B. Base-Catalyzed Reactions of Phenylacetone with Para-Substituted Benzaldehydes. Reaction of Phenylacetone with Benzaldehyde.—Phenylacetone (24.9 g, 0.186 mol) and benzaldehyde (19.7 g, 0.186 mol) were added to a rapidly mechanically stirred solution of NaOH (1.50 g) in water (800 ml) at 65°. After 18 hr the mixture was cooled to room temperature and extracted with five 100-ml portions of CH_2Cl_2. The extract was washed with water and dried ($MgSO_4$) and solvent was evaporated under reduced pressure. A small sample of the crude product was set aside for glc and nmr analysis. The remainder of the product was recrystallized from methanol, affording 18.2 g (44%) of *trans*-1,4-diphenyl-3-buten-2-one (IIId): mp 72–75° (lit.[27] mp 73–76°); nmr δ 7.57 (d, 1, J = 16 Hz) and 6.70 (d, 1, J = 16 Hz) (trans CH=CH), 7.3 (m, 10, aryl H), 3.82 (s, 2, CH_2).

Glc analysis of the *crude* product showed a relative yield of 91:9 of IIId:VId; glc and nmr analysis[28] showed a total yield of 92% for IIId + VId.[29]

Reaction of Phenylacetone with *p*-Tolualdehyde.—The same procedure as with benzaldehyde was followed. Washing of the crude product with petroleum ether (bp 20–40°) and recrystallization from ethanol afforded 8.2 g (19%) of *trans*-1-phenyl-4-(*p*-tolyl)-3-buten-2-one (IIIe): mp 112.5–114° (lit.[16] mp 115°); nmr δ 7.57 (d, 1, J = 16 Hz) and 6.66 (d, 1, J = 16 Hz) (trans CH=CH), 7.2 (m, ~9, aryl H), 3.84 (s, 2, CH_2), 2.26 (s, 3, CH_3). Repetition of the reaction at 80° for 24 hr increased the yield to 21.9 g (50%).

Glc and nmr analysis of the crude products, as above, showed a relative yield of 92:8 for IIIe:VIe for the 65° reaction and 90:10 for the 80° reaction. A total yield (IIIe + VIe) of 88% was found in the latter reaction.

Reaction of Phenylacetone with *p*-Anisaldehyde.—The standard procedure was followed. Trituration of the crude product with cold ether and filtration afforded 11.2 g (24%) of *trans*-4-(*p*-anisyl)-1-phenyl-3-buten-2-one (IIIf): mp 98–100° (lit.[16] mp 98–100°); nmr δ 7.58 (d, 1, J = 16 Hz) and 6.62 (d, 1, J = 16 Hz) (trans CH=CH), 7.25 (m, ~9, aryl H), 3.87 (s, 2, CH_2), 3.72 (s, 3, OCH_3).

Glc and nmr analysis of the crude products showed relative yields of 90:10 for IIIf:VIf in both reactions. The total yield (IIIf + VIf) was 88% in the 80° reaction.

Reaction of Phenylacetone with *p*-Chlorobenzaldehyde.—The standard procedure was used. Two recrystallizations of the crude product from ethanol gave 11.4 g (24%) of *trans*-4-(*p*-chlorophenyl)-1-phenyl-3-buten-2-one (IIIg) as white crystals: mp 102–104°; ir 1655 cm^{-1} (C=O), 970 (trans CH=CH); nmr δ 7.53 (d, 1, J = 16 Hz) and 6.66 (d, 1, J = 16 Hz) (trans CH=CH), 7.27 (m, 9, aryl H), 3.89 (s, 2, CH_2).

Anal. Calcd for $C_{16}H_{13}ClO$: C, 74.85; H, 5.10; Cl, 13.81. Found: C, 74.77; H, 5.02; Cl, 13.80.

Glc and nmr analysis of the crude product showed a ratio of IIIg:VIg of 87:13. A total yield (IIIg + VIg) of 68% was found.

