with those of authentic samples.[5] Compound **2** was identified by comparison of its melting point[4] and infrared[6] and proton nmr[4] spectra with literature data. Compound **3** was characterized by elemental analysis and by comparison of its infrared spectrum with literature data.[6] Characteristic bands for β CH and ring breathing vibrational modes were identified in the 1300–1000 cm^{-1} region, as well as diagnostic substitution pattern bands below 1000 cm^{-1} (Table II) and

TABLE II

PHYSICAL PROPERTIES OF PRODUCTS[a]

Compd	Bp, °C (mm)	Mp, °C	Mp of chloroaurate,[b] °C	Ir,[c] cm^{-1}
1	90–93 (20)		184–185[d]	993, 890, 817, 750
2	115–120 (20)	70.9–71.2[e]	277–278 dec	1022, 998, 875
3	100–102 (17)		197.5–199 dec	1150, 995, 887, 839
4		122.5–123[f]		1140, 1083, 990, 805, 757
5	63–67 (20)			

[a] Compounds **1** and **2** were obtained in >99% purity by a single distillation or by sublimation. Compound **3** required a second distillation of combined fractions of >90% purity to achieve >99% purity. No attempt was made to purify **5** beyond 95% purity. Satisfactory analytical values (±0.3% for C, H, N) were reported for compounds **1**, **2**, and **3**: Ed. [b] Prepared according to procedure of Brown.[2] Compounds **1**, **2**, and **3** did not give picrates. [c] Only those bands pertinent to characterization are given. [d] Lit.[2] 184.2–184.5°. [e] Lit.[4] 69°. [f] Crystallized out of the reaction residues. Lit.[2] 122.3–122.8°.

their characteristic overtone patterns in the 2100–1700-cm^{-1} region. In addition, the splitting patterns in the δ 6.5–8.5 region of the proton nmr spectra of **1**, **2**, and **3** are quite comparable to those of 2,6-lutidine, 2,4,6-trimethylpyridine, and 2,4-lutidine, respectively.

Experimental Section

General.—Melting points (Mel-Temp apparatus) are corrected. Boiling points are uncorrected. The infrared spectra were recorded on a Perkin-Elmer Model 337 spectrophotometer. Nmr spectra were determined in spectrograde carbon tetrachloride using tetramethylsilane as reference and measured with a Varian T60 spectrometer. Both infrared and proton nmr spectra have been subsequently published by the Sadtler Research Laboratories, Inc., for compounds **1**, **2**, and **3**.[7] All distillations were performed on a manually operated, 24-in. Teflon annular spinning-band column (Nester-Faust) at approximately 20-mm pressure, which resolved a persistant foaming problem encountered with other columns. Glpc analysis of reagents, crude reaction mixture, and purified products were performed on a Perkin-Elmer Model 800 instrument equipped with thermal conductivity and flame ionization detectors. One or both of the following columns were used throughout this work: column A (11 ft × 0.25 in., 20% Siponate Ds-10 on 45–60 mesh Chromosorb W, 5% NaOH, carrier gas flow 60 ml/min) and column B (6 ft × 0.25 in., 15% Carbowax 6000 on 40–60 mesh Chromosorb W, 5% NaOH, carrier gas flow 60 ml/min). Pyridine (Fisher or Baker reagent grade), *tert*-butyllithium, 2 *M* in pentane (Ventron ALFA), and heptane (Phillips pure grade) were all used without further purification. The microanalyses were performed by Crobaugh Laboratories, Cleveland, Ohio, or on a F & M CHN analyzer Model 185.

General Procedures for Alkylation. A. Addition of *tert*-Butyllithium to Pyridine.—Pyridine (15.8 g, 0.20 mol) in 200 ml of heptane was placed in a flask equipped with magnetic or mechanical stirrer, dewar condenser, alcohol thermometer, pressure-compensated addition funnel, CO_2–acetone cooling bath, and provision for introducing dry nitrogen below the surface of the reaction mixture. With thorough flushing with dry nitrogen, the solution was cooled to −75°. The volume of *tert*-butyllithium, 2 *M* in pentane, necessary to provide the desired molar ratio (Table I) of *tert*-butyllithium to pyridine was introduced to the addition funnel by expelling it with dry nitrogen pressure from a glass wash bottle previously filled in a glove bag under dry nitrogen.[8] Addition required 2 hr and stirring at −75° was continued for 1 hr. The mixture was then allowed to warm to room temperature. Under a dry nitrogen stream, the pentane was removed by distillation and the reaction mixture was refluxed for 7 hr. After being cooled to 10°, the reaction was carefully quenched by dropwise addition of water. The aqueous layer was thoroughly extracted with pentane and the combined organic layers were washed once with water and dried ($MgSO_4$). Removal of solvents left a red-brown oil (*ca.* 44 g) which was distilled and analyzed by glpc. Yields are given in Table I and physical properties in Table II.

B. Addition of Pyridine to *tert*-Butyllithium.—The volume of *tert*-butyllithium, 2 *M* in pentane, necessary to provide the desired molar ratio (Table I) of *tert*-butyllithium to pyridine was carefully introduced into the apparatus as described in procedure A. After the mixture was cooled to −75°, pyridine (1.58 g, 0.02 mol) in 50 ml of heptane was added dropwise (45 min) with dry nitrogen flush and the stirring was continued an additional hour. Procedure A was then followed. The resulting oil (*ca.* 5.8 g) was either distilled or allowed to crystallize at room temperature. Filtration and vacuum sublimation gave pure **2**.

Registry No.—**1**, 585-48-8; **2**, 20336-15-6; **2** chloroaurate, 29930-36-7; **3**, 29939-31-9; **3** chloroaurate, 29930-37-8; **5**, 5944-41-2; pyridine, 110-86-1; *tert*-butyllithium, 594-19-4.

