in thiophenol. This manipulation of figures provides a plausible rationale for the conjugative-magnitude donor category but it should be clear that other experimental observations may be more difficult to dissect.

The alternatives set out in Table IV are sometimes difficult to sort out: in any given system the balance of nonconjugative and conjugative effects may be changing; the measured property may be dependent on medium, on both reactant and product, or ground state and excited state, etc. In other cases, misunderstandings have arisen because the type of results found in one situation, donor conjugative transmission, were not found or perhaps contradicted in another situation, acceptor conjugative transmission. The ultraviolet spectral transitions of certain oxygen and sulfur compounds have been discussed and fall in our conjugative donor category;[20c,22b,31] aspects of the reactivity toward nucleophiles of ethynyl ethers and thioethers have been clearly elucidated and clearly fall into the conjugative acceptor category:[20c,23] it is no contradiction to propose sulfur d-orbital participation in the latter case and not in the former.

Acknowledgment.—We wish to thank Mr. A. Caplan for preparing one of the thioanisoles and Mr. D. Sardella for providing his unpublished data on the benzoylacetones.

(31) L. Goodman and R. W. Taft, *J. Am. Chem. Soc.*, **87**, 4385 (1965). Ultraviolet spectral evidence in this paper places sulfur in the conjugative acceptor–donor category.

Proton Magnetic Resonance Studies of Pyrazoles

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4-Proton chemical shift data for 54 pyrazoles are correlated in the empirical equation $\delta_4 = \delta_4(s) + \alpha_1 + \alpha_3 + \alpha_5$, where $\delta_4(s)$ is a constant for each solvent, and α_1, α_3, and α_5 are empirical constants that represent the effect of replacing a methyl substituent by another group at positions 1, 3, and 5 of the pyrazole nucleus. The equation can be used for isomer identification and for the study of tautomers. The α constants of the equation are correlated with Hammett σ constants. It was observed in the nmr spectra that a phenyl group attached to a pyrazole ring appears as a multiplet resonance unless a substituent is α to it. Under the latter condition the phenyl resonance is a singlet. Chemical shift data are used to distinguish relative coplanarity of the phenyl and pyrazole rings. Ring proton coupling constants of pyrazoles are discussed.

Proton magnetic resonance data for substituted pyrazoles are of utility in the assignment of isomers and tautomers, and yield parameters of theoretical interest. Williams[1] found that the spin–spin coupling constants of the annular protons in 1-acylpyrazoles fell into narrow ranges and made structural assignments on that basis. For 1-alkyl-3- or -5-methylpyrazole pairs synthesized unequivocally, Habraken and Moore[2] found a paramagnetic displacement of the C-3(5) ring proton peak and a diamagnetic shift of the methyl peak on going from the 3-methyl to the 5-methyl isomer. Finar and Mooney[3] have noted that the 3-, 4-, and 5-protons of pyrazoles can generally be distinguished by the region of their chemical shifts and shift behavior in trifluoroacetic acid. Other nmr publications on substituted pyrazole have appeared.[4]

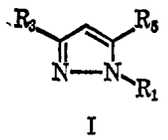
This paper presents additional nmr data for 54 pyrazoles all unsubstituted at the 4-position. An additive relationship, involving empirical constants, for calculating the chemical shift of the 4-proton in substituted pyrazoles has been found. This expression appears to be unambiguous for isomer identification of 1-substituted compounds and would seem to indicate which tautomer predominates in 1-H pyrazoles. The constants correlate with electron densities.[5–7] Chemical shift data of the phenyl series reflect coplanarity or noncoplanarity of the aromatic ring[8] and would seem to be of value in the study of induced currents and aromaticities in the pyrazole ring.

Experimental Section

The nmr spectra were measured at 60 Mc with either a Varian A-60 or a Varian HA-60 spectrometer, or both. The audiofrequency side-banding technique was used on the HA-60 to obtain accurate frequency values for chemical shifts and coupling constants. Shifts are reported in δ values (parts per million) downfield from internal tetramethylsilane. Solution concentrations were 0.5–2.5 *M* (*ca.* 5% w/v) in deuteriochloroform.

Results and Discussion

General.—The chemical shifts of 1,3,5-tribsustituted pyrazoles I and 1-H 3,5-disubstituted pyrazoles have been measured. They are tabulated in Tables I and II, respectively.



