

hydrolysis of IIIb with 2 *N* potassium hydroxide in butan-1-ol (43 hr) gave the hydrazine IV in good yield as evidenced by absence of carbonyl peaks and appearance of NH peaks in the infrared spectrum, absence of N-phenyl peaks at  $\delta$  7.4 in the pmr spectrum, satisfactory elemental analysis, and the trapping of the aniline formed in the hydrolysis as diphenylurea.

I also reacted instantly with ergosterol (V) in acetone-benzene solution at 0° as shown by disappearance of the color of I. The adduct VIa was characterized by the disappearance of the ring-diene absorption pattern for ergosterol at  $\lambda_{\max}$  282 m $\mu$ , appearance of a carbonyl doublet at 1675 and 1735 cm<sup>-1</sup>, and the pmr spectrum which showed peaks at  $\delta$  7.4 (N-phenyl), 5.2 and 5.26 (multiplet, integrating for the two vinyl protons at C-22 that were in the same position in ergosterol), and 6.24 and 6.33 (two vinyl protons at C-6 and C-7, *J* = 4 cps). No hydrogen abstraction-addition product<sup>3</sup> could be isolated.

The adduct VIa was hydrogenated to the tetrahydro adduct VIb, whose pmr spectrum failed to reveal vinylic protons. Hydrolysis of VIb to the hydrazine VII required more drastic conditions compared to IIIb, namely, 120-hr reflux in 3 *N* potassium hydroxide in butan-1-ol. VII was characterized by absence of the N-phenyl peak in the pmr spectrum, by the absence of a carbonyl doublet and the presence of NH peaks in the infrared spectrum, and by elemental analysis.

It has been established that adduct formation in rings A and B of  $\Delta^{2,4}$ -cholestadiene and ergosterol takes place from the less hindered  $\alpha$  side<sup>6</sup> and we therefore assume that the stereochemistry of IIIa and VIa is as depicted.

#### Experimental Section<sup>7</sup>

**$\Delta^{2,4}$ -Cholestadiene (II).**—The procedure of Stavely and Bergmann<sup>8</sup> was employed with some modification. A cholesterol-alumina (Fischer chromatographic grade) mixture (3:2) was heated for 2.5 hr at 225° (0.4 mm). The yellow mixture was cooled and extracted with methylene chloride, and the extracts were chromatographed (Woelm neutral alumina) using benzene as the eluent to give II in 64% yield: mp and mmp 60–62°.

**Adduct IIIa of II with 4-Phenyl-1,2,4-triazoline-3,5-dione (I).**—To a solution of II (0.368 g) in dry acetone (25 ml) and a little benzene (to homogeneity) was added dropwise at 0° a freshly prepared<sup>8</sup> solution of I in dry acetone until the reaction mixture remained pale pink. The reaction mixture was chromatographed (Woelm neutral alumina) using benzene and ethyl acetate (95:5) as eluent and recrystallized from ethanol to give IIIa (0.47 g, 90%): mp 200–204°;  $\nu_{\text{Nujol}}$  1705, 1760 cm<sup>-1</sup> (C=O).

*Anal.* Calcd for C<sub>33</sub>H<sub>46</sub>N<sub>2</sub>O<sub>2</sub>: C, 77.30; H, 9.08; N, 7.7. Found: C, 77.3; H, 9.3; N, 7.4.

**Catalytic Reduction of Adduct IIIa.**—IIIa (0.9 g) in ethanol (100 ml) was hydrogenated for 19 hr at 45 psi with 5% Pd-C (300 mg). The solution was evaporated *in vacuo* and the solid material was chromatographed (Woelm neutral alumina) using benzene and ethyl acetate (95:5) as eluent and crystallized from ethanol to give IIIb in near quantitative yield: mp 208–209°;  $\nu_{\text{Nujol}}$  1705, 1760 cm<sup>-1</sup> (C=O).

*Anal.* Calcd for C<sub>33</sub>H<sub>46</sub>N<sub>2</sub>O<sub>2</sub>: C, 77.00; H, 9.42; N, 7.7. Found: C, 77.26; H, 9.42; N, 7.4.

(6) R. Antonucci and K. J. Sax, *J. Org. Chem.*, **16**, 1356 (1951); K. Tsuda and S. Nozoe, *Chem. Pharm. Bull.* (Tokyo), **8**, 1128 (1960).