Acknowledgments.—The assistance of a number of Hiram College students is appreciated. In particular, early scouting and development were performed by R. Waller, J. Wansack, W. Toth, C. Brininger, and G. Luteri. The writers also thank Professor Peter Kovacic for discussions and suggestions. Financial support by the Hiram College Faculty Research Assistance Fund is gratefully acknowledged.

(5) We are indebted to Professor H. C. Brown for providing authentic samples of **1** and **5**.

(6) A. R. Katritzky and A. P. Ambler in "Physical Methods in Heterocyclic Chemistry," Vol. II, A. R. Katritzky, Ed., Academic Press, New York, N. Y., 1963, Chapter 10, pp 276–279.

(7) "Sadtler Standard Spectra" references, compound (ir spectrum no, nmr spectrum no): **1** (702339, 9708M); **2** (702340, 9709M); **3** (708021, 10509M).

(8) For an alternative procedure, see S. Farber and R. T. Conley, *J. Chem. Educ.*, **45**, 704 (1968).

New General Methods for the Substitution of 5-Chloropyrazoles. The Synthesis of 1,3-Dialkyl-5-chloropyrazol-4-yl Aryl Ketones and New 1,3-Dialkyl-2-pyrazolin-5-ones

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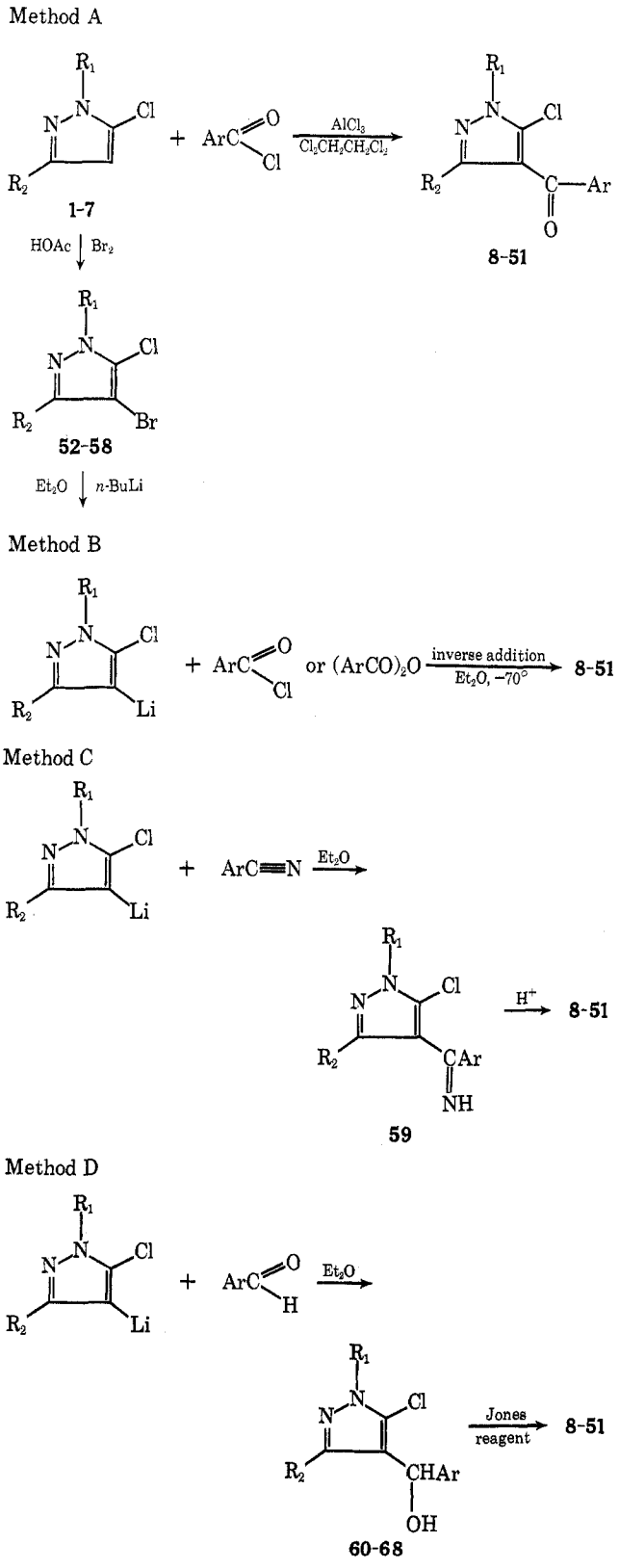
Received February 3, 1971

In connection with other synthetic studies underway in this laboratory, we required a large variety of the previously unknown 1,3-dialkyl-5-chloropyrazol-4-yl aryl ketones. Based on the ready availability of

SCHEME I

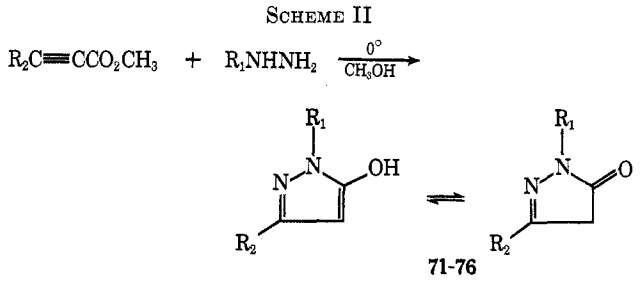


1,3-dialkyl-5-chloropyrazoles[1-4] and aroyl chlorides, the Friedel–Crafts reaction between these components was reinvestigated. Michaelis and Rojahn[5-7] had earlier reported the failure of this reaction with substituted pyrazoles of this type using relatively mild conditions. We have found that the synthesis can be performed easily in high yield in refluxing *s*-tetrachloroethane (Scheme I).