Reaction of phenylacetone with *p*-nitrobenzaldehyde at temperatures varying from 50 to 75° and times of 6–24 hr afforded either unreacted starting materials and/or a dark red glassy substance which could not be purified. Glc analysis of the crude products showed a trace of VIh but no products other than starting materials could be detected.[30]

Registry No.—IIId, 38661-84-6; IIIe, 38661-85-7; IIIf, 38661-86-8; IIIg, 37562-70-2; IVd, 103-79-7; VId, 38661-88-0; VIe, 38661-89-1; VIf, 13938-22-2; VIg, 38661-91-5; VIl, 8661-92-6.

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[27] S. A. Fine and R. L. Stern, *J. Org. Chem.*, **32**, 4132 (1967).

[28] Glc analyses were based on comparisons of peak areas of standardized solutions of the pure compounds with peak areas in solutions of the crude product mixtures. Nmr analysis was used as confirmatory evidence. The areas of suitable peaks due to III and VI in the nmr spectrum of the crude product mixtures were compared with the areas of peaks due to unreacted phenylacetone and/or unreacted aldehyde. Total yields obtained by the two methods always differed by less than 4%.

[29] Since the glc retention times of VId–h in the crude product mixtures were precisely the same as the retention times of authentic samples, and since the nmr shifts due to VId–h in the crude product mixtures were identical with those in authentic samples, we conclude that the stereochemistry of VI in our product mixtures is identical with that of the authentic samples, namely cis with respect to the aryl groups. Similar stereochemical results have been observed in a related base-catalyzed condensation: H. E. Zimmerman and L. Ahramjian, *J. Amer. Chem. Soc.*, **81**, 2086 (1959).

[30] The retention times of type VI ketones (d–g) were almost exactly double the retention times of the corresponding type III ketones under the conditions used. The conclusion that IIIh was absent is based on the fact that no peak appeared on the chromatogram even after 15 times the retention time of VIh.

A Reinvestigation of the Condensation of Aliphatic Ketones with Benzil

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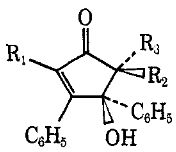
An extensive investigation of the base-catalyzed condensation of acetone and other aliphatic ketones with benzil was carried out many years ago by Japp and his coworkers.[1] The product from the reaction of acetone with benzil was proved to be 4-hydroxy-3,4-diphenyl-2-cyclopenten-1-one (**1**). From the reaction of other aliphatic ketones with benzil, cyclopentenones bearing alkyl groups at C-2 or C-5 were obtained. The structures of these products, however, were not completely established. In the present study some of these products were reinvestigated, and their structures were determined using nmr spectroscopy.

The structure of **1** and that of **2**, which is produced from 3-methyl-2-butanone, are unambiguous, and these compounds serve as models. In addition to signals for aromatic and hydroxylic hydrogens, the spectrum of **1** has a one-proton singlet at δ 6.66 and an AB pattern [δ_A 2.98, δ_B 2.84 (J_{AB} = 19 Hz)]. The spectrum of **2** has a one-proton singlet at δ 6.74 and three-proton singlets at 1.32 and 0.64. The substituents at C-4 cause these latter to be displaced from δ 1.03, the reported position for the methyl hydrogen resonance of 5,5-dimethyl-2-cyclopenten-1-one.[2] The methyl group cis to the phenyl group on C-4 lies in the region shielded by the aromatic ring, and this methyl group thus gives rise to the higher field peak.[3]



1, $R_1 = R_2 = R_3 = H$
2, $R_1 = H$; $R_2 = R_3 = CH_3$
3, $R_1 = R_2 = CH_3$; $R_3 = H$
4, $R_1 = R_3 = CH_3$; $R_2 = H$
5, $R_1 = CH_3$; $R_2 = R_3 = H$
6, $R_1 = R_3 = H$; $R_2 = CH_3$
7, $R_1 = R_2 = H$; $R_3 = CH_3$

From the reaction of 3-pentanone with benzil Japp and Meldrum obtained two products, one melting at 150° and the other at 128.°[1a] They concluded

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[1] (a) F. R. Japp and A. N. Meldrum, *J. Chem. Soc.*, **79**, 1024 (1901); (b) F. R. Japp and J. Knox, *ibid.*, **87**, 673 (1905); (c) F. R. Japp and A.C. Michie, *ibid.*, **83**, 276 (1903).

