[CONTRIBUTION FROM STANFORD RESEARCH INSTITUTE AND VARIAN ASSOCIATES]

# Identities of Ethyl Benzoylacetate 2,4-Dinitrophenylhydrazone and Its Derived Pyrazolone. Absolute Configuration of *syn* and *anti* Isomers

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Neither ethyl benzoylacetate 2,4-dinitrophenylhydrazone nor its cyclization product, the corresponding pyrazolone, has been correctly identified in the literature. The present work establishes these identities and the absolute configurations of the *syn* and *anti* isomers of the 2,4-dinitrophenylhydrazone. The argument rests on spectrometric evidence for coplanarity in the *anti* form and steric interference with coplanarity in the *syn* form.

The ease and the convenience by which deeply colored, high melting, crystalline 2,4-dinitrophenylhydrazones of aldehydes and ketones may be prepared often make them derivatives of choice for characterization. Unfortunately polymorphism and stereoisomerism occur frequently enough to warrant a *caveat.*[1] Characterization of β-keto esters with 2,4-dinitrophenylhydrazine under the usual strongly acidic conditions presents two additional hazards—decarboxylation, and cyclization to pyrazolones.

In the course of earlier work[2] we treated ethyl benzoylacetate at room temperature with a 2,4-dinitrophenylhydrazine reagent[3] and obtained a product which on recrystallization from acetic acid melted at 163–164° and had a correct analysis for a 2,4-dinitrophenylhydrazone plus a mole of acetic acid of crystallization. Recrystallization from ethanol–ethyl acetate followed by drying at 78° (1 mm.) gave a compound which melted at 164–166° and which gave the expected analytical values for the nonsolvated 2,4-dinitrophenylhydrazone. The infrared ($\lambda_{max}^{CHCl_3}$ 3.05 μ and 5.77 μ) and NMR spectra (Fig. 1b) were in accord with the postulated structure. The ultraviolet absorption peak was at 378 mμ.

The identity of the product was of some concern because it was also obtained by treating ethyl thiobenzoylacetate with 2,4-dinitrophenylhydrazine.[2] The literature reported that the 2,4-dinitrophenylhydrazone of ethyl benzoylacetate melted at 222–223°[4] or at 246–247°[5] and absorbed maximally in chloroform at 379 mμ.[5] As a further complication, a more recent report by Khromos-Borisov[6] described the product of reaction between ethyl benzoylacetate and 2,4-dinitrophenylhydrazine as a pyrazolone, m.p. 160–161°.

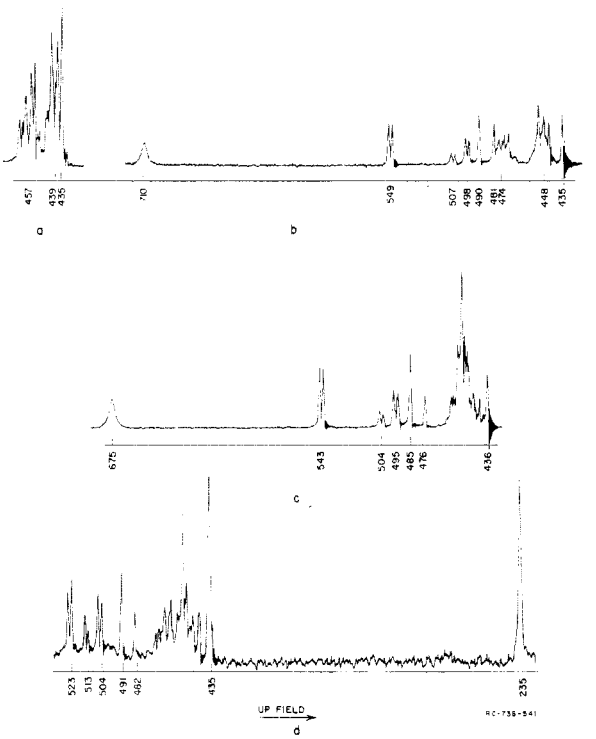



Fig. 1. NMR spectra

a. 2,4-DNP of acetophenone
b. 2,4-DNP of ethyl benzoylacetate (stable)
c. 2,4-DNP of ethyl benzoylacetate (unstable)
d. 1-(2,4-Dinitrophenyl)-3-phenyl-5-pyrazolone