The Friedel–Crafts reaction would be expected to fail when the aroyl chloride is susceptible to the action of aluminum chloride or self aroylation. Therefore, a second approach was developed. Hüttel and Schön[8] have shown that treatment of 4-bromo-1-methylpyrazole with phenyllithium results in a mixture of 4-lithio-1-methylpyrazole and 4-bromo-5-lithio-1-methylpyrazole. We have found that the easily prepared 1,3-dialkyl-4-bromo-5-chloropyrazoles[1] react with *n*-butyllithium resulting in reasonably stable 1,3-dialkyl-5-chloro-4-lithiopyrazoles. These reagents undergo the usual reactions of aryllithiums[9] including those leading to the desired ketones. While extra steps are involved in this sequence, the reactions are simple to perform, result in high yields, and constitute a general approach to the desired compounds. As demonstrations of the versatility of the second approach, a few examples of alkyl, cycloalkyl, and 1- or 3-phenyl-substituted pyrazolyl ketones were prepared and are included with the other new ketones in Table I.

A variety of 1,3-dialkyl-2-pyrazolin-5-ones was also needed. As stated by Büchi, Ursprung, and Lauener,[10] the classical 2-pyrazolin-5-one synthesis of Knorr[11] gives very poor yields when alkylhydrazines other than methylhydrazine are condensed with ethyl acetoacetate. These workers condensed alkyl bromides or iodides in a bomb with 3-methyl-2-pyrazolin-5-one to produce 1-alkyl-3-methyl-2-pyrazolin-5-ones in yields of 10–44% depending on the alkyl group. A large number of workers have condensed acetylenic esters with hydrazine and phenylhydrazine but little or nothing has been done with alkylhydrazines.[12,13] With the commercial availability of methylhydrazine and other alkylhydrazines available by alkylation and other procedures,[14] we investigated the reaction of a number of methyl esters of alkylacetylenecarboxylic acids with alkylhydrazines. Shown in Scheme II, this appears to be

SCHEME II



(1) K. von Auwers and F. Niemeyer, *J. Prakt. Chem.*, **110**, 153 (1925).
(2) L. C. Behr, R. Fusco, and C. H. Jarboe in "Pyrazoles, Pyrazolines, Pyrazolidines, Indazoles and Condensed Rings," Interscience, New York, N. Y., 1967, pp 87, 88.
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(7) Reference 3, p 100.
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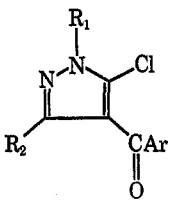
(12) Reference 4, p 15.
(13) Reference 3, p 120.
(14) P. A. Smith in "The Chemistry of Open-Chain Organic Nitrogen Compounds," Vol. II, W. A. Benjamin, Chapter 9, pp 139–144, New York, N. Y., 1966, and references therein.

TABLE I



Compd no.	Registry no.	R_1	R_2	Ar	Method[a]	Yield,[b] %	Mp (recrystn solvent[c]) or bp (mm),[d] °C
8	29938-70-3	CH_3	CH_3	C_6H_5	A	79	49–52 (J),
					D	88	128–130 (0.2)
9	29938-71-4	CH_3	CH_3	2-FC_6H_4	A	82	73–75 (F)
10	29938-72-5	CH_3	CH_3	3-FC_6H_4	A	52	44–46 (J),
							156–160 (0.5)
11	29938-73-6	CH_3	CH_3	4-FC_6H_4	A	55	158–160 (0.3)
12	29938-74-7	CH_3	CH_3	2-ClC_6H_4	A	71	70–72 (J)
13	29938-75-8	CH_3	CH_3	3-ClC_6H_4	A	77	81–83 (L)
14	30093-77-7	CH_3	CH_3	4-ClC_6H_4	A	78	65–68 (M)
15	29938-76-9	CH_3	CH_3	2-BrC_6H_4	B	70	135–137 (0.15)
16	30093-78-8	CH_3	CH_3	2-$CF_3C_6H_4$	B	75	77–79 (J),
							105–107 (0.15)
17	29938-77-0	CH_3	CH_3	3-$CF_3C_6H_4$	B	70	64–66 (J)
18	29938-78-1	CH_3	CH_3	2-$CH_3OC_6H_4$	B	62	86–88 (J),
							131–133 (0.15)
19	29938-79-2	CH_3	CH_3	4-$CH_3OC_6H_4$	C	75	128–130 (G)
20	29938-80-5	CH_3	CH_3	2-$CH_3C_6H_4$	B′	70	51–53 (J),
							105–106 (0.15)
21	30093-79-9	CH_3	CH_3	3-$CH_3C_6H_4$	A	76	60–62 (J),
							175–180 (0.5)
22	29938-81-6	CH_3	CH_3	4-$CH_3C_6H_4$	A	54	160–170 (0.3)
23	29938-82-7	CH_3	CH_3	2-Cl,3-$CH_3OC_6H_3$	D	75	108–109 (H)
24	29938-83-8	CH_3	CH_3	C_6H_{11}	B	67	78–80 (J)
25	29938-84-9	C_2H_5	CH_3	C_6H_{11}	B	72	110–111 (0.15)
26	29938-85-0	CH_3	CH_3	2-C_4H_3S	B	71	97–99 (J)
					D	85	
27	29938-86-1	CH_3	CH_3	3-C_4H_3S	D	84	86–88 (J)
28	29938-87-2	CH_3	CH_3	2,3-$(CH_3O)_2C_6H_3$	B	65	75–76 (J),
							146–148 (0.025)
29	29938-88-3	CH_3	CH_3	2,6-$(CH_3O)_2C_6H_3$	B	60	158–160 (I)
30	29938-89-4	CH_3	CH_3	2-(HOOC)C_6H_4	B′	31	150–152 (H)
31	29938-90-7	CH_3	CH_3	2-(5-BrC_4H_2S)	D	71	103–105 (J)
32	29938-91-8	CH_3	C_2H_5	2-ClC_6H_4	A	64	77–79 (J)
33	30093-80-2	CH_3	C_3H_7	2-ClC_6H_4	A	90	180–182 (0.2)
34	30093-81-3	CH_3	*i*-C_3H_7	2-ClC_6H_4	A	70	148–150 (0.2)
35	29938-92-9	CH_3	C_4H_9	2-ClC_6H_4	A	90	188–190 (0.2)
36	29938-93-0	C_2H_5	CH_3	2-ClC_6H_4	A	68	62–64 (K)
37	29938-94-1	C_3H_7	CH_3	2-$CH_3OC_6H_4$	B	60	153–155 (0.2)
38	29938-95-2	C_3H_7	CH_3	2-$CF_3C_6H_4$	B	78	123–125 (0.2)
39	29938-96-3	C_3H_7	C_2H_5	2-ClC_6H_4	A	94	138–140 (0.15)
40	29938-97-4	C_6H_{11}	CH_3	2-ClC_6H_4	A	90	115–117 (J)
41	29938-98-5	CH_3	C_2H_5	3-FC_6H_4	A	46	160–165 (0.3)
42	30093-82-4	CH_3	C_2H_5	C_6H_5	A	90	55–57 (J)
43	29938-99-6	CH_3	CH_3	3,5-$(CH_3O)_2C_6H_3$	C	72	88–90 (I)
44	29939-00-2	C_6H_{11}	CH_3	2-C_4H_3S	D	70[e,f]	148–150 (0.15)
45	30093-83-5	CH_3	C_3H_7	2-C_4H_3S	D	74	108–110 (0.15)
46	29939-01-3	CH_3	*i*-C_3H_7	2-C_4H_3S	D	79[e]	128–130 (0.4)
47	29939-02-4	CH_3	C_4H_9	2-C_4H_3S	D	80[e]	128–130 (0.17)
48	30115-50-5	C_6H_5	CH_3	2-C_4H_3S	D	88	84–86 (J)
49	29939-03-5	CH_3	C_6H_5	2-C_4H_3S	D	80	181–183 (J)
50	29939-04-6	C_6H_5	CH_3	2-$CH_3OC_6H_4$	B	60	107–109 (J)
51	29939-05-7	CH_3	C_6H_5	2-$CH_3OC_6H_4$	D	80	112–114 (J)