I

We have observed an additive relationship among the chemical shifts of the 4-proton in 1,3,5-trisubstituted pyrazoles. It takes the form

$$\delta_4 = \delta_4(s) + \alpha_1 + \alpha_3 + \alpha_5 \quad (1)$$

(1) J. K. Williams, *J. Org. Chem.*, **29**, 1377 (1964).

(2) C. L. Habraken and J. A. Moore, *ibid.*, **30**, 1892 (1965); *cf.*, also, J. A. Moore and C. L. Habraken, *J. Am. Chem. Soc.*, **86**, 1456 (1964).

(3) I. L. Finar and E. F. Mooney, *Spectrochim. Acta*, **20**, 1269 (1964).

(4) (a) M. Cola and A. Perotti, *Gazz. Chim. Ital.*, **94**, 1268 (1964); (b) V. Papesch and R. M. Dodson, *J. Org. Chem.*, **30**, 199 (1965); (c) T. Yamauchi and J. A. Moore, *ibid.*, **31**, 42 (1966); (d) J. D. Albright and L. Goldman, *ibid.*, **31**, 273 (1966).

(5) C. G. Hall, A. Hardisson, and L. M. Jackman, *Tetrahedron*, **19**, Suppl. **2**, 101 (1963).

(6) T. Schaefer and W. G. Schneider, *Can. J. Chem.*, **41**, 966 (1963).

(7) B. P. Dailey, *J. Chem. Phys.*, **41**, 2304 (1964).

(8) B. M. Lynch and Y. Y. Hung, *Can. J. Chem.*, **42**, 1605 (1964).

where δ_4 (s) is the chemical shift of the 4-proton of 1,3,5-trimethylpyrazole in a specific solvent s, and α_1, α_3, and α_5 are empirical constants representing the effect of replacing a methyl group by another group at positions 1, 3, and 5, respectively. The value of the constant δ_4 (s) for 5% solution in deuteriochloroform is 5.79 ppm and in carbon tetrachloride it is 5.66 ppm.

Data for the compounds in Tables I and II were used to obtain the averaged empirical α values tabulated in Table III. Values of δ_4 calculated from eq 1 and Table III are in agreement with the experimental values of Table I to within 0.01 ppm in nearly all examples except the carboxylic acids. The difference between the calculated and observed values for the acids of Table I was within ±0.04 ppm except for compound 28, which was 0.09 ppm.

Chemical reactions leading to 1,3,5-trisubstituted pyrazoles are usually such that both the 3 and 5 isomers are formed. The calculated chemical shifts of the 4-proton signals provided by eq 1, when the 3 and 5 substituents are of different chemical type, permit identification of the isomers. Four broadly different chemical classes (H, alkyl, aryl, and carbonyl) have been investigated. In a mixture of such isomers the spectrum integral provides a good estimate of the relative amounts.

Calculations of 4-proton shifts in 1-H 3,5-unsymmetrically disubstituted pyrazoles readily distinguish tautomers. The observed 4-proton resonances for compounds 48, 49, and 51 are in almost exact agreement with those calculated from eq 1 for tautomers R_3R_5 (Table II) and considerably different from the values calculated for the tautomers $R_{(5)}R_{(3)}$. This is in agreement with the conclusions of von Auwers[9] from molar refraction studies who found that compounds 48 and 49 (our tables) existed predominantly as the 3-phenyl tautomers. Although the observed value for compound 42 is in exact agreement with the calculated value for R_3R_5 tautomer (the reverse was proposed in ref 2), this tautomer is not necessarily the predominant form since the difference between calculated values is so small.

Several 1-H pyrazoles exhibited experimental 4-proton chemical shifts that were intermediate between the shifts calculated for the two tautomeric forms. These data are not inconsistent with the existence of cyclic dimers and trimers in solution.[10] If separate tautomers exist in solution, the nmr data indicate that the exchange is extremely rapid.[1]

The major effect of the substituents listed in Table III on the 4-proton chemical shift is inductive in nature rather than being magnetic anisotropic. This is demonstrated by the correlation of the α values with Hammett σ_p values. A plot of the data (Figure 1) shows the phenyl groups to be an exception, which is perhaps not surprising in view of the large magnetic anisotropy of the phenyl ring.