It seems likely that the high melting derivative (246–247°) was the 2,4-dinitrophenylhydrazone of acetophenone resulting from decarboxylation. In fact, the properties of the authentic acetophenone derivative (m.p. 247–248°, $\lambda_{max}^{CHCl_3}$ 378 mμ) reported in the same paper[5] were almost identical with those for the compound purported to be the ethyl benzoylacetate derivative. Incomplete decarboxylation probably accounts for the melting point given[4] as 222–223°. The procedure of Khromos-Borisov[6] afforded us a product which melted at 163–164°, gave no melting point depression on admixture with our sample (m.p. 164–166°), and gave an infrared spectrum identical with that of our sample.

Attempts to cyclize the 2,4-dinitrophenylhydrazone of ethyl benzoylacetate under acidic condi-

(1) For a recent review of 2,4-dinitrophenylhydrazones, see M. E. Umstead (Penn State) Dissertation Abstract Vol. XVII No. 5, Publ. No. 20,982, microfilm 57-1520, University Microfilms, Ann Arbor, Mich.

(2) Z. Reyes and R. M. Silverstein, *J. Am. Chem. Soc.*, **80**, 6367, 6373 (1958).

(3) R. L. Shriner and R. C. Fuson, *Systematic Identification of Organic Compounds*, John Wiley & Sons, New York, N. Y., 1948, p. 171.

(4) N. R. Campbell, *Analyst*, **61**, 391 (1936).

(5) G. D. Johnson, *J. Am. Chem. Soc.*, **75**, 2720 (1953).

(6) M. V. Khromos-Borisov, *Zhurn. Obshchei Khemii*, **25**, 136 (1955).

tions were unsuccessful; under forcing conditions, the 2,4-dinitrophenylhydrazone of acetophenone (m.p. 247–249°) was obtained. Rapid cyclization to the desired 1-(2,4-dinitrophenyl)-3-phenyl-5-pyrazolone was effected with sodium ethoxide in ethanol at room temperature. The pyrazolone melted at 203–204° and gave the required analytical values. There was no N–H absorption in the 3.0 $\mu$ region. The NMR spectrum (Fig. 1d) provided further confirmation for the identity of the pyrazolone.

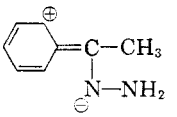
Addition of base to the 2,4-dinitrophenylhydrazone of ethyl benzoylacetate immediately produced the deep magenta color of the anion. Disappearance of the color concomitant with cyclization afforded a convenient measure of rate of reaction. It should also afford a method for determining absolute configuration if the other isomer could be isolated, and if the rate of cyclization were faster than the rate of isomerization. The isomer in which the benzene ring and the 2,4-dinitro-substituted benzene ring are in the *syn* configuration must undergo isomerization prior to cyclization.

There are not very many reported instances of isolation of *syn* and *anti* isomers of 2,4-dinitrophenylhydrazone derivatives, and those usually depended either on the absence of an $\alpha$-hydrogen as in substituted benzophenones, or on the presence of a group with which the NH group can effect hydrogen bonding and consequent stabilization of one isomer.[1,7] We were also aware that 2,4-dinitrophenylhydrazine derivatives undergo enolization at rates many times greater than those of parent ketones[1]; and the lability of $\beta$-keto-esters would argue against the likelihood of isolating both forms of the 2,4-dinitrophenylhydrazone of ethyl benzoylacetate. However, the *syn* and *anti* isomers of the 2,4-dinitrophenylhydrazone acetophenone had been prepared[6] by heating the reactants in the absence of acid. Attempts to use this technique with ethyl benzoylacetate failed, but exposure of a benzene solution of the 2,4-dinitrophenylhydrazone to sunlight over a period of two weeks yielded a small amount of lower-melting (121–122.5°) orange material whose infrared spectrum (in chloroform) differed from that of the starting material only beyond 6 $\mu$, and whose ultraviolet absorption maximum (in chloroform) occurred at 364 m$\mu$—*i.e.*, a hypsochromic shift of 14 m$\mu$. The maximum yield of low melting isomer was 5%. The low melting (unstable) form could be converted to the high melting (stable) form by acid catalysis, and there was virtually no detectable amount of the unstable form at equilibrium.