(7) Melting points were recorded on a Thomas-Kofler hot stage and are corrected. Infrared and ultraviolet spectra were recorded on Perkin-Elmer spectrophotometers, Models 237 and 202, respectively. Pmr spectra were recorded on a Varian A-60 spectrophotometer and are reported as  $\delta$  values in deuteriochloroform with tetramethylsilane as internal standard. Elemental analyses were by Galbraith Laboratories, Knoxville, Tenn.

(8) H. E. Stavely and W. Bergmann, *J. Org. Chem.*, **1**, 575 (1936).

**Alkaline Hydrolysis of Reduced Adduct IIIb.**—IIIb (1.08 g) and potassium hydroxide-butan-1-ol (40 ml, 2 *N*) were refluxed in a nitrogen atmosphere for 43 hr. The solution was evaporated *in vacuo* and the solid material was extracted into methylene chloride, chromatographed (Woelm neutral alumina) using benzene and ethyl acetate (80:20) as eluent, and crystallized from ethanol-ether to give IV (0.439 g, 60%): mp 115–118°,  $\nu_{\text{Nujol}}$  3400 cm<sup>-1</sup> (NH) (br).

*Anal.* Calcd for C<sub>27</sub>H<sub>48</sub>N<sub>2</sub>: C, 80.91; H, 12.08; N, 6.99. Found: C, 80.97; H, 11.90; N, 6.93.

**Adduct VIa of V and 4-Phenyl-1,2,4-triazoline-3,5-dione (I).**—This was prepared in a similar manner to adduct IIIa from 0.8 g of ergosterol in acetone-benzene. The reaction mixture was evaporated under reduced pressure and crystallized three times from aqueous acetone to give VIa (0.93 g, 85%): mp 190–191.5°;  $\nu_{\text{Nujol}}$  1675, 1735 (C=O), 3450 cm<sup>-1</sup> (OH).

*Anal.* Calcd for C<sub>36</sub>H<sub>50</sub>N<sub>2</sub>O<sub>3</sub>: C, 75.63; H, 8.64; N, 7.35. Found: C, 75.47; H, 8.77; N, 7.54.

**Catalytic Reduction of Adduct VIa.**—VIa (0.57 g) in ethanol (40 ml) was hydrogenated for 16 hr at 50 psi with 5% Pd-C (300 mg). The solution was evaporated under reduced pressure, chromatographed (Woelm neutral alumina) using benzene and ethyl acetate (95:5) as eluent, and crystallized from ethanol to give VIb (0.49 g, 86%): mp 178–182°;  $\nu_{\text{Nujol}}$  1675, 1740 (C=O), 3435 cm<sup>-1</sup> (OH).

*Anal.* Calcd for C<sub>36</sub>H<sub>50</sub>N<sub>2</sub>O<sub>3</sub>: C, 75.1; H, 9.2; N, 7.3. Found: C, 74.89; H, 9.02; N, 6.8.

**Alkaline Hydrolysis of Reduced Adduct VIb.**—VIb (1.7 g) and potassium hydroxide-butan-1-ol (100 ml, 3 *N*) were refluxed in a nitrogen atmosphere for 120 hr and extracted as for adduct IIIb to give VII (0.3 g, 25%): mp 189–192°,  $\nu_{\text{Nujol}}$  3410 cm<sup>-1</sup> (NH) (br).

*Anal.* Calcd for C<sub>28</sub>H<sub>50</sub>N<sub>2</sub>O: C, 78.1; H, 11.6; N, 6.5. Found: C, 77.92; H, 11.66; N, 6.4.

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### The Preparation of Triazines Related to 6-Cyano-2,2'-bipyridine<sup>1</sup>

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For the preparation of 6-cyano-2,2'-bipyridine, 6-chloro- or -bromobipyridine was needed. The chloro compound was prepared by converting 2,2'-bipyridine methiodide by an alkaline oxidation with potassium ferricyanide to the hitherto unreported 1-methyl-2,2'-bipyridin-6-one and treating the latter with phosphoryl chloride and phosphorus pentachloride. However, since the halogen in this compound was too unreactive to yield the cyanobipyridine, 6-bromo-2,2'-bipyridine was prepared from the bipyridinone using phosphoryl bromide, phosphorus tribromide, and bromine. This compound had previously been prepared by direct vapor phase bromination of 2,2'-bipyridine.<sup>2</sup> The bromobipyridine was then converted smoothly to 6-cyano-2,2'-bipyridine by cuprous cyanide in pyridine. The melting point observed for the cyanobipyridine was considerably lower than that previously reported.<sup>2</sup>

