, and Paquin (6). Bond assignments were made tentatively for the C=O group at 1700 cm.$^{-1}$ and the C=N group at 1600 cm.$^{-1}$. Gagnon, Boivin, MacDonald, and Yaffe (5) have studied the absorption spectra of 2-substituted-3-hydroxy-5-pyrazolones and assigned a band in the region of 3300 cm.$^{-1}$ to an OH group. The presence of

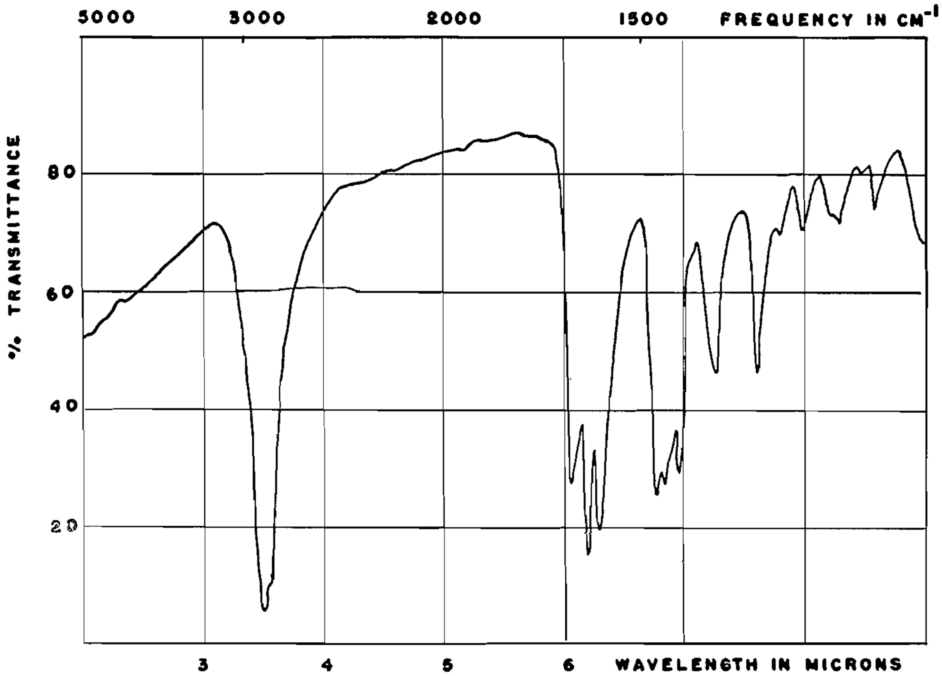

FIG. 5. Infrared absorption spectrum of 1-*m*-chlorophenyl-3-phenyl-4-butyl-5-pyrazolone.