[a] The methods are those represented by capital letters A–D in Scheme I. [b] The yields on the products using methods C and D are calculated from the amount of 1,3-dialkyl-4-bromo-5-chloropyrazole charged. [c] Recrystallization solvents are represented by the following capital letters: F, ethyl acetate–petroleum ether; G, 95% ethanol; H, anhydrous diethyl ether; I, ethanol; J, benzene–petroleum ether; K, hexane; L, carbon tetrachloride; M, petroleum ether; N, tetrahydrofuran–petroleum ether; O, toluene–petroleum ether. [d] Satisfactory analytical values (±0.4% for C, H, and N) were reported for compounds **8–14, 16–19, 21–23, 26–31,** and **38–51**; values within these limits for C and H were reported for the remaining compounds in the table (not analyzed for N). [e] The intermediate alcohols reacted upon attempted distillation and the reactions were repeated and the alcohols oxidized without purification. [f] The parent alcohol of this compound underwent dehydration to the ether upon attempted distillation. The resulting 4,4′-(oxydi-2-thenylidene)bis[5-chloro-1-cyclohexyl-3-methylpyrazole] had mp 223–225° (purified by boiling with acetone and filtering). *Anal.* Calcd for $C_{30}H_{36}Cl_2N_4OS_2$: C, 59.68; H, 6.02; N, 9.27. Found: C, 59.69; H, 6.08; N, 9.30.

a simple, general, high-yield procedure for the preparation of 1,3-dialkyl-2-pyrazolin-5-ones. This route also avoids the difficulty involved in a crossed Claisen reaction to prepare ω-alkylacetoacetic acid esters.

In summary (a) 1,3-dialkyl-5-chloropyrazol-4-yl aryl ketones can be prepared using the Friedel–Crafts reaction between 1,3-dialkyl-5-chloropyrazoles and aroyl chlorides; (b) 5-chloro-1,3-disubstituted 4-lithiopyrazoles can be prepared and used to synthesize these ketones directly or indirectly; and (c) 1,3-dialkyl-2-pyrazolin-5-ones can be synthesized in high yield by the reaction of alkylhydrazines with the methyl ester of an alkylacetylenecarboxylic acid.

Experimental Section[15]

The aroyl chlorides were commercially available or were prepared from the commercially available aromatic carboxylic acids using thionyl chloride and distilled before use. The arylcarbonitriles were commercially available as were the arylcarboxaldehydes with the following exceptions: (a) 2-chloro-3-methoxybenzaldehyde, mp 56–57°, was prepared by a modification of the method of Hodgson and Beard;[16,17] and (b) 3-thiophenecarboxaldehyde, bp 86–88° (20 mm), was prepared as described by Gronowitz.[18] 1,3-Dimethyl-2-pyrazolin-5-one was prepared from ethyl acetoacetate as described by Knorr,[11] mp 117–118° (lit. mp 117°). 1-Ethyl-3-methyl-2-pyrazolin-5-one was prepared by the method of Büchi, Ursprung, and Lauener,[10] mp 108–109° (lit. 109°). 1-Cyclohexyl-3-methyl-2-pyrazolin-5-one was prepared by hydrogenation of 3-methyl-1-phenyl-2-pyrazolin-5-one as described by Schuster and Krzikalla,[19] mp 149–151° (lit. mp 139°). 5-Chloro-1,3-dimethylpyrazole, bp 156–157° (lit. bp 157°), 5-chloro-1-ethyl-3-methylpyrazole, bp 166–167° (lit. bp 167°), and 4-bromo-5-chloro-1,3-dimethylpyrazole, mp 35–36°, bp 85–87° (10 mm) (lit. mp 35–36°), were prepared as described by von Auwers and Niemeyer.[1] Because of the importance of this type of intermediate to our synthetic purposes, a brief description of the preparation of this compound has been included in the Experimental Section. 4-Bromo-5-chloro-1-methyl-3-phenylpyrazole, mp 65–66°, bp 95–97° (0.2 mm) (lit. mp 65°), and 4-bromo-5-chloro-3-methyl-1-phenylpyrazole, mp 56–57°, bp 93–95° (0.2 mm) (lit. mp 56°), were prepared as described by Michaelis with Dorn[20] and Pasternach,[21] respectively. The α-acetylenic acids and their methyl esters were prepared as described by Zoss and Hennion.[22] Methylhydrazine was commercially available (Olin). *n*-Propylhydrazine, bp 118–120° (lit. bp 119°),[23] was prepared by alkylation and continuous extraction with diethyl ether.