Starting from 6-cyano-2,2'-bipyridine and using reactions previously described<sup>3,4</sup> for cyanopyridine

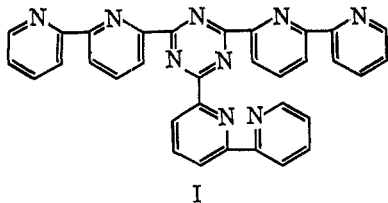
(1) This work was supported by a grant (G-9645) from the National Science Foundation.

(2) F. H. Burstall, *J. Chem. Soc.*, 1662 (1938).

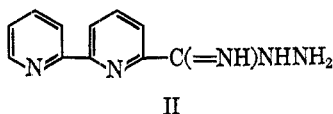
(3) F. H. Case and E. Koft, *J. Am. Chem. Soc.*, **81**, 905 (1959).

(4) F. H. Case, *J. Org. Chem.*, **30**, 931 (1965).

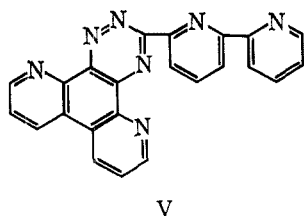
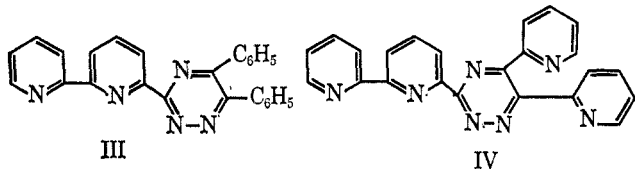
derivatives there were synthesized 2,4-diamino-6-(2,2',6-bipyridyl)-1,3,5-triazine (by the action of dicyanodiamide), 2-amino-4,6-bis(2,2',6-bipyridyl)-1,3,5-triazine (from guanidine), and 2,4,6-tris(2,2',6-bipyridyl)-1,3,5-triazine (I) (by the action of sodium hydride). The hydrazidine (II) was prepared by the



action of hydrazine and from it 3-(2,2',6-bipyridyl)-



5,6-diphenyl-*as*-triazine (III) (by the action of benzil), 3-(2,2',6-bipyridyl)-5,6-bis(2-pyridyl)-*as*-triazine (IV) (on treatment with pyridil), and 3-(2,2',6-bipyridyl)-*as*-triazino[5,6-*f*][4,7]phenanthroline (V) (on treatment with 4,7-phenanthroline-5,6-dione). The triazines de-



scribed in this paper, all of which contain the ferrioin group ( $=N-C(=)-C(=)-N=$ ), will be tested for metal-chelating ability.

#### Experimental Section

**1-Methyl-2,2'-bipyridin-6-on.**—To a stirred saturated solution of potassium ferricyanide maintained at 25° there was added in alternate portions 50 g of 2,2'-bipyridine methiodide<sup>5</sup> and sufficient concentrated sodium hydroxide solution to maintain a constant alkalinity. The reaction was completed by stirring for 0.5 hr at this temperature. Repeated extraction of the aqueous solution with chloroform, removal of solvent, and vacuum distillation yielded 17 g (54.3%) of product, bp 205–210° (8 mm). A sample of the solidified compound, crystallized from benzene-petroleum ether (bp 60–70°), melted at 74–75°.

*Anal.* Calcd for  $C_{11}H_{10}N_2O$ : C, 70.97; H, 5.38. Found: C, 71.28; H, 5.53.

**6-Chloro-2,2'-bipyridine.**—A mixture of 16 g of 1-methyl-2,2'-bipyridin-6-one, 16 g of phosphorus pentachloride, and 90 g of phosphoryl chloride was heated at reflux for 3 hr. After removal of excess phosphoryl chloride using an aspirator at 100°, the contents of the flask were poured on ice and neutralized with ammonium hydroxide. The precipitate was removed by filtra-

tion, dried, and crystallized from petroleum ether (bp 60–70°). The yield of pure product, melting at 61–62°, was 13 g (79.3%).

*Anal.* Calcd for  $C_{10}H_7N_2Cl$ : C, 62.98; H, 4.12. Found: C, 62.68; H, 3.91.