Thus in general the change in chemical shift of the 4-proton reflects the change in the electron density at the 4-position produced by the substituent. Schaefer and Schneider[6] studying benzene have suggested a value of *ca.* 10-ppm shift/unit of π-electron charge and

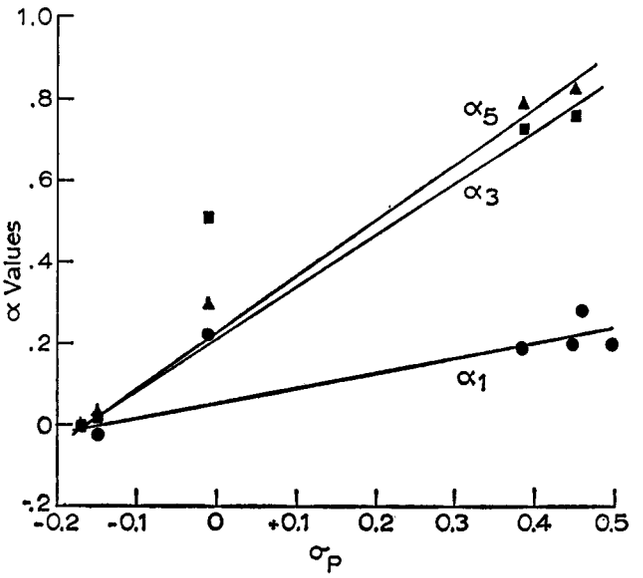


Figure 1.—Correlation of shift parameters with Hammett constants.

calculations of Lynch and Dou[11] find a value of 7.7 ± 0.2 for pyrazole.

Temperature and Concentration Studies.—The chemical shift of the proton on nitrogen varies with concentration owing to changes in hydrogen bonding.[10] The signals for protons on carbon are more constant, but it is important to know the extent of their shift variation with concentration, temperature and solvents. Accordingly, the shift of the 4-proton was studied as a function of temperature using compounds 52 and 25 representing 1-H and 1-substituted pyrazoles. In the region of probe temperature (37°) the temperature dependence of the 4-proton signal for both examples was ~0.0003 ppm/degree. Temperature variation was therefore not further considered in this study.

Chemical shift variation with concentration was investigated for pyrazole and compound 26, representing 1-H and 1-phenylpyrazoles. The studies demonstrated that the use of eq 1 for substituted pyrazoles requires that measurements be made at or below 5% concentration or that concentration dependence be otherwise taken into account. For a limited number of additional pyrazoles studied, the shift value for the 4-proton from 5% concentration to infinite dilution was 0.01 ppm measured in deuteriochloroform.[12]

The 4-proton signal of pyrazoles at 5% concentration occurred consistently at lower field in deuteriochloroform than in carbon tetrachloride by 0.13 ± 0.01 ppm.

Phenyl Resonance.—The phenylpyrazoles of this study fall into two groups, those with essentially singlet phenyl peaks and those with multiplet phenyl resonances. A summary of these data is given in Table IV. In the examples where the phenyl resonance occurs as a multiplet, the *ortho* protons are deshielded about 0.4 ppm, compared with the *meta* and *para* protons that are not significantly different from benzene. Inspection of Table IV reveals that a phenyl group attached to a nitrogen or carbon atom of pyrazole has a multiplet

(9) K. von Auwers, *Ann.*, **508**, 51 (1934).

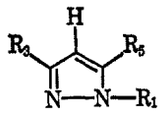
(10) V. F. Bystov, I. I. Grandberg, and G. I. Scharova, *Opt. Spectry. (USSR)*, **17**, 31 (1964).

(11) B. M. Lynch and H. J. M. Dou, *Chem. Commun.*, in press. The authors are grateful to Professor Lynch for providing this information prior to its publication.

(12) Habraken and Moore[2] in a similar study found that the shift variation of protons on carbon for pyrazoles varied no more than ±1 cps. over a fourfold concentration range.