[2] T. Matsumato, H. Shirahama, A. Ichihara, H. Shin, S. Kagawa, N. Ito, T. Hisamitsu, T. Kamada, and F. Sakan, *Tetrahedron Lett.*, 4097 (1967).

[3] L. M. Jackman and S. Sternhell, "Applications of Nuclear Magnetic Resonance Spectroscopy in Organic Chemistry," 2nd ed, Pergamon Press, Oxford, 1969, p 234.

that the product of higher melting point is a cyclopentenone bearing methyl groups at C-2 and C-5 and that the other product is an acyclic compound, 3-methyl-1,2-diphenyl-2-hexene-1,4-dione. The nmr spectra of these compounds clearly show that the two are, in fact, diastereoisomeric. Each has a three-proton singlet near δ 2.0 and a one-proton quartet and a three-proton doublet. The spectrum of the higher melting product has the doublet at δ 1.24, and the compound is therefore **3** with the methyl group on C-5 trans to the phenyl group on C-4. The spectrum of the other isomer has the doublet at δ 0.74, and the compound is therefore **4**.

The compounds equilibrate under basic conditions, and the equilibrium mixture in ethanol contains very nearly equal amounts of the two. That the two are of nearly equal stability is surprising since one would expect steric interference of the methyl group with phenyl to be far more severe than interference of methyl with hydroxyl. A reasonable explanation is that clustering of solvent molecules about the hydroxyl group increases its apparent size. Although the equilibrium mixture contains nearly equal amounts of the two compounds, in preparative experiments **3** is produced in nearly quatitative yield because this more insoluble compound preferentially crystallizes from the basic solution.

Condensation of 2-butanone with benzil can give three different monomethyl-substituted products. When the reaction was carried out in dilute alcoholic potassium hydroxide, Japp and Meldrum obtained a product melting at 118° to which they assigned structure **5**.[1a,4] The nmr spectrum clearly confirms the correctness of the assignment of structure. The spectrum has an easily exchangable one-proton singlet, a two-proton singlet at δ 2.96 (accidentally equivalent methylene protons), and a three-proton singlet at 1.93.[5a] From a heterogeneous reaction carried out in the presence of hot concentrated aqueous base, Japp and Meldrum obtained, in addition to **5**, a compound melting at 180° and a small amount of a compound melting at 157°.[1a] They concluded that the higher melting product is a cyclopentenone with a methyl group at C-5 and that the compound melting at 157° is 1,2-diphenyl-2-hexene-1,4-dione. The nmr spectra of the compounds show them to be diastereoisomeric. In addition to signals for aromatic and hydroxylic hydrogens, each has a one-proton singlet near δ 6.8 and a one-proton quartet and a three-proton doublet. The doublet in the spectrum of the higher melting compound lies at δ 1.24, and the compound is **6**. The doublet at δ 0.72 in the spectrum of the other compound proves it to be **7**, the diastereomer of **6**.

In agreement with the properties of the related dimethyl compounds, an equilibrium mixture of **6** and **7** in ethanolic base contains appreciable amounts of both isomers, but the higher melting **6** preferentially crystallizes. Compounds **6** and **7** are not readily interconverted with the structurally isomeric **5**. Compound **5** was unaffected by base, and appreciable conversion of a mixture of **6** and **7** to **5** was accomplished only by heating in 1 *M* ethanolic potassium hydroxide for an extended period during which extensive destruction of the compounds took place. Since these conditions are far more vigorous than those under which the three compounds are formed in the same reaction mixture, the production of the structurally isomeric compounds is the result of independent, rather than consecutive reactions.

The uv absorption maximum of those compounds which have hydrogen at C-2 occurs near 285 nm. The maximum lies near 275 nm for the compounds in which C-2 bears a methyl group. The explanation, given some years ago, for these observations is that the alkyl group interferes with the ability of the phenyl group on C-3 and the cyclopentenone ring to be coplanar.[6]

Experimental Section

All melting points are uncorrected. The nmr spectra were recorded on a Perkin-Elmer Model R12A instrument, and chemical shifts are reported in parts per million downfield from internal tetramethylsilane. The ir spectra were taken on a Perkin-Elmer Model 467 grating instrument, and uv spectra were recorded on a Cary 14 spectrophotometer.