**6-Bromo-2,2'-bipyridine.**—To 3.4 ml of ice-cold phosphorus tribromide was added 2.3 ml of bromine, followed by 50 g of phosphoryl bromide and 7.5 g of 1-methyl-2,2'-bipyridin-6-one. The mixture was heated at 120–130° for 2.5 hr, then poured onto ice and made alkaline with ammonium hydroxide. The dried precipitate, after crystallization from petroleum ether (bp 60–70°), melted at 70–71° (lit.<sup>3</sup> 74°). The yield was 4.5 g (47.4%).

*Anal.* Calcd for  $C_{10}H_7N_2Br$ : C, 51.06; H, 3.00. Found: C, 51.15; H, 3.12.

**6-Cyano-2,2'-bipyridine.**—A mixture of 9 g of 6-bromo-2,2'-bipyridine, 3.9 g of cuprous cyanide, and 15 ml of pyridine was heated at 140–150° for 3 hr. The contents of the flask were then poured into an excess of a concentrated solution of potassium cyanide and allowed to stand overnight. The resulting precipitate was filtered, dried, and extracted with benzene. The residue from the removal of benzene on crystallization from methanol yielded 4.5 g (65.2%) of pure product, mp 130–131° (lit.<sup>2</sup> 151°).

*Anal.* Calcd for  $C_{11}H_7N_3$ : C, 72.89; H, 3.90. Found: C, 72.76; H, 4.04.

**2,4,6-Tris(2,2',6-bipyridyl)-1,3,5-triazine.**—6-Cyano-2,2'-bipyridine (1.5 g) and sodium hydride (0.15 g) were heated at 130–140° in a test tube in absence of air for 9 hr. After cooling 5 ml of ethanol was added, and the solution was evaporated and treated with water. The precipitate, after extraction with ethanol to remove soluble material, was crystallized from dimethylformamide. The yield of pure product melting at 312–313° was 0.4 g (26.7%).

*Anal.* Calcd for  $C_{33}H_{21}N_9$ : C, 72.89; H, 3.90. Found: C, 72.97; H, 4.29.

**2,4-Diamino-6-(2,2',6-bipyridyl)-1,3,5-triazine.**—A mixture of 0.75 g of dicyanodiamide, 1.3 g of 6-cyano-2,2'-bipyridine, 0.1 g of potassium hydroxide, and 5 ml of Methyl Cellosolve was heated at 130–140° for 3 hr, and then poured into water. The resulting precipitate, on crystallization from aqueous dimethylformamide, yielded 1.6 g (72.7%) of pure dihydrate, melting at 284–285°.

*Anal.* Calcd for  $C_{13}H_{11}N_7 \cdot 2H_2O$ : C, 51.79; H, 5.01. Found: C, 51.38; H, 5.21.

Drying at 120° for 24 hr yielded the anhydrous material.

*Anal.* Calcd for  $C_{13}H_{11}N_7$ : C, 59.07; H, 4.11. Found: C, 58.85; H, 4.18.

**2-Amino-4,6-bis(2,2',6-bipyridyl)-1,3,5-triazine.**—To a cooled solution of 0.55 g of guanidine hydrochloride in 20 ml of absolute ethanol was added 0.15 g of sodium. After complete solution of the sodium, 1.8 g of 6-cyano-2,2'-bipyridine was added and the mixture was refluxed for 20 hr. The solution was then poured into water, and the precipitate was removed by filtration and dried. Crystallization from dimethylformamide yielded 0.8 g (20%) of pure product melting at 318–319°.

*Anal.* Calcd for  $C_{23}H_{16}N_8$ : C, 68.28; H, 3.99. Found: C, 68.05; H, 4.12.

**Hydrazidine of 6-Cyano-2,2'-bipyridine.**—A mixture of 1.6 g of 6-cyanobipyridine, 5 ml of ethanol, and 5 ml of 95% hydrazine was stirred at room temperature for 2.5 hr. The contents of the flask were then poured into water, and the resulting precipitate was removed by filtration and dried. Crystallization from benzene yielded 1.1 g (57.9%) of product melting at 155–156°.

*Anal.* Calcd for  $C_{11}H_{11}N_5$ : C, 61.97; H, 5.21. Found: C, 62.25; H, 5.46.