TABLE I

CHEMICAL SHIFTS[a] OF 1-SUBSTITUTED PYRAZOLES IN DEUTERIOCHLOROFORM



Compd	R_1	δ_1, ppm	R_3	δ_3, ppm	δ_4, ppm Obsd	δ_4, ppm Calcd[b]	R_5	δ_5, ppm
1	CH_3	3.69	CH_3	2.20	5.79	5.79	CH_3	2.20
2	CH_3	3.63	CH_3	2.28	6.01	6.02	H	7.26
3	CH_3	3.83	CH_3	2.30	6.09	6.09	C_6H_5	7.43
4	CH_3	4.10	CH_3	2.26	6.58	6.58	CO_2CH_3	3.86
5	CH_3	4.13	CH_3	2.27	6.61	6.62	$CO_2C_2H_5$	~4.32 ~1.36
6	CH_3	4.13	CH_3	2.29	6.78	6.74	CO_2H	...
7	CH_3	3.80	H	7.31	5.99	6.00	CH_3	2.30
8	CH_3	3.80	C_6H_5	7.78 7.37	6.30	6.30	CH_3	2.30
9	CH_3	3.86 or 3.83	CO_2CH_3	3.83 or 3.86	6.53	6.52	CH_3	2.30
10	CH_3	3.85	$CO_2C_2H_5$	~4.36 ~1.36	6.55	6.55	CH_3	2.30
11	CH_3	3.89	CO_2H	~10.9	6.63	6.61	CH_3	2.31
12	CH_3	3.88	H	7.33	6.23	6.23	H	7.55
13	CH_3	4.17	C_6H_5	7.82 7.40	7.09	7.09	CO_2CH_3	3.86
14	CH_3	4.19	C_6H_5	7.83 7.45	7.11	7.13	$CO_2C_2H_5$	~4.00 ~1.37
15	CH_3	4.22	C_6H_5	7.83 7.42	7.13	7.14	$CO_2C_3H_7$ (n)	~4.27 ~1.82 ~1.03
16	CH_3	4.26	C_6H_5	7.82 7.37	7.25	7.25	CO_2H	~10.7
17	CH_3	3.63	C_6H_5	7.7 7.3	5.82	...	NH_2	~3.6
18[c]	CH_3	~4.2	CO_2CH_3	~3.9	6.85	6.82	C_6H_5	7.45
19	CH_3	3.91	$CO_2C_2H_5$	~4.00 ~1.37	6.84	6.85	C_6H_5	7.44
20	CH_3	3.94	$CO_2C_3H_7$ (n)	~4.31 ~1.82 ~1.03	6.85	6.86	C_6H_5	7.50
21	CH_3	4.00	CO_2H	~11.6	6.93	6.91	C_6H_5	7.50
22	C_2H_5	4.40 1.37	$CO_2C_2H_5$	~4.23 ~1.37	6.82	6.82	C_6H_5	7.40
23	C_2H_5	4.62 1.45	C_6H_5	7.82 7.33	7.12	7.11	$CO_2C_2H_5$	~4.30 ~1.33
24	C_2H_5	4.68 1.50	C_6H_5	7.82 7.40	7.25	7.23	CO_2H	~11.5
25	C_6H_5	7.39	CH_3	2.27	6.01	6.01	CH_3	2.30
26[d]	C_6H_5	7.7 7.2	CH_3	2.35	6.23	6.24	H	7.78
27	C_6H_5	7.43	H	7.56	6.19	6.22	CH_3	2.34
28	C_6H_5	7.42	CH_3	2.36	6.87	6.96	CO_2H	...
29	C_6H_5	7.46	CO_2H	...	6.80	6.83	CH_3	2.33
30[d]	C_6H_5	7.6 7.2	H	7.74	6.45	6.45	H	7.94
31	$CO_2C_2H_5$	4.48 1.44	CH_3	2.27	5.99	5.99	CH_3	2.53
32	$CO_2C_2H_5$	4.54 1.46	H	7.77	6.44	6.43	H	8.18
33	CH_2CO_2-C_2H_5	4.76 4.23 1.25	CH_3	2.20	5.84	5.87	CH_3	2.24
34	CH_2CO_2-C_2H_5	4.90 4.22 1.25	H	7.47	6.31	6.31	H	7.54
35	CON-HCH_3	7.3 2.92	CH_3	2.18	5.88	5.88	CH_3	2.55
36	$COCH_3$	2.64	CH_3	2.22	5.96	5.98	CH_3	2.52
37	$COCH_3$	2.70	H	7.71	6.44	6.42	H	8.25