Typical Preparation of 1,3-Dialkyl-4-aroyl-5-chloropyrazoles Using Friedel–Crafts Conditions. Method A. 5-Chloro-1,3-dimethylpyrazol-4-yl Phenyl Ketone (8).—5-Chloro-1,3-dimethylpyrazole,[1] 39 g (0.3 mol), was added slowly to a suspension of 40 g (0.3 mol) of anhydrous aluminum chloride in 200 ml of *s*-tetrachloroethane. Benzoyl chloride, 46 g (0.33 mol), was added in one portion and the mixture was stirred and refluxed 18 hr. The reaction mixture was poured into 200 ml of ice–water and 50 ml of concentrated hydrochloric acid. The organic layer was separated and stirred with 200 ml of 4 *N* sodium hydroxide for 1 hr. The organic layer was separated, dried ($MgSO_4$), and distilled *in vacuo* to yield **8**: 57 g (79%); bp 128–130° (0.2 mm); mp 49–52°; nmr ($CDCl_3$) 7.2–7.84 (5 H, aromatic CH), 3.77 (3 H, singlet, 1-CH_3), 2.26 (3 H, singlet, 3-CH_3); ir 1655 cm^{-1} (ketone C=O).

Typical Preparation of 1,3-Dialkyl-5-chloro-4-lithiopyrazoles. 5-Chloro-1,3-dimethyl-4-lithiopyrazole.—4-Bromo-5-chloro-1,3-dimethylpyrazole[1] (**52**), 21 g (0.1 mol), was dissolved in 400 ml of anhydrous diethyl ether under N_2. The solution was maintained between 20 and 25° by cooling and a solution of commercial *n*-butyllithium, 60 ml (0.1 mol), was added rapidly with stirring. The lithio reagent was present as a white precipitate and could be used in any typical aryllithium reaction. No attempt was made to isolate these compounds.

Typical Preparation of 1,3-Dialkyl-4-aroyl-5-chloropyrazoles Using the Lithio Reagent. Method B. Addition to an Aroyl Chloride. 5-Chloro-1,3-dimethylpyrazol-4-yl *o*-Methoxyphenyl Ketone (18).—5-Chloro-1,3-dimethyl-4-lithiopyrazole (0.1 mol), prepared as in the example, was poured into a −70° solution of 34 g (0.2 mol) of *o*-anisoyl chloride with stirring. The flask in which the lithio reagent was prepared was washed into the second solution with two 100-ml portions of anhydrous diethyl ether. The reaction mixture was allowed to warm to room temperature and 200 ml of methanol was added, followed by 500 ml of 0.5 *N* sodium hydroxide. The mixture was stirred overnight to complete the esterification of the excess aroyl chloride. The organic layer was separated, washed with water, dried ($MgSO_4$), concentrated, and distilled *in vacuo* to yield **18**: 16.5 g (62%); bp 131–133° (0.15 mm); mp 76–78; nmr ($CDCl_3$) δ TMS 6.8–7.5 (4 H, aromatic CH), 3.76 (6 H, singlet, 1-CH_3 and *o*-CH_3O), 2.3 (3 H, singlet, 3-CH_3); ir (KBr) 1628 cm^{-1} (ketone C=O). The analysis is in Table I.

Method B′. Addition to an Aryl Anhydride. 5-Chloro-1,3-dimethylpyrazol-4-yl *o*-Tolyl Ketone (20).—5-Chloro-1,3-dimethyl-4-lithiopyrazole, prepared from **52**, 60 g (0.287 mol), was added to a −70° suspension–solution of *o*-toluic anhydride, 127 g (0.5 mol) in 1 l. of anhydrous diethyl ether. The reaction mixture was stirred 1 hr and refluxed 1 hr, and 150 ml of methanol was added. The mixture was refluxed 1 hr, 500 ml of 2 *N* sodium hydroxide was added, and the layers were separated. The organic layer was dried ($MgSO_4$) and evaporated, and the residue distilled *in vacuo* to yield **20**: 44 g (70%); bp 105–107° (0.15 mm); nmr ($CDCl_3$) δ TMS 7.1–7.3 (4 H, aromatic CH), 3.7 (3 H, singlet, 1-CH_3), 2.3 (3 H, singlet, 3-CH_3), 2.2 (3 H, singlet, *o*-CH_3); ir (thin film) 1635 cm^{-1} (ketone C=O). The analysis is in Table I.