The following compounds were prepared by published procedures. **4-Hydroxy-3,4-diphenyl-2-cyclopenten-1-one** (**1**): mp 147–148° (lit.[1b] mp 149°); nmr ($CDCl_3$) δ 7.2–7.7 (m, 10), 6.66 (s, 1), 3.53 (s, 1, OH), 2.91 (AB q, 2, $\Delta_{AB} = 8$ Hz, $J_{AB} = 19$ Hz); uv max (95% EtOH) 288 nm (log ϵ 4.26); ir ($CHCl_3$) 3600, 3400, 1725 (sh), 1695 cm^{-1}. **4-Hydroxy-5,5-dimethyl-3,4-diphenyl-2-cyclopenten-1-one** (**2**): mp 181–183° (lit.[1a] mp 181°); nmr ($CDCl_3$) δ 7.2–7.7 (m, 10), 6.74 (s, 1), 2.46 (s, 1, OH), 1.32 (s, 3), 0.64 (s, 3); uv max (95% EtOH) 287 nm (log ϵ 4.29); ir ($CHCl_3$) 3610, 3400, 1705 cm^{-1}. **(4*SR*,5*SR*)-4-Hydroxy-2,5-dimethyl-3,4-diphenyl-2-cyclopenten-1-one** (**3**): mp 150–151° (lit.[5] mp 152–153°); nmr ($CDCl_3$) δ 7.1–7.5 (m, 10), 2.71 (q, 1, J = 7 Hz), 2.32 (s, 1, OH), 1.98 (s, 3), 1.24 (d, 3, J = 7 Hz); uv max (95% EtOH) 275 nm (log ϵ 4.18); ir ($CHCl_3$) 3600, 3400, 1705 cm^{-1}. **4-Hydroxy-2-methyl-3,4-diphenyl-2-cyclopenten-1-one** (**5**): mp 116–118° (lit.[1a] mp 118°); nmr ($CDCl_3$) δ 7.0–7.5 (m, 10), 2.96 (s, 2), 2.57 (s, 1, OH), 1.93 (s, 3); uv max (95% EtOH) 276 nm (log ϵ 4.30); ir ($CHCl_3$) 3580, 3400, 1705 cm^{-1}. **(4*SR*,-5*SR*)-4-Hydroxy-5-methyl-3,4-diphenyl-2-cyclopenten-1-one** (**6**): mp 182–183° (lit.[1a] mp 180°); nmr ($CDCl_3$) δ 7.2–7.7 (m, 10), 6.74 (s, 1), 2.68 (q, 1, J = 7 Hz), 2.35 (s, 1, OH), 1.24 (d, 3, J = 7 Hz); uv max (95% EtOH) 286 nm (log ϵ 4.32); ir ($CHCl_3$) 3600, 3400, 1705 cm^{-1}.

Preparation of (4*SR*,5*RS*)-4-Hydroxy-2,5-dimethyl-3,4-diphenyl-2-cyclopenten-1-one (4).—To a warm solution of 6.3 g of **3** in 25 ml of ethanol was added a solution of 2.5 g of KOH in 10 ml of ethanol. After 15 min the solution was slowly added to 5 ml of acetic acid in 25 ml of ethanol, and 100 ml of water was slowly added to the resulting solution. The precipitated product, 5.7 g, a 3:2 mixture of **4** and **3**, was filtered and dried. A portion of this product (0.69 g) was chromatographed on 50 g of silica gel. Elution by 1:150 ether–benzene gave **3** followed by a mixture of **3** and **4**. The latter was recrystallized twice from carbon tetrachloride–hexane to give 0.26 g of **4**: mp 129–130° (lit.[1a] mp 128°); nmr ($CDCl_3$) δ 7.0–7.5 (m, 10), 2.91 (q, 1, J = 7 Hz), 2.45 (s, 1, OH), 2.02 (s, 3), 0.74 (d, 3, J = 7 Hz); uv max (95% EtOH) 274 nm (log ϵ 4.12); ir ($CHCl_3$) 3580, 3400, 1705 cm^{-1}.

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(4) Under the same conditions a few years later Japp and Michie obtained a product melting at 134° which they considered to be a second crystalline modification.[1b] In the present work only the product of lower melting point was obtained.