**3-(2,2',6-Bipyridyl)-5,6-diphenyl-*as*-triazine.**—A mixture of 1 g of the hydrazidine of 6-cyano-2,2'-bipyridine and 1 g of benzil in 25 ml of ethanol was refluxed for 2 hr. It was then poured into water, and the precipitate was removed by filtration and dried. Crystallization from ethanol yielded 1.6 g (88.9%) of triazine melting at 184–185°.

*Anal.* Calcd for  $C_{25}H_{17}N_5$ : C, 77.48; H, 4.43. Found: C, 77.48; H, 4.66.

**3-(2,2',6-Bipyridyl)-5,6-bis(2-pyridyl)-*as*-triazine.**—A solution of 1 g of the hydrazidine of 6-cyano-2,2'-bipyridine and 1.3 g of pyridil in 20 ml of ethanol was allowed to stand overnight. The resulting precipitate was removed by filtration, dried, and crystallized from methanol. The yield of triazine was 1.2 g (66.7%) melting at 164–165°.

*Anal.* Calcd for  $C_{23}H_{15}N_7$ : C, 70.92; H, 3.88. Found: C, 71.07; H, 4.08.

(5) F. H. Westheimer and O. T. Benfey, *J. Am. Chem. Soc.*, **78**, 5309 (1956).

**3-(2,2',6-Bipyridyl)-as-triazino[5,6-f][4,7]-phenanthroline.**—A mixture of 1 g of 6-cyano-2,2'-bipyridine hydrazidine, 1 g of 4,7-phenanthroline-5,6-dione, and 30 ml of ethanol was refluxed 3 hr. The contents of the flask were then poured into water, and the precipitate was removed by filtration, dried, and crystallized from dimethyl sulfoxide, yielding 1.2 g of product melting at 369–370° (57.1%). An analytical sample, melting at 372°, was prepared by crystallization from dimethylformamide.

*Anal.* Calcd for C<sub>23</sub>H<sub>13</sub>N<sub>7</sub>: C, 71.28; H, 3.88. Found: C, 71.66; H, 3.69.

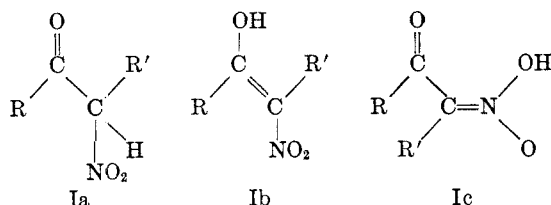
### The Structure of $\alpha$ -Nitro Ketones

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Based on work done in 1914<sup>1</sup> it has been thought that  $\alpha$ -nitro ketones could best be represented by three tautomeric structures, Ia, b, and c.<sup>2</sup> This early work done by bromine titration indicated that  $\alpha$ -nitroaceto-



R = alkyl or aryl; R' = alkyl or H

phenone existed in solution as a mixture of material of ketonic and enolic structures. The compound was found to be most enolic in toluene (10.3%) and least so in aqueous methanol (2.7%).

Using spectral techniques Campbell and Pitzer<sup>3</sup> have shown that 2-nitro-1-indanone is isolable as a pure nitro enol. These authors found that the pure enol partially isomerized on standing to a mixture of nitro ketone and nitro enol. Schaub, *et al.*,<sup>4</sup> have determined that 2 $\alpha$ -nitro-17 $\beta$ -hydroxy-17 $\alpha$ -methyl-5 $\alpha$ -androstan-3-one and 2 $\alpha$ -nitro-17 $\beta$ -hydroxy-5 $\alpha$ -androstan-3-one are mixtures of material of nitro ketone and nitro enol structure. In addition, these workers showed that due to steric interactions the corresponding 4-nitro-3-keto and 16-nitro-17-keto steroids were not enolic. We would like to present data which demonstrates that in general acyclic  $\alpha$ -nitro ketones exist in neutral media in the nitro ketone form Ia and that  $\alpha$ -nitrocyclohexanone, representative of the cyclic compounds, which was isolatable in the nitro ketone form, isomerizes under mild conditions to a mixture of tautomers.