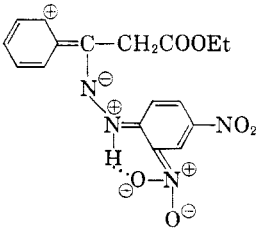
Reaction rate studies were carried out by adding excess sodium ethoxide in absolute ethanol to an absolute ethanolic solution of each isomer, and following the rate at which the absorption peak decreased. A clean pseudo-first-order reaction rate was obtained, and the rate constants for the stable and the unstable forms were identical ($k = 9.40 \times 10^{-3}$ sec.$^{-1}$). Obviously then, isomerization is much more rapid than cyclization, and nothing is learned about absolute configuration.

Molecular models show that coplanarity of both benzene rings and the C=N bond are possible in the *anti* configuration but sterically impossible in the *syn* (*syn* and *anti* refer to the configurations in which the benzene rings are on the same side and opposite sides of the C=N bond, respectively). The 14-m$\mu$ hypsochromic shift noted above can thus be taken as presumptive evidence for the syn configuration of the unstable form.

Nuclear magnetic resonance proved to be a remarkably informative tool for observing the effects of coplanarity or the lack of it in the system under consideration. The unsubstituted hydrazone of acetophenone[8] was prepared for orientation purposes. Its NMR spectrum (Fig. 1a) shows that resonance forms such as



contribute strongly to its structure. The shift due to reduction of electron density and magnetic anisotropy effects at the *ortho* positions is greater than that at the *meta* or *para* positions. This accounts for the down-field shifts of absorption peaks corresponding to two protons (multiplet centered on 457 cps.[9]); the remaining three protons show absorption centered on 439 cps. In the spectrum of the stable form (Fig. 1b) of the 2,4-dinitrophenylhydrazone of ethyl benzoylacetate, we find the same two groups of peaks (centered at 474 and 448 cps. respectively) separated by 26 cps. compared with 18 cps. in acetophenone hydrazone. This increased separation would appear to be the result of additional resonance stabilization from a structure such as



which is permitted only to the *anti* configuration. In contrast, the unstable isomer (Fig. 1c) shows practically no separation of *ortho* from *meta* and

(7) F. Ramirez and A. F. Kirby, *J. Am. Chem. Soc.*, **76**, 1037 (1954). D. Schulte-Frohlinde, *Ann.*, **622**, 43 and 47 (1959). H. van Duin, *Rec. trav. chim.*, **73**, 78 (1954). F. A. Isherwood and R. G. Jones, *Nature* **175**, 419 (1955).

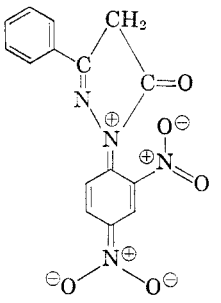
(8) H. Staudinger, *Ber.*, **49**, 1907 (1916).

(9) At 60 mc., relative to internal tetramethylsilane as reference; see Experimental.

*para* protons in the benzene ring because steric interference in the *syn* configuration between the benzene ring and the NH group prevents the necessary coplanarity.