Method C. Addition to an Arylcarbonitrile and Hydrolysis of the Imine. 5-Chloro-1,3-dimethylpyrazol-4-yl *p*-Methoxyphenyl Ketone (19).—5-Chloro-1,3-dimethyl-4-lithiopyrazole, prepared from **52**, 58 g (0.28 mol), in 500 ml of anhydrous diethyl ether was treated with a diethyl ether solution of 40 g (0.3 mol) of *p*-anisonitrile. The reaction mixture was stirred and refluxed overnight, cooled, and treated with 300 ml of a saturated solution of ammonium chloride. The mixture was diluted with ethyl acetate, and the organic layer was separated and washed with water. The organic layer was extracted with 350 ml of 3 *N* hydrochloric acid. The acid extract was swiftly made basic with concentrated ammonium hydroxide and extracted with benzene. The benzene solution was dried ($MgSO_4$) and concentrated *in vacuo* to yield 5-chloro-1,3-dimethylpyrazol-4-yl *p*-methoxyphenyl ketone imine **59**: 63 g (85%); mp 94–96° (from diethyl ether–petroleum ether); ir (KBr) 1600 cm^{-1} (C=N).

Anal. Calcd for $C_{13}H_{14}ClN_3O$: C, 59.21; H, 5.35; N, 15.94. Found: C, 59.47; N, 5.49; N, 15.96.

The imine **59** was hydrolyzed to **19** in 90% yield by heating 30 min on the steam bath in 4 *N* hydrochloride acid. The mixture was allowed to cool and the **19** filtered: mp 128–130° (from 95% ethanol); ir (KBr) 1630 cm^{-1} (ketone C=O). The analysis is in Table I.

Method D. Addition to an Arylcarboxaldehyde Followed by Oxidation Using Jones Reagent.[24] 5-Chloro-1,3-dimethylpyrazol-

(15) Melting points (uncorrected) were taken in open capillary tubes in a Thomas-Hoover melting point apparatus. Ir spectra were determined on a Beckman IR-9 instrument and nmr spectra with a Varian A-60 spectrophotometer at ambient temperature (Me_4Si). We are indebted to Mr. C. E. Childs and associate for microanalyses, Mr. W. Pearlman for the catalytic hydrogenations and pressure reactions and to Dr. J. M. Vandenbelt and associates for spectral data,

(16) H. H. Hodgson and H. G. Beard, *J. Chem. Soc.*, 147 (1926).

(17) The chlorination of *m*-hydroxybenzaldehyde was performed between 0 and −30° using tetrahydrofuran as the solvent. The yield and the by-products were the same as those reported by Hodgson and Beard; however, much larger amounts can be chlorinated in a shorter time.

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(19) C. Schuster and H. Krzikalla, *ibid.*, **33**, 180 (1939); U. S. Patent 2,132,193 (1938).

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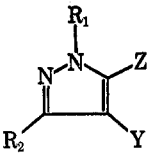
TABLE II



Compd no.	Registry no.	R_1	R_2	Z	Y	Yield, %	Mp (recrystn solvent[d]) or bp (mm),[b] °C
1	29938-63-4	CH_3	C_2H_5	Cl	H	80	82–83 (28)
2	29938-64-5	CH_3	C_3H_7	Cl	H	88	78–79 (10)
3	29938-65-6	CH_3	i-C_3H_7	Cl	H	81	72–74 (10)
4	29938-66-7	CH_3	C_4H_9	Cl	H	85	90–92 (10)
5	29938-67-8	C_3H_7	CH_3	Cl	H	71	83–84 (22)
6	29938-68-9	C_3H_7	C_2H_5	Cl	H	82	104–105 (30)
7	29938-69-0	C_6H_{11}	CH_3	Cl	H	62	109–111 (10)
52	29939-06-8	CH_3	CH_3	Cl	Br	95	35–36[c,d]
53	30093-84-6	C_2H_5	CH_3	Cl	Br	90	93–94 (10)
54	29939-07-9	C_3H_7	CH_3	Cl	Br	93	93–95 (6)
55	29939-08-0	C_6H_{11}	CH_3	Cl	Br	96	166–168 (24)
56	30093-85-7	CH_3	C_3H_7	Cl	Br	90	105–107 (17)
57	29939-09-1	CH_3	i-C_3H_7	Cl	Br	92	98–100 (16)
58	29939-10-4	CH_3	C_4H_9	Cl	Br	95	118–120 (16)
60	29939-12-6	CH_3	CH_3	Cl	C_6H_5CHOH	95	96–98 (P)
61	29939-13-7	CH_3	CH_3	Cl	2-C_4H_3SCHOH	97	101–103 (J)
62	29939-14-8	CH_3	CH_3	Cl	2-(5-BrC_4H_2S)CHOH	88	118–120 (J)
63	29939-15-9	CH_3	CH_3	Cl	3-C_4H_3SCHOH	95	158–160 (0.2)
64	29939-16-0	CH_3	CH_3	Cl	2-Cl-3-$CH_3OC_6H_3CHOH$	90	148–150 (H)
65	30093-86-8	CH_3	C_3H_7	Cl	2-C_4H_3SCHOH	90	125–127 (0.1)
66	29939-17-1	C_6H_5	CH_3	Cl	2-C_4H_3SCHOH	93	100–102 (J)
67	29939-18-2	CH_3	C_6H_5	Cl	2-C_4H_3SCHOH	97	122–124 (J)
68	29939-19-3	CH_3	C_6H_5	Cl	2-$CH_3OC_6H_4CHOH$	85	136–138 (J)
69	29939-20-6	CH_3	CH_3	Cl	$CH_3C{=}O$[a]	75	54–55 (J)
70	27006-82-2	CH_3	CH_3	Cl	CO_2H[e]	85	195–197 (P)
71	29939-22-8	CH_3	C_2H_5	OH	H	92	101–103 (J)
72	29939-23-9	CH_3	C_3H_7	OH	H	93	109–111 (J)
73	29939-24-0	CH_3	i-C_3H_7	OH	H	92	113–115 (J)
74	29939-25-1	CH_3	C_4H_9	OH	H	95	102–104 (N)
75	29939-26-2	C_3H_7	CH_3	OH	H	96	107–109 (O)[f]
76	29939-27-3	C_3H_7	C_2H_5	OH	H	75	96–97 (H)

[a] This compound was prepared by method B′ using acetic anhydride. [b] Satisfactory analytical values (±0.4% for C, H, and N) were reported for compounds 55–70; values within these limits for C and H were reported for the remaining compounds in the table (not analyzed for N). Exceptions: compound 52 was old and the melting point checked the literature; see *c*. [c] Seet ext, ref 1. [d] See footnote *c* in Table I for recrystallization solvents, P = methanol. [e] This compound was prepared by adding the lithio reagent to chunks of Dry Ice in anhydrous ether and acidification of the lithio salt. [f] See text, ref 10; these workers had mp 115°, and isolated the product in 22.8% yield.