TABLE I (*continued*)

Compd	R_1	δ_1, ppm	R_3	δ_3, ppm	δ_4, ppm Obsd	δ_4, ppm Calcd[b]	R_5	δ_5, ppm
38	COC_6H_5	8.03 7.54	CH_3	2.24	6.07	6.07	CH_3	2.64
39	COC_6H_5	8.19 7.54	H	7.81	6.49	6.51	H	8.46
40	CH_2- C_6H_5	5.17 7.17	H	7.25	6.17	...	H	7.50

[a] In Tables I and II multiplet phenyl resonances reported to 0.01 are accurate to ±0.03 ppm, those reported to 0.1 ppm are less certain, owing to multiplet broadness. The 4-proton shifts are accurate to ±0.01 ppm, as are all other shifts except those prefaced ∽, which were not side banded. [b] Calculated using eq 1. [c] Compound 18 was obtained as a very minor component from the preparation of 13; its methyl resonances are obscured by the methyl signals of 13. [d] The 4- and 5-absorptions were identified by decoupling experiments.

TABLE II
CHEMICAL SHIFTS OF 1-H PYRAZOLES IN DEUTERIOCHLOROFORM

Compd	δ_1,[a] ppm	$R_{3(5)}$	δ, ppm	$R_{5(3)}$	δ, ppm	δ_4, ppm Obsd	δ_4, ppm Calcd[b]	δ_4, ppm Calcd[c]
41	...	CH_3	2.27	CH_3	2.27	5.82	5.82	5.82
42	...	CH_3	2.32	H	7.47	6.05	6.05	6.03
43	13.1	CH_3	2.38	Cl	...	5.97	...	...
44	...	CH_3	2.34	CO_2CH_3	3.87	6.55	6.61	6.55
45	13.2	CH_3	2.37	$CO_2C_2H_5$	∼4.20 ∼1.30	6.56	6.65	6.58
46	9.9	C_2H_5	2.67 1.25	C_2H_5	2.67 1.25	5.86	5.86	5.86
47	...	H	7.65	H	7.65	6.36	6.26	6.26
48	13.8	C_6H_5	∼7.77 ∼7.3	H	∼7.52	∼6.53	6.56	6.33
49	11.2	C_6H_5	7.73 7.35	CH_3	2.25	6.32	6.33	6.12
50	10.3	C_6H_5	7.70 7.37	C_6H_5	7.70	6.79	6.63	6.63
51	14.0	C_6H_5	7.78 7.42	CO_2CH_3	3.94	7.12	7.12	6.85
52	13.5	C_6H_5	7.73 7.37	$CO_2C_2H_5$	∼4.15 ∼1.15	6.93	7.16	6.88
53	13.5	C_6H_5	7.73 7.37	$CO_2C_3H_7$ (*n*)	4.08 1.59 0.87	6.97	7.17	6.89
54	...	C_6H_5	7.6 7.2	NH_2	∼5.1	5.94	...	...

[a] The shift of δ_1 varied with concentration and the value when reported, is not necessarily the maximum value. [b] Calculated using eq 1 as tautomer R_3R_5. [c] Calculated using eq 1 as tautomer $R_{(5)}R_{(3)}$.

TABLE III
ADDITIVE PARAMETERS α (PARTS PER MILLION) FOR 4-PROTON CHEMICAL SHIFTS AND HAMMETT *para*-SUBSTITUENT PARAMETERS (σ_p)

Substituent	α_1	α_3	α_5	σ_p[a]
CH_3	0	0	0	−0.170
C_2H_5	−0.02	0.02	0.02	−0.151
H	0.03	0.21	0.23	
C_6H_5	0.22	0.51	0.30	−0.01
CO_2CH_3	(0.19)[b]	0.73	0.79	+0.385
$CO_2C_2H_5$	0.20	0.76	0.83	+0.45
$CO_2C_3H_7$ (*n*)	(0.20)[b]	0.77	0.84	
CO_2H	...	0.82	0.95	+0.406
$CH_2CO_2C_2H_5$	0.08	...	...	
$CONHCH_3$	0.09	...	...	
$COCH_3$	0.19	...	...	+0.502
COC_6H_5	0.28	...	...	+0.459
m-$NO_2C_6H_4$[c]	0.28	...	...	
m-$NH_2C_6H_4$[c]	−0.05	...	...	