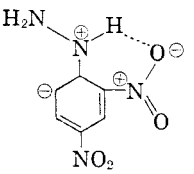
In the stable 2,4-dinitrophenylhydrazone, we also identify the doublet at 549 cps. as the proton between the two nitro groups, the pair of doublets at 507 and 498 cps. as the proton adjacent to one nitro group, and the pair of peaks at 490 and 481 cps. as the third proton on the nitro substituted ring. Looking at the peaks at 710 cps. (Fig. 1b) and at 675 cps. (Fig. 1c), which correspond to the NH proton in the stable and unstable forms respectively, we note that the strong intramolecular hydrogen bonding which leads to this large concentration-independent down-field shift is apparently weakened slightly in the unstable form presumably by steric interference between the benzene ring and the NH group. It will also be noted that, in the unstable form, all three protons on the nitro substituted ring are shifted upfield a few cycles per second. This could be due either to magnetic anisotropy of the adjacent aromatic ring or to decreased importance of electron withdrawing resonance structures.

The spectrum of 1-(2,4-dinitrophenyl)-3-phenyl-5-pyrazolone (Fig. 1d) shows that the doublet absorption peak of the proton between the two nitro groups is shifted upfield considerably (523 cps.) while those of the proton adjacent to one nitro group are shifted downfield slightly (513 and 504 cps.) and the peaks of the third proton are essentially unaffected (491 and 482 cps.). This behavior can be explained by considering the resonance form



which contributes to the structure of this molecule. The nitro group *ortho* to the pyrazolone ring is hindered by the carbonyl group; this would twist it out of the plane of the ring and diminish its tendency to withdraw electrons from the ring. Therefore, the shift of the absorption peak of the proton between the nitro groups would be decreased. On the other hand, if one of the nitro groups were unable to engage in resonance, the other would encounter less competition and should be more heavily involved than usual; this interpretation would account for the downfield shift of the other proton adjacent to it. Evidence for appreciable contribution to the structure by the resonance form having a plus charge in the *ortho* positions of the unsubstituted ring is seen in the moderate downfield shift (*ca.* 465 cps.) of those *ortho* proton peaks. However, steric resistance to complete coplanarity of the three rings is apparent from comparison with the greater shift noted above in the stable form of the 2,4-dinitrophenylhydrazone compound.

The spectrum of 2,4-dinitrophenylhydrazine itself shows essentially the same pattern for the three protons on the nitro substituted ring as was found for the 2,4-dinitrophenylhydrazones. The proton *ortho* to the hydrazine nitrogen is, however, shifted upfield about 18 cps., and this suggests that the resonance structure



is perhaps somewhat more important in this molecule than in the 2,4-dinitrophenylhydrazones.

In view of the discrepancies in the literature[4-6] regarding the identity of the 2,4-dinitrophenylhydrazone of ethyl benzoylacetate and the pyrazolone derived therefrom, we note the presence in the 2,4-dinitrophenylhydrazone spectra of the NH peak (described above) and of the ethoxy proton peaks, $CH_2$ centered at about 249 cps. and $CH_3$ at about 75 cps. (off-scale in the Figures). None of these peaks appears in the pyrazolone spectrum. Although tautomeric forms for pyrazolone rings are frequently written,[10] the absence of NH or OH peaks in both the NMR and infrared spectra argues against appreciable equilibrium concentration of these forms in this compound. Furthermore, the ratio of the peak areas of the $CH_2$ protons (235 cps.) to the peak areas of the protons on the nitro substituted ring is in accord with the structure as written above.

## EXPERIMENTAL

Visible and ultraviolet spectra and kinetic data were obtained on a Cary recording spectrophotometer model 14M. Infrared spectra were obtained on a Beckman spectrophotometer model IR 4. The proton nuclear magnetic resonance spectra were obtained on a Varian Associates high resolution 60 mc. spectrometer. Samples were dissolved in deuterated chloroform (traces of chloroform account for the peak at 435 cps.) containing tetramethylsilane as an internal reference standard. Shifts were measured in cycles per second relative to the reference.