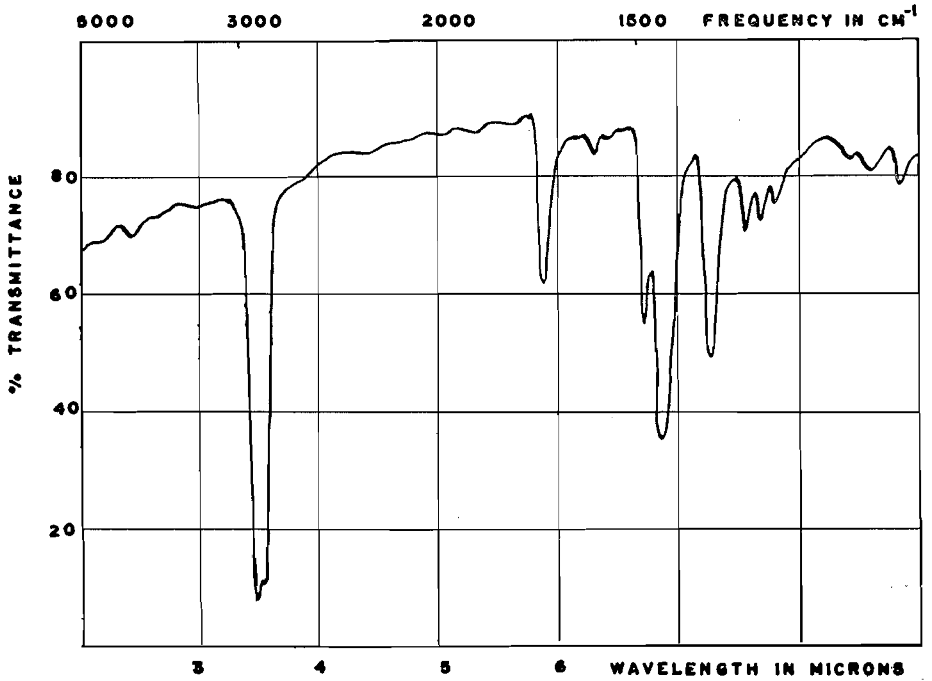

FIG. 6. Infrared absorption spectrum of 1-*p*-chlorophenyl-3-phenyl-4-propyl-5-pyrazolone.

that group was also proved by chemical methods. Another band occurring in the region of 1670–1700 cm.$^{-1}$ was attributed to a C=O group. A third band in the region of 1590–1680 was attributed to a C=N band as suggested by Randall (10) after studying many cyclic nitrogen compounds such as thiazolidines, imidazolines, and pyridines.

In the present investigation band assignments can be made for two functional groups. An absorption band of high intensity occurring in the region of 1630–1710 cm.$^{-1}$ is attributed to a C=O group. Randall and his co-workers have assigned an absorption band in this region to the carbonyl group for the lactams; therefore it is reasonable to do the same for pyrazolones. Furthermore the absence of a band in the region of 3300 cm.$^{-1}$ characteristic of an OH group is another proof for the presence of a carbonyl group.

A second band occurs in the double band region and absorbs in the range of 1565–1610 cm.$^{-1}$. This band is attributed to a C=N group as suggested by Randall after having studied many cyclic nitrogen compounds.

From those results, one might conclude that in the solid state the pyrazolones prepared have the form CH—C=N while in alcoholic solution this form is in equilibrium with its tautomer C=C—NH.

EXPERIMENTAL PART*

1-o-Chlorophenyl-3-phenyl-4-alkyl-5-pyrazolones

A mixture of ethyl-α-monosubstituted-α-benzoylacetate (0.02 mole) and *o*-chlorophenylhydrazine hydrochloride (0.02 mole) was heated under reduced pressure for three hours at 110–120° C. The red viscous liquid obtained was cooled and dissolved in sodium hydroxide (5%, 200 ml.). The solution was filtered and washed with ether until the extracts were no longer colored. The alkaline solution was cooled and acidified with acetic acid (50%). The precipitate obtained was recrystallized from alcohol or petroleum ether. The pyrazolones are listed together with their melting points, analyses, and ultraviolet absorption spectra in Table I and the infrared data are given in Table IV. Typical ultraviolet absorption curves are plotted in Fig. 1 while some infrared data are plotted in Fig. 4.

1-m-Chlorophenyl- and 1-p-Chlorophenyl-3-phenyl-4-monosubstituted-5-pyrazolones

A mixture of ethyl-α-monosubstituted-α-benzoylacetate (0.02 mole) and *m*-chlorophenyl- or *p*-chlorophenyl-hydrazine was heated under reduced pressure for three hours at 110–120° C. and then for one hour at 170–180° C. The red viscous liquid was treated in a manner similar to that used to obtain the 1-*o*-chlorophenylpyrazolones. The melting points, analyses, and ultraviolet absorption maxima are given in Tables II and III. The infrared absorption bands are given in Tables V and VI and some data are plotted in Figs. 5 and 6.

Preparation of Ethyl Benzoylacetate-α-C^{14}

Magnesium (5.6 gm., 0.23 mole) was placed in a flask equipped with a condenser and a mechanical stirrer. Ethyl malonate (32 gm., 0.20 mole) and

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**All melting points are uncorrected.*

ethyl malonate-2-C^{14} (10 mgm. containing 0.1 mc. of activity) were added. The reaction was initiated with a few drops of carbon tetrachloride and when it subsided, dried ether (75 ml.) was introduced. After all the magnesium had reacted, benzoyl chloride (31 gm., 0.22 mole) was added dropwise while the mixture was refluxed and stirred. When the reaction was completed the solution was cooled and diluted with water (100 ml.). The compound $C_6H_5COCH(CO_2C_2H_5)_2.3H_2O$ crystallized from ether. That substance was decomposed with dilute sulphuric acid. The product was extracted with ether, dried, and distilled. B.p.: 185–190° C. at 12 mm. The benzoyl malonate-2-C^{14} was decarboxylated by steam distillation in dilute sulphuric acid solution. The distillate was neutralized with sodium bicarbonate, extracted with ether, dried, and distilled. B.p.: 113–116° C. at 2 mm.