[a] D. H. McDaniel and H. C. Brown, *J. Org. Chem.*, **23**, 420 (1958). [b] Estimated from α_3 and α_5 values. [c] Value was calculated from the data of Finar and Mooney.[3]

resonance, unless there is a substituent α to it, under which condition the phenyl resonance is a singlet. The phenyl singlet resonances have the same chemical shift whether attached to the nitrogen or a carbon of the pyrazole ring. *meta*- and *para*-phenyl resonances are also essentially independent of the point of attachment of the phenyl to the pyrazole ring.

It is apparent from these observations that inductive and resonance electron-withdrawal effects cannot be responsible for the selective paramagnetic shift of the *ortho* protons where multiplet phenyl resonances occur. This *ortho*-shift phenomenon must, therefore, be attributed to the magnetic anisotropy of the neighboring pyrazole ring as suggested by Lynch and Hung.[8] When multiplet resonances occur, the *ortho*-phenyl protons reside preferentially near the plane of the pyrazole ring and are shifted downfield by the magnetic field of the pyrazole ring current. The effect of substituents on the pyrazole ring α to the point of phenyl attachment is to reduce the coplanarity of the aromatic rings and place the *ortho*-phenyl protons above the plane of the pyrazole ring. The time-averaged magnetic field on the phenyl protons due to the pyrazole ring is then essentially 0, and a singlet phenyl resonance occurs.

To assess the effect of two α-pyrazole protons on the phenyl spectrum, the nmr spectra of 4-phenylpyrazole and 1-methyl-4-phenylpyrazole were determined. Un-

TABLE IV

PHENYL PROTON CHEMICAL SHIFTS (δ) OF PHENYLPYRAZOLES MEASURED IN DEUTERIOCHLOROFORM

Compd class	Singlet, δ, ppm (all protons)	Multiplet, δ, ppm		
		ortho	*meta, para*	$\delta_o - \delta_{m,p}$
1-Phenyl (5-position substituted)	7.41 ± 0.02[a]	...	...	...
1-Phenyl (5-position *not* substituted)	...	7.7–7.8	7.2	0.5
5-Phenyl (N–R)	7.44 ± 0.03[a]	...	...	...
3-Phenyl (N–R)	...	7.82 ± 0.01	7.39 ± 0.03[b]	0.43 ± 0.04
3(5)-Phenyl (N–H)	...	7.73 ± 0.02	7.37 ± 0.02[b]	0.36 ± 0.01

[a] These values are not significantly different; average δ = 7.43 ± 0.03 ppm. [b] Observed chemical shift of benzene in deuteriochloroform is 7.37 ppm.

TABLE V

NMR DATA OF 4-PHENYLPYRAZOLES

Compd	Solvent	Phenyl multiplet			Ring protons		1-Methyl
		ortho	*meta, para*	$\delta_o - \delta_{m,p}$	3	5	
4-Phenylpyrazole[a]	$CDCl_3$[b]	...	...	...	...	...	...
4-Phenylpyrazole	DMSO-d_6	7.58	7.29	0.29	8.00	8.00	...
1-Methyl-4-phenylpyrazole[a]	$CDCl_3$[c]	7.40	7.27	0.13	7.58	7.75	3.92
1-Methyl-4-phenylpyrazole	DMSO-d_6	7.57	7.30	0.27	7.88	8.08	3.87

[a] Prepared according to the method of E. Klingsberg, *J. Am. Chem. Soc.*, **83**, 2934 (1961). [b] Insoluble. [c] Measured at 4% w/v.

fortunately 4-phenylpyrazole was highly insoluble in chloroform but was soluble in dimethyl sulfoxide; thus both compounds were measured in that solvent. The nmr data for these two compounds are shown in Table V. The *ortho*-phenyl protons are separated from the *meta–para* protons by 0.13 ppm measured in deuteriochloroform. Thus, two α-pyrazole protons are somewhat less effective in reducing coplanarity than is a single α-methyl substituent.