Kinetic runs were carried out at 25° as follows: Approximately 5 mg. of the 2,4-dinitrophenylhydrazone was dissolved in 100 ml. of a 20% benzene-80% absolute ethanol solution. To 2 ml. of this solution contained in a 1 cm. cell, 1 ml. of a solution of 1.90 g. of sodium in 100 ml. of absolute ethanol was added with a syringe. The cell was quickly shaken and placed immediately in the spectrophotometer set at the predetermined absorption peak. Log $A_0/A_t$ was

(10) G. de Stevens, A. Halamandaris, P. Wenk, and L. Dorfman, *J. Am. Chem. Soc.*, **81**, 6292 (1959).

plotted against time (sec.). The following tabulation presents crude data from a typical run:

ETHYL BENZOYLACETATE 2,4-DINITROPHENYLHYDRAZONE (STABLE)

$\lambda_{max}$ 550 m$\mu$, $A_o$ 2.25

| Time, sec. | 20 | 40 | 60 | 80 | 100 | 120 | 140 |
|---|---|---|---|---|---|---|---|
| $A_t$ | 1.92 | 1.57 | 1.28 | 1.06 | 0.90 | 0.75 | 0.65 |

*2,4-Dinitrophenylhydrazone of ethyl benzoylacetate* (stable). To a solution at room temperature of 6.5 g. (33.8 mmoles) of ethyl benzoylacetate in 25 ml. of 95% ethanol was added sufficient reagent (prepared according to Shriner and Fuson[3]) to furnish an equimolar amount of 2,4-dinitrophenylhydrazine. Precipitation occurred within a minute. The precipitate was filtered after 2 hr. at room temperature, washed with ethanol, and recrystallized from ethanol–ethyl acetate. Yield of orange crystals 10.7 g. (85%), m.p. 161.5–163.5°. An analytical sample was recrystallized from glacial acetic acid and air dried, m.p. 163–164°.

*Anal.* Calcd. for $C_{17}H_{16}O_6N_4 \cdot C_2H_4O_2$: C, 53.0; H, 4.64; N, 13.0. Found: C, 53.3, 53.2; H, 4.82, 4.61; N, 13.2, 13.3.

It was recrystallized from ethanol–ethyl acetate and dried overnight at 78° (1 mm.), m.p. 164–166°, $\lambda_{max}^{CHCl_3}$ 378 m$\mu$ ($\epsilon$ = 27,500), 241 m$\mu$ ($\epsilon$ = 16,350); $\lambda_{max}^{CHCl_3}$ 3.05 $\mu$ (NH), 5.77 $\mu$ (ester C = O). Peaks at 6.93 $\mu$ and 9.05 $\mu$ are present in the stable, but not present or very weak in the unstable form.

*Anal.* Calcd. for $C_{17}H_{16}O_6N_4$: C, 54.8; H, 4.33; N, 15.0. Found: C, 54.8; H, 4.50; N, 15.0.

*2,4-Dinitrophenyl hydrazone of ethyl benzoylacetate* (unstable form). Saturated solutions of the stable form of the 2,4-dinitrophenylhydrazone of ethyl benzoylacetate in benzene were exposed in borosilicate glass flasks to sunlight over a period of 2 weeks. The solvent was removed *in vacuo*, and the residue was extracted with two 5-ml. portions of 95% ethanol. The ethanolic solution was evaporated *in vacuo*, and the residue was recrystallized four times from benzene–petroleum ether (b.p. 65–110°). The best yield was 5% of orange crystals, m.p. 121–122.5°. $\lambda_{max}^{CHCl_3}$ 364 m$\mu$ ($\epsilon$ = 24,760); 257 m$\mu$ ($\epsilon$ = 13,380); $\lambda_{max}^{CHCl_3}$ 3.05 $\mu$ (NH), 5.77 $\mu$ (C = O). A peak at 9.28 $\mu$ is present in the unstable form, but absent in the stable.