1-o-Chlorophenyl-3-phenyl-5-pyrazolone-4-C^{14}

Ethyl benzoylacetate-α-C^{14} (3.84 gm., 0.02 mole) was heated with *o*-chlorophenylhydrazine hydrochloride (3.58 gm., 0.02 mole) during three hours at 110–120° C. The product of the reaction was dissolved in sodium hydroxide solution and purified by several extractions with ethyl ether. Acidification with acetic acid (50%) gave the labelled pyrazolone, which was crystallized from ethyl alcohol. Yield, 3.3 gm., 61%.

1-m-Chlorophenyl- and 1-p-Chlorophenyl-3-phenyl-5-pyrazolones-4-C^{14}

A mixture of ethyl benzoylacetate-α-C^{14} (1.92 gm., 0.01 mole) and *m*-chlorophenyl- or *p*-chlorophenyl-hydrazine (1.43 gm., 0.01 mole) was heated under reduced pressure for three hours at 110–120° C. and then for one hour at 170–180° C. The product obtained was treated in a manner similar to that used to obtain the 1-*o*-chlorophenylpyrazolone. The chemical yields varied from 60 to 70%, after purification from ethyl alcohol.

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

Samples weighing about fifteen milligrams were completely transformed into carbon dioxide by burning them in a closed system in the presence of oxygen. The carbon dioxide evolved was absorbed in two traps containing carbonate-free sodium hydroxide. After some ammonium chloride was added, the carbonate was precipitated with barium chloride. The barium carbonate was transferred to an aluminum counting plate by centrifuging. Sufficient barium carbonate was added to each plate to ensure "infinite thickness". When dry, the samples were counted using an end window Geiger-Müller counter. The results obtained are given in Table VII.

TABLE VII

COUNTING DATA OF 1-CHLOROPHENYL-3-PHENYL-5-PYRAZOLONES-4-C^{14}

1-Chloro	Weight, mgm.	Total count	Time, min.	Thickness, mgm./cm.^{2}	Net activity, c./min.
Ortho	13.1	20758	25	30.4	801
Meta	13.6	23082	25	30.8	894
Para	13.9	21896	25	31.0	847

Ultraviolet Absorption Spectra

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

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 (6). The spectra covering the range 5000–1100 cm.$^{-1}$ only are given in Figs. 4, 5, and 6. The curves all show the four specific bands of nujol. The other absorption bands are listed in Tables IV, V, and VI, and have been discussed in the theoretical part.

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REFERENCES

1. Breslow, D. S., Baumgarden, E., and Hauser, C. R. J. Am. Chem. Soc. 66: 1288. 1944.
2. Gagnon, P. E., Boivin, J. L., and Boivin, P. A. Can. J. Research, B, 28: 720. 1950.
3. Gagnon, P. E., Boivin, J. L., and Chisholm, A. Can. J. Chem. 30: 904. 1952.
4. Gagnon, P. E., Boivin, J. L., and Jones, R. N. Can. J. Research, B, 27: 190. 1949.
5. Gagnon, P. E., Boivin, J. L., MacDonald, R., and Yaffe, L. Can. J. Chem. 32: 823. 1954.
6. Gagnon, P. E., Boivin, J. L., and Paquin, R. Can. J. Chem. 31: 1025. 1953.
7. Gagnon, P. E., Savard, K., Gaudry, R., and Richardson, E. M. Can. J. Research, B, 25: 28. 1947.
8. Lund, H. Ber. 67: 937. 1934.
9. Perkin, W. A., Jr. J. Chem. Soc. 45: 179. 1884.
10. Randall, H. M., Fowler, R. O., Fuson, N., and Dangl, J. R. Infrared determination of organic structures. D. Van Nostrand Company, Inc., New York. 1949.