Coupling Constants.—Coupling constants for pyrazole ring protons were determined where possible (Table VI). For 1-carbonyl- and 1-phenylpyrazoles, J_{45} was

TABLE VI

RING PROTON COUPLING CONSTANTS (CYCLES PER SECOND) OF PYRAZOLES[a] MEASURED IN DEUTERIOCHLOROFORM

Compd	N Substituent	J_{34}	J_{45}	J_{35}	3(5) subst.	J_{34} (J_{45})
31	$CO_2C_2H_5$	1.3	2.8	0.6		
38	COC_6H_5	1.5	3.0	*b*		
37[c]	$COCH_3$	1.5	2.9	0.6		
26	C_6H_5	...	2.56[d]	...		
27	C_6H_5	1.5	...	...		
30	C_6H_5	1.9	2.5	0.7		
33	$CH_2CO_2C_2H_5$	2.0	2.5	~1.0		
40	$CH_2C_6H_5$	1.92	2.35	0.6		
12	CH_3	~2.0	~2.2	~0.7		
2	CH_3	...	2.20	...		
7	CH_3	1.9	...	...		
42	H				CH_3	~2.0
48	H				C_6H_5	~2.5

[a] For compounds in this table (except 48) only hydrogen or a methyl group appears at the 3- or 5-position. [b] Not determined. [c] See ref 1. [d] Value measured in carbon tetrachloride, J_{45} = 2.27 cps.

numerially much larger than J_{34}. On the basis of this observation for 1-acylpyrazoles, Williams[1] confirmed von Auwers' classical work concerning isomer assignments of pyrazoles. The difference decreased for 1-alkyl derivatives, although for all of the compounds studied J_{45} remained larger than J_{34}. For 1-H pyrazoles, of course, the distinction no longer exists.

Preparation of Materials.—All of the compounds listed in Tables I and II except numbers 15, 17, 20, 33, and 53 are reported in the literature.

The esters 44, 45, 51, and 52 were prepared from the appropriate acylpyruvate and hydrazine according to the method of Bulow[13] and illustrated below for the preparation of compound 53. Use of methyl hydrazine in place of hydrazine gave the esters 4, 5, 9, 10, 13, 14, 18, and 19 as described below for the preparation of compounds 15 and 20. The use of phenyl hydrazine in place of hydrazine yielded esters that were used as intermediates and are not included in Table I. Alkylation of compound 52 using sodium ethoxide and ethyl iodide according to the method of von Auwers[14] gave compounds 22 and 23. Hydrolysis of the above esters using 5% sodium hydroxide in 75% methanol–water mixture yielded the acids 6, 11, 16, 21, 24, 28, and 29.

The 3(5)-alkyl-5(3)-aryl compounds 1, 3, 8, 25, 41, 46, 48, 49, and 50 were prepared from the appropriate 1,3-dicarbonyl compound and corresponding hydrazine according to the general method of von Auwers.[15]

Compounds 2 and 7 were prepared[16] by the thermal decarboxylation of compounds 6 and 11. The decarboxylation of the carboxylic acids 28 and 29 according to the procedure of Claisen[17] gave compounds 26 and 27.

Compounds 12 and 40 were prepared by the alkylation of pyrazole.[18] Compound 30 was prepared according to the method of Finar and Hurlock.[19] Compounds 31, 37, and 39 were prepared according to Knorr.[20] Compounds 32,[21] 36,[22] and 38[23] were prepared according to reported methods. Compound 42 was prepared by the thermal decarboxylation of 3(5)-methyl-5(3)-pyrazolecarboxylic acid and it had the same

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physical constants as reported by Knorr.[24] Compound 43 was prepared according to Michaelis.[25]

The preparation of compounds 15, 17, 20, 33, 34, 35, 53, and 54 are given below.

n-Propyl Benzoylpyruvate and Hydrazines. A.—A solution of equimolar quantities of *n*-propyl benzoylpyruvate[26] (mp 63–64°) and hydrazine hydrate in *n*-propyl alcohol was heated on a steam bath for 0.5 hr to give 3(5)-phenyl-5(3)-carbo-*n*-propoxypyrazole (53), mp 117–118°.

Anal. Calcd for $C_{13}H_{14}N_2O_2$: C, 67.81; H, 6.13; N, 12.17. Found: C, 67.83; H, 6.16; N, 12.00.