*Anal.* Calcd. for $C_{17}H_{16}O_6N_4$: N, 15.0. Found: N, 15.2.

*Conversion of unstable to stable isomer.* A solution of 2 mg. of the 2,4-dinitrophenylhydrazone of ethyl benzoylacetate in 2 ml. of 95% ethanol containing a droplet (approx. 20 mg.) of concd. hydrochloric acid was boiled for 1 min. Removal of the solvent *in vacuo* left a residue which melted at 160–163° and gave an ultraviolet spectrum identical with that of the stable form. Thermal isomerization was relatively slow; thus a melt held at 140° took about 15 min. to resolidify so that remelting occurred at about 155–161°.

*1-(2,4-Dinitrophenyl)-3-phenyl-5-pyrazolone.* To a solution of 0.100 g. (0.260 mmole) of the 2,4-dinitrophenylhydrazone of ethyl benzoylacetate in a mixture of 3 ml. benzene and 1 ml. of absolute ethanol at room temperature was added 0.5 ml. of a solution of 2.55 g. of sodium in 100 ml. of absolute ethanol. After 15 min. at room temperature, the solution was acidified with glacial acetic acid, and petroleum ether (b.p. 30–65°) was added until precipitation was complete. The precipitate was recrystallized twice from benzene–petroleum ether. Yield of light yellow crystals was 0.062 g. (71%), m.p. 203–204°. $\lambda_{max}^{CHCl_3}$ 350 m$\mu$ ($\epsilon$ = 10,800), 300 m$\mu$ ($\epsilon$ = 16,000); $\lambda_{max}^{CHCl_3}$ 5.86 $\mu$ (C = O), no peak at 3 $\mu$.

*Anal.* Calcd. for $C_{15}H_{10}O_5N_4$: N, 17.2. Found: N, 17.5.

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[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, DUKE UNIVERSITY]

# The Synthesis of 2-Aza-1,2-dihydrodicyclopentadienes[1,2]

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The synthesis of the isomeric *endo*- and *exo*-2-aza-1,2-dihydrodicyclopentadienes and several *N*-alkyl derivatives is described.

The facile rearrangement of *endo*-dicyclopentadiene and its 1,2-dihydro derivative (I) to 9-substituted *exo* compounds by addition of halogen acids, sulfuric acid, acetic acid, or formic acid has been fully demonstrated.[3–5] Recently a study of 2-oxa-1,2-dihydro-*endo*-dicyclopentadiene (II) has indicated that under similar conditions, addition of acids to the norbornylene double bond leads to little or no structural rearrangement.[6] An investigation of the effects of a nitrogen atom in the 2-position of 1,2-dihydro-*endo*-dicyclopentadiene upon reactions with acidic reagents[7] has lead to the synthesis of several 2-aza derivatives. Only three *N*-alkylated derivatives of 2-aza-1,2-dihydro-*endo*-

(1) Presented in part before the Division of Organic Chemistry, 135th National Meeting of the American Chemical Society, Boston, Mass., April 5–10, 1959.

(2) Taken in part from a dissertation submitted by Chicita F. Culberson to the Graduate School of Duke University in partial fulfillment of the requirements for the Ph.D. degree (1959).

(3) P. D. Bartlett and A. Schneider, *J. Am. Chem. Soc.*, **68**, 6 (1946).

(4) H. A. Bruson and T. W. Riener, *J. Am. Chem. Soc.*, **67**, 723, 1178 (1945); *J. Am. Chem. Soc.*, **68**, 8 (1946).

(5) P. Wilder, Jr., Chicita F. Culberson, and G. T. Youngblood, *J. Am. Chem. Soc.*, **81**, 655 (1959).

(6) Chicita F. Culberson, J. H. Seward, and P. Wilder, Jr., *J. Am. Chem. Soc.*, **82**, 2541 (1960).

(7) P. Wilder, Jr. and Chicita F. Culberson, *J. Am. Chem. Soc.*, **81**, 2027 (1959).