(5) (a) In a recent report it was mentioned briefly that reaction according to the original procedure gave 3-methyl-1,2-diphenyl-2-pentene-1,4-dione rather than **5**.[5b] No properties were given for the product, and the compound is not reported elsewhere in the literature. In the present work no difficulty was encountered in repeating the original experiment. A possible explanation for the discrepancy lies in the observation that under some conditions (*e.g.*, 21 mg/ml in CCl_4 at 35°) the signal for the hydroxylic proton is coincident with that for the accidentally equivalent methylene protons and the nmr spectrum of **5** contains two three-proton singlets. A deceptive spectrum and the tendency for **5** to remain noncrystalline may have caused misidentification of the product. (b) P. Bladon, S. McVey, P. L. Pauson, G. D. Broadhead, and W. M. Horspool, *J. Chem. Soc. C*, 306 (1966).

(6) P. Yates, N. Yoda, W. Brown, and B. Mann, *J. Amer. Chem. Soc.*, **80**, 202 (1958).

Preparation of (4*SR*,5*RS*)-4-Hydroxy-5-methyl-3,4-diphenyl-2-cyclopenten-1-one (7).—By a procedure analogous to that used to prepare 4, 6 was isomerized to give a 6:5 mixture of 7 and 6. Chromatography of 0.90 g of this mixture on 50 g of silica gel (elution with dilute ether in benzene mixtures) gave 0.24 g of 6, followed by 0.36 g of a mixture of 6 and 7, and finally 0.24 g of a 6:1 mixture of 7 and 6. Four recrystallizations of the last from carbon tetrachloride gave 0.10 g of 7: mp 159–160° (lit.[1a] mp 157°); nmr ($CDCl_3$) δ 7.2–7.7 (m, 10), 6.77 (s, 1), 2.92 (q, 1, J = 7 Hz), 2.88 (s, 1, OH), 0.72 (d, 3, J = 7 Hz); uv max (95% EtOH) 285 nm (log ϵ 4.29); ir ($CHCl_3$) 3600, 3400, 1705 cm^{-1}.

Equilibration of 3 and 4 in Basic Solution.—A solution of 0.23 g of 3 in 15 ml of ethanol was heated under reflux with 0.05 g of K_2CO_3. Aliquots were withdrawn at intervals and prepared for analysis by nmr by precipitation in water, extraction into ether, and evaporation of the ether. An equilibrium mixture containing 52% 4 and 48% 3 was formed after 90 min of heating. An identical mixture was formed by heating a 3:2 mixture of 4 and 3 in ethanol with K_2CO_3. A mixture containing a somewhat greater proportion of 4 was formed by allowing a solution of 3 in ethanol containing KOH to stand at room temperature. In another experiment, upon allowing a warm solution of 7.5 g of a mixture of 3 and 4 in 30 ml of ethanol containing 0.1 g of KOH to cool slowly, 5.5 g of a 16:1 crystalline mixture of 3 and 4 was slowly deposited. Analysis of the supernatant liquid at intervals showed it continuously to contain an equilibrium mixture of 3 and 4.

Action of Base upon 5, 6, and 7.—A solution of 0.96 g of a mixture of 6 and 7 in 5 ml of 1 M ethanolic KOH was heated under reflux for 1 hr. The solution became very dark. After neutralization with acetic acid, the solution was poured into water, and the precipitated material was extracted into ether. The ether was evaporated, and 0.8 g of the residue was chromatographed on 45 g of neutral alumina (activity grade III). Eluted by benzene were 0.2 g of material, the ir spectrum of which lacked hydroxyl absorption, and 0.1 g of highly colored material. Eluted by 1:10 ether–benzene was 0.39 g of a mixture of 5, 6, and 7 which contained, according to analysis by nmr, 0.08 g of 5. Other treatments of 5 and of mixtures of 6 and 7 did not effect interconversion of the structural isomers. Among the experiments in which no change was observed were treatment of 5 with boiling 1 M ethanolic KOH for 30 min, treatment of 5 with 0.1 M ethanolic KOH for 5 days, treatment of a mixture of 6 and 7 with 0.1 M ethanolic KOH for 5 days, and stirring, while heating under reflux, for 2 hr a heterogeneous mixture of 30% aqueous KOH and a solution of 6 and 7 in DME.