B.—A solution of equimolar quantities of *n*-propyl benzoylpyruvate and methyl hydrazine in *n*-propyl alcohol was heated on a steam bath for 0.5 hr. The product was distilled by heating under reduced pressure to give 15 and 20 in the ratio of 3:1.

1-Methyl-3-phenyl-5-carbo-*n*-propoxypyrazole (15) boiled at 195° at 10 mm.

Anal. Calcd for $C_{14}H_{16}N_2O_2$: C, 68.83; H, 6.60; N, 11.47. Found: C, 68.49; H, 6.52; N, 11.30.

1-Methyl-5-phenyl-3-carbo-*n*-propoxypyrazole (20) boiled at 205° at 10 mm.

Anal. Found: C, 68.83; H, 6.90; N, 11.22.

Ethyl 1-(3,5-Dimethylpyrazolyl)acetate (Compound 33).—A solution of equimolar quantities of 3,5-dimethylpyrazole, sodium ethoxide and ethyl bromoacetate in ethanol was treated according to the method used by Jones[27] for the preparation of compound 34. The yield of 33, bp 135° at 15 mm, was very low.

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5-Amino-1-methyl-3-phenylpyrazole (Compound 17).—Equimolar quantities of benzoyl acetonitrile and methyl hydrazine dissolved in ethanol was heated under reflux for 1 hr. The product was recrystallized from benzene–methylcyclohexane mixture, mp 129–131°. From the nmr data the material was assigned structure 17.

Anal. Calcd for $C_{10}H_{11}N_3$: N, 24.26. Found: N, 24.03.

In a similar procedure benzoyl acetonitrile and hydrazine hydrate gave 3(5)-amino-5(3)-phenylpyrazole (54), mp 123–125° (lit.[28] mp 125°).

1-Methylcarbamoyl-3,5-dimethylpyrazole (Compound 35).—A solution of 0.1 mole of 3,5-dimethylpyrazole, 0.1 mole of methyl isocyanate, and 0.5 g of triethylenediamine dissolved in 100 ml of dry dioxane was allowed to stand at room temperature for 4 days. The solvent was removed by evaporation and the residue was recrystallized from petroleum ether (bp 60–70°) to give a nearly quantitative yield of 35, mp 75° (lit.[29] mp 71°).

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Synthesis of the 1,8-Naphthalic Anhydride Obtained by Degradation of Trimethylherqueinone B[1]

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Starting material for the successful synthesis of 7-methyl-2,3,4,5-tetramethoxy-1,8-naphthalic anhydride (**2**) was 3,4,5-trimethoxybenzoic acid. This acid was converted to its homolog, whose ester (**5**) was condensed with methyl crotonate to give the glutaric acid derivative, **6**. Cyclization of the substituted glutaric acid with polyphosphoric acid yielded the tetralone **7**, which has the oxygen function and the methyl group in the positions required for the synthesis. The route chosen for eventual introduction of carboxyl groups in the *peri* positions involved initial decarboxylation of tetralone **7** to yield 3-methyl-6,7,8-tetramethoxy-1-tetralone (**8**). Dehydrogenation yielded the corresponding naphthol **9**, which was methylated and subjected to reaction with diphenyloxalimide chloride. The resultant acenaphthenequinone, **10**, was readily oxidized with alkaline hydrogen peroxide to yield the desired 1,8-naphthalic anhydride **2**. The synthetic anhydride proved identical with that previously obtained by a degradative sequence from trimethylherqueinone B.

The copper-red pigment from *Penicillium herquei*, first reported by Stodola and co-workers,[2] was subsequently named herqueinone.[3] The herqueinone structure has proved so sensitive to rather deep-seated changes that some aspects of this structure remain uncertain. In contrast, the structure of one of the ethers of herqueinone,[4] designated trimethylherqueinone B, has been established with reasonable firmness. The structure assigned[5] to trimethylherqueinone B is that shown in formula **1**. The alicyclic features of the ring system were established by a combination of chemical and spectroscopic methods, while the structure of the basic naphthalene nucleus was assigned from isolation of the degradation product shown in formula **2**. Since the degradation anhydride was formulated to a major extent on the basis of spectral interpretations, verification by synthesis of this key structure is

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