4-yl 2-Thienyl Ketone (26).—5-Chloro-1,3-dimethyl-4-lithiopyrazole, prepared from **52**, 209.5 g (1.0 mol), was stirred and cooled to 10° and 124 g (1.1 mol) of 2-thiophenecarboxaldehyde was added. The reaction mixture was stirred 15 min and 1 l. water was added. The layers were separated and the water layer was extracted with two portions of diethyl ether. The organic layers were combined, dried ($MgSO_4$), and concentrated. The residue was triturated with petroleum ether to yield 5-chloro-1,3-dimethyl-α-2-thienylpyrazole-4-methanol (**61**): 235 g (97%); mp 101–103°; nmr ($CDCl_3$) δ TMS 6.7–7.5 (3 H, aromatic CH), 5.9–6.15 (1 H, broad singlet, CHO), 3.7 (4 H, singlet with a broad base, 1-CH_3 and OH, 1 H removed by D_2O wash), 2.11 (3 H, singlet, 3-CH_3). The analysis is in Table II.

The carbinol, 194 g (0.8 mol), **61** was dissolved in 2 l. of reagent acetone and cooled with stirring to 10°. Jones reagent, 205 ml (0.8 equiv), was added rapidly with stirring and cooling. The temperature rose to 45° during the addition. The liquid was filtered through Celite and concentrated. The inorganic sludge was treated with excess saturated sodium bicarbonate solution and extracted with diethyl ether. The concentrate was dissolved in diethyl ether and treated with excess sodium bicarbonate solution. The organic layers were combined, dried ($MgSO_4$), concentrated, and distilled *in vacuo* to yield **26**: 168 g (88%); bp 120–121° (0.15 mm); mp 97–99°; nmr ($CDCl_3$) δ TMS 7.45–7.7 (2 H, multiplet, aromatic CH), 6.95–7.18 (1 H, multiplet, aromatic CH), 3.8 (3 H, singlet, 1-CH_3), 2.33 (3 H, singlet, 3-CH_3); ir (KBr) 1628 cm^{-1} (ketone C=O). The analysis is in Table I.

Typical Bromination of 1,3-Dialkyl-5-chloropyrazoles. 4-Bromo-5-chloro-1,3-dimethylpyrazole (**52**).—5-Chloro-1,3-dimethylpyrazole,[1] 390 g (3.0 mol), was dissolved in 1.5 l. of glacial acetic acid and 496 g (3.1 mol) of bromine was added rapidly with stirring. The reaction mixture was concentrated and treated with diethyl ether and excess ice cold 2 *N* sodium hydroxide. The organic layer was dried ($MgSO_4$) and concentrated using a Vigreux column and distilled *in vacuo* to yield **52**: 597 g (95%); bp 95–96° (15 mm); mp 35–36° (lit. mp 35–36°); nmr ($CDCl_3$) δ TMS 3.8 (3 H, singlet, 1-CH_3), 2.3 (3 H, singlet, 3-CH_3). This was patterned after the synthesis of von Auwers and Niemeyer.[1]

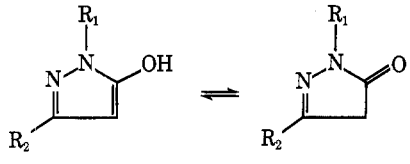
Typical Preparation of 1,3-Dialkyl-2-pyrazolin-5-one. 3-Methyl-1-propyl-2-pyrazolin-5-one (**75**).—A solution of 81 g (1.1 mol) of propylhydrazine in 1 l. of methanol was cooled to 0° and 98 g (1.0 mol) of methyl tetrolate was added dropwise with stirring. The mixture was stirred at 0° for 4 hr and then refluxed 1 hr and concentrated to dryness. The residue was recrystallized from toluene–petroleum ether to yield **75**: 135 g (96%); mp 107–109° (lit. 115°);[10] nmr ($CDCl_3$) δ TMS 10.2–10.6 (0.5 H), 5.0–5.25 (0.25 H), 3.4–4.0 (2 H, broad ill-defined triplet, 1-CH_2), 3.1–3.4 (1.25 H, broad singlet, $CH_2C{=}O$), 2.13 (3 H, singlet, 3-CH_3),

1.4–2.1 (2 H, multiplet, CH_2), 0.85–1.15 (3 H, triplet, CH_3).[25] The analysis is in Table II.

Typical Preparation of 1,3-Dialkyl-5-chloropyrazoles. 5-Chloro-3-methyl-1-propylpyrazole (5).—**75**, 100 g (0.714 mol), was dissolved in 453 g (2.95 mol) of phosphoryl chloride and the mixture was refluxed 24 hr. The reaction mixture was concentrated *in vacuo* at 60° (water bath temperature) and the residue was poured into water. The resulting oil–water mixture was made strongly basic with concentrated ammonium hydroxide with cooling and extracted with diethyl ether. The extracts were dried ($MgSO_4$) and distilled through a Vigreux column, finally under vacuum to yield **5**: 81 g (71%); bp 83–84° (22 mm); nmr ($CDCl_3$) δ TMS 5.82 (1 H, 4-H), 3.8–4.15 (2 H, triplet, 1-CH_2), 2.18 (3 H, singlet, 3-CH_3), 1.6–2.1 (2 H, multiplet, CH_2), 0.75–1.15 (3 H, triplet, CH_3). The analysis is in Table II.