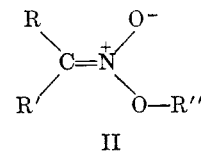
The proton magnetic resonance (pmr) spectra<sup>5</sup> of 1-nitro-2-pentanone, 2-nitro-3-pentanone, and 3-methyl-3-nitrobutanone in carbon tetrachloride of  $\alpha$ -nitro-

acetophenone and  $\alpha$ -nitrocyclohexanone<sup>6</sup> in deuteriochloroform and of  $\alpha$ -nitroacetophenone in benzene show only the presence of material of nitro ketone structure. The neat pmr spectra of 1-nitro-2-pentanone, 2-nitro-3-pentanone, and  $\alpha$ -nitropropiophenone also give no indication of the presence of enol or *aci*-nitro species in the system. In Table I is given the pmr data on the several  $\alpha$ -nitro ketones.

The infrared spectra of the  $\alpha$ -nitro ketones also indicated that only material of nitro ketone structure was present. The spectra were run neat and in carbon tetrachloride solution. In neither case was any absorption due to enolic OH observed, no absorption being found below 3.2  $\mu$ . The principal absorptions of the compounds occurred at 5.76  $\mu$  ( $\epsilon \sim 300$ ) and 6.41  $\mu$  ( $\epsilon \sim 800$ ). These bands are assignable to the carbonyl stretching and the asymmetric nitro stretching vibrations of the molecules. The locations and intensities of these bands were unaltered in going from primary to secondary to tertiary  $\alpha$ -nitro ketones.

Isomerization of  $\alpha$ -nitrocyclohexanone was carried out either by heating [vacuum distillation at  $\sim 100^\circ$  (0.1 mm)] or by passing the compound through a silica gel column. The other nitro ketones were stable to both the distillation and chromatography conditions. In addition, treatment of the acyclic nitro ketones with excess aqueous sodium hydroxide or excess triethylamine in carbon tetrachloride did not cause isomerization. The compounds were recovered unchanged.

In agreement with other workers<sup>3,4</sup> the infrared spectrum of the cyclic enol showed strong absorption at 6.14  $\mu$  and weak absorption at 6.55  $\mu$ . Though the 6.14- $\mu$  band has been assigned<sup>3,4</sup> to olefin absorption it is equally consistent with C=N absorption. Kornblum<sup>7</sup> has found that nitronic esters II absorb in the region 6.05–6.2  $\mu$  and therefore no definite conclusion



R, R' = H, alkyl or aryl; R'' = alkyl

as to enol structure of the  $\alpha$ -nitro ketones can be drawn. The pmr spectrum of the tautomeric mixture shows sharp absorption at  $\tau - 3.93$ . This has been assigned<sup>4</sup> to the OH proton of the nitro enol but is equally consistent with the *aci*-nitro ketone structure; *via* pmr the mixture was determined to be 30.6% enol.

The isomerization of the cyclic  $\alpha$ -nitro ketone to an enolic structure is best interpreted in terms of the instability of the cyclic  $\alpha$ -nitro ketone rather than to the stability of the enol. Stuart-Briegleb models indicate that there is severe crowding of the nitro and carbonyl groups in the boat and both chain conformers of the molecule; enolization alleviates this. Enolization also decreases the unfavorable electrostatic interactions between the two polar functionalities.

That the acyclic  $\alpha$ -nitro ketones do not substantially exist in a stable enolic form is interpretable in terms of the known weak hydrogen bonding ability of aliphatic nitro compounds. It has been shown *via* infrared and ultraviolet spectra that aliphatic nitro groups form

- (1) K. H. Meyer and P. Wertheimer, *Ber.*, **47**, 2374 (1914).
- (2) G. W. Wheland, "Advanced Organic Chemistry," John Wiley and Sons, Inc., New York, N. Y., 1949, p 633.
- (3) R. D. Campbell and C. L. Pitzer, *J. Org. Chem.*, **24**, 1531 (1959).
- (4) R. E. Schaub, W. Fulmor, and M. J. Weiss, *Tetrahedron*, **20**, 373 (1964).
- (5) It is estimated that an enol concentration of  $>1\%$  would have been observable in both the pmr and infrared spectra. We have determined by neat pmr spectra that ethyl acetoacetate contains 7.5% enol. This is in excellent agreement with Burdett and Rogers [J. L. Burdett and M. T. Rogers, *J. Am. Chem. Soc.*, **86**, 2105 (1964)] who determined the compound to be 8% enolic.

- (6) The pure nitro ketone isomer.
- (7) N. Kornblum and R. A. Brown, *J. Am. Chem. Soc.*, **86**, 2681 (1964).