Registry No.—**1**, 5587-78-0; **2**, 38661-94-8; **3**, 38661-95-9; **4**, 38661-96-0; **5**, 38661-97-1; **6**, 38661-98-2; **7**, 38677-74-6; benzil, 134-81-6.

New Adducts of Hexafluoroacetone with Hydrogen Cyanide

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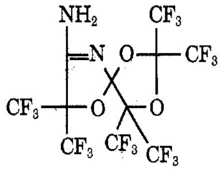
Two adducts of hexafluoroacetone with hydrogen cyanide are known. A 1:1 adduct, hexafluoroacetone cyanohydrin (6), was prepared by the piperidine-catalyzed addition of hydrogen cyanide to the ketone,[1] and a 2:1 adduct, 2,2,5,5-tetrakis(trifluoromethyl)-4-oxazolidinone (4), was prepared by reaction of hexafluoroacetone with sodium cyanide in acetonitrile.[2]

We noted that large, transparent crystals separated from a sample of hexafluoroacetone cyanohydrin that had been standing for more than a year in a clear glass bottle at room temperature. Elemental and mass spectral analysis showed that these crystals are a new, 3:2 adduct of hexafluoroacetone with hydrogen cyanide.

The spiro structure 1 was assigned to this 3:2 adduct on the basis of infrared and nmr spectral analysis. The ^{19}F nmr showed six nonequivalent CF_3 groups. The ^1H nmr showed two different absorptions of equal intensity that coalesced on warming, similar to the ^1H nmr spectrum of the closely analogous 4-amino-2,2,5,5-tetrakis(trifluoromethyl)-3-oxazoline (2).[3] The ir spectra of both 1 and 2 were also similar, with a band at 5.88 μ for C=N.



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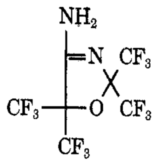

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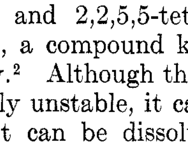
Chemically, the spiro compound 1 was also similar to 2. Both compounds are stable to concentrated sulfuric acid at 100°, and both compounds are nitrated by fuming nitric acid in fuming sulfuric acid to form nitramines.

Attempts to prepare 1 under controlled conditions resulted in additional new adducts of hexafluoroacetone with hydrogen cyanide. A 3:1 adduct resulted when excess hexafluoroacetone was added to either hydrogen cyanide or the preformed cyanohydrin in the presence of basic catalyst at or below room temperature. The structure of this new adduct is believed to be the dioxolane 3 instead of the isomeric oxazoline 3a, because attempts to distil the adduct at atmospheric pressure decomposed it to hexafluoroacetone and hexafluoroacetone cyanohydrin. Thermal decomposition of 3a should result in hexafluoroacetone and 2,2,5,5-tetrakis(trifluoromethyl)-4-oxazolidinone, a compound known to possess high thermal stability.[2] Although this new 3:1 adduct is somewhat thermally unstable, it can be distilled at reduced pressure. It can be dissolved in cold alkali and reprecipitated with acid, but warm alkali converts it to the cyanohydrin. Methylation of 3 with diazomethane gives a stable *O*-methyl ether. Reaction of 3 with sodium hydride followed by acidification gives the 2:1 adduct 4. Pyrolysis of 3 in the presence of a few drops of sulfuric acid gave a product that appeared to be a mixture of 3 and a new 2:1 adduct, 5. Evidence



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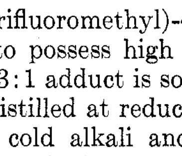

3a

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(1) I. L. Knunyants, E. M. Rokhlin, N. P. Gambaryan, Yu. A. Cheburkov and T-Y. Chen, *Khim. Nauka Prom.*, **4**, 802 (1959); *Chem. Abstr.*, **54**, 10851 (1959).

(2) W. J. Middleton and C. G. Krespan, *J. Org. Chem.*, **32**, 951 (1967).

(3) W. J. Middleton, D. Metzger, K. B. Cunningham, and C. G. Krespan, *J. Heterocycl. Chem.*, **7**, 1045 (1970).