Registry No.—**59**, 29939-11-5; 4,4′-(oxydi-2-thenylidene)bis[5-chloro-1-cyclohexyl-3-methylpyrazole],[26] 29939-28-4.

(25) The absorption between 10.2–10.6 and 5.0–5.25 was observed in all of the 1,3-dialkyl-2-pyrazolin-5-ones prepared in this study and was independent of the synthetic route used. It is the result of the equilibrium with the 1,3-dialkylpyrazol-5-ol tautomer in solution.



Thus the absorption between 3.1 and 3.4 due to the hydrogens at position 4 in the 1,3-dialkyl-2-pyrazolin-5-one is diminished proportionally. This was demonstrated by taking the same spectrum in DMSO-d_6. In this solvent the equilibrium is shifted almost exclusively to the 1,3-dialkylpyrazol-5-ol tautomer. The absorption between 10.2 and 10.6 accounts for 0.9 protons and is assigned to the 5-OH as salt-like, the absorption at 5.15 is a singlet accounting for 0.9 protons and is due to the hydrogen at position 4, and the absorption at 3.1–3.4 accounts for 0.2 protons. Equilibration with deuterium oxide in both solvent systems results in rapid removal of the absorption at all three of the given areas.

(26) See Table I, footnote *e*.

Reductions with Organosilicon Hydrides. III. Reduction of Acyl Fluorides to Esters

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Received January 8, 1971

The previous paper[1] in this series dealt with the palladium-catalyzed reaction of silicon hydrides with acyl chlorides (eq 1). Since it is known, in contrast to the

$$R_3SiH + RCOCl \xrightarrow{Pd} R_3SiCl + RCHO \quad (1)$$

other halogens, that carbon–fluorine bonds of fluorocarbons are not cleaved readily by silicon hydrides in the presence of palladium catalysts,[2] it was of interest to discover if this was also true of acyl fluorides.

A mixture of pentanoyl fluoride, triethylsilane, and 5% Pd/C showed no sign of reaction, and this was confirmed by infrared spectrum (the chloride would have reacted vigorously under these conditions). However, it was found that the reaction with the fluoride proceeded thermally to yield pentyl pentanoate (eq 2),

$$2n\text{-}C_4H_9COF + 2Et_3SiH \longrightarrow n\text{-}C_4H_9CO_2C_5H_{11}\text{-}n + 2Et_3SiF \quad (2)$$

with no trace of pentanal in the product mixture (a test with 2,4-dinitrophenylhydrazine solution was negative). Table I summarizes the results of this and other similar reactions. The reduction of terephthaloyl fluoride yielded a polymer, whose pmr and infrared spectra indicated that it was a polyester of terephthalic acid, *p*-hydroxymethylbenzoic acid, and *p*-bis(hydroxymethyl)benzene. Highly hindered esters can also be prepared, as exemplified by the high yield of 2,2-dimethylpropyl 2,2-dimethylpropionate obtained. However, a silicon dihydride, diphenylsilane, yielded only a complex mixture of carbonyl compounds.

The reaction products could be altered by the addition of other compounds, such as aldehydes. Reduction of pentanoyl fluoride in the presence of equimolar hexanal led to the formation of hexyl pentanoate. As judged from chromatography, no pentyl pentanoate was formed. As noted in Table I, benzonitrile seemed to have no effect upon the reaction. The aldehydes had another effect on the reaction, that of increasing the rate. This was especially true of crotonaldehyde, but only a mixture of carbonyl compounds was isolated from this reaction (a referee has pointed out that this very rapid reaction may not necessarily be the reduction to the ester).

These data are strikingly similar to those obtained in the analogous reductions of tin hydrides.[3] In those reductions of acyl fluorides, esters are also the only products.[4] Based on the mechanism developed for tin hydrides,[3] the steps involved in the present reaction are probably as shown in eq 3–6. The unpaired species

$$R_3Si\cdot + RCOF \longrightarrow RCO\cdot + R_3SiF \quad (3)$$

$$RCO\cdot + R_3SiH \longrightarrow RCHO + R_3Si\cdot \quad (4)$$

$$RCO\cdot + RCHO \longrightarrow RC(=O)\text{—}O\text{—}\dot{C}HR \quad (5)$$

$$RC(=O)\text{—}O\text{—}\dot{C}HR + R_3SiH \longrightarrow RCO_2CH_2R + R_3Si\cdot \quad (6)$$

(radicals) represented in eq 3–6 may or may not actually exist (they may only be transition states) but they are useful in visualizing the mechanism. There are two other experiments which tend to substantiate this pathway. After 19 hr at 75°, equimolar amounts of Et_3SiH and pentanoyl fluoride with 0.9 mol % of α,α′-azobisisobutyronitrile contained 19% of the original silicon hydride; a control reaction without the azonitrile initiator contained 43% of Et_3SiH. Thus, as expected, a radical source increased the reaction rate. Another alternate mechanism, addition of the silicon hydride across aldehydic carbonyl, followed by reaction of the resulting alkoxysilane with the acyl fluoride[5] (eq 7), is much less likely because the first step does not

$$R'CHO + R_3SiH \longrightarrow R'CH_2OSiR_3 \xrightarrow{R''COF} R''CO_2CH_2R' + R_3SiF \quad (7)$$

(1) For part II, see J. D. Citron, *J. Org. Chem.*, **34**, 1977 (1969).
(2) J. D. Citron, J. E. Lyons, and L. H. Sommer, *ibid.*, **34**, 638 (1969).
(3) E. J. Walsh, Jr., and H. G. Kuivila, *J. Amer. Chem. Soc.*, **88**, 576 (1966).
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(5) J. D. Citron, *J. Organometal. Chem.*, in press.