4-*O*-Acetyl-1,5-anhydro-2-*O*-benzoyl-3-oxo-L-*arabino*-pentitol (105). Oxidation of **104** with pyridinium chlorochromate followed a procedure identical with that used in the preparation of **80**. The yield was 80%. ^{1}H NMR ($CDCl_3$) δ 8.06 (2 H, d, J = 8.0, ortho H's), 7.59 (1 H, t, J = 7.4, para H), 7.45 (2 H, dd, J = 8.0, 7.4, meta H's), 5.61 (1 H, dd, J = 6.1, 4.5, 2-H), 5.46 (1 H, dd, J = 6.3, 4.3, 4-H), 4.15 (1 H, dd, J = 12.0, 4.5, 1-H), 4.10 (1 H, dd, J = 12.1, 4.3, 5-H), 4.08 (1 H, dd, J = 12.0, 6.1, 1-H), 3.96 (1 H, dd, J = 12.1, 6.3, 5-H), 2.18 (3 H, s, CH_3C=O). ^{13}C NMR ($CDCl_3$) δ 196.6 (C-3), 169.3 (CH_3C=O), 165.0 (PhC=O), 133.7, 130.0, 128.8, 128.6 (Ar C's), 75.0, 74.7, 71.6, 71.5 (C-1,2,4,5), 20.6 (CH_3C=O). The hydrate form of **105** was also detected by NMR. ^{1}H NMR ($CDCl_3$) of the hydrate form: δ 8.05 (2 H, d, J = 8.0, ortho H's), 7.57 (1 H, t, J = 7.4, para H), 7.43 (2 H, dd, J = 8.0, 7.4, meta H's), 5.26 (1 H, dd, J = 5.7, 3.3, 2-H), 5.09 (1 H, dd, J = 6.7, 3.7, 4-H), 3.99-3.87 (2 H, m, 1-H, 5-H), 3.79 (1 H, dd, J = 11.8, 5.7, 1-H), 3.64 (1 H, dd, J = 11.6, 6.7, 5-H), 2.18 (3 H, s, CH_3C=O). ^{13}C NMR ($CDCl_3$) of the hydrate form: δ 171.1 (CH_3C=O), 166.7 (PhC=O), 133.8, 130.1, 129.4, 128.7 (Ar C's), 92.7 (C-3), 72.9, 72.2, 67.1, 66.8 (C-1,2,4,5), 21.1 (CH_3C=O).

4-*O*-Acetyl-1,5-anhydro-2-*O*-benzoyl-3-oxo-L-*arabino*-pentitol (*p*-Tolylsulfonyl)hydrazone (55). This compound was prepared from **105** based on the coupling described in the general procedures. Both syn and anti isomers (2:1) were obtained and separated by flash chromatography (25% EtOAc/hexane). The total yield was 90%. ^{1}H NMR ($CDCl_3$) of the major isomer: δ 9.35 (1 H, b s, NH), 8.04 (2 H, d, J = 7.3, ortho H's), 7.65 (1 H, t, J = 7.1, para H), 7.52 (2 H, dd, J = 7.3, 7.1, meta H's), 7.43, 6.88 (2 H each, d, J = 8.2, Ts H's), 5.65 (1 H, dd, J = 10.8, 6.2, 2-H), 5.26 (1 H, b s, 4-H), 4.28 (1 H, dd, J = 10.8, 6.2, 1-H), 4.15 (1 H, d, J = 13.0, 5-H), 3.72 (1 H, dd, J = 13.0, 1.6, 5-H), 3.65 (1 H, t, J = 10.8, 1-H), 2.30 (3 H, s, Ts-Me), 2.12 (3 H, s, CH_3C=O). ^{13}C NMR ($CDCl_3$) of the major isomer: δ 172.0 (CH_3C=O), 164.8 (PhC=O), 146.9 (C-3), 143.8, 133.6, 130.0, 129.4, 129.2, 128.5, 128.1 (Ar C's), 70.3, 69.9, 66.6, 66.5 (C-1, 2, 4, 5), 21.6 (Ts-Me), 20.5 (CH_3C=O). High-resolution FAB-MS: calcd for $C_{21}H_{23}N_2O_7S$ $(M + H)^+$ 447.1226, found 447.1222. ^{1}H NMR ($CDCl_3$) of the minor isomer: δ 9.79 (1 H, b s, NH), 8.00 (2 H, d, J = 7.8, ortho H's), 7.61 (1 H, t, J = 7.5, para H), 7.45 (2 H, dd, J = 7.8, 7.5, meta H's), 7.75, 7.23 (2 H each, d, J = 8.3, Ts H's), 5.44 (1 H, b s, 4-H), 5.41 (1 H, dd, J = 10.7, 6.3, 2-H), 4.25 (1 H, d, J = 13.2, 5-H), 4.19 (1 H, dd, J = 10.7, 6.3, 1-H), 3.76 (1 H, dd, J = 13.2, 1.9, 5-H), 3.57 (1 H, t, J = 10.7, 1-H), 2.35 (3 H, s, Ts-Me), 2.05 (3 H, s, CH_3C=O). ^{13}C NMR ($CDCl_3$) of the minor isomer: δ 169.0 (CH_3C=O), 168.0 (PhC=O), 146.2 (C-3), 144.1, 134.3, 130.2, 129.4, 128.7, 128.1, 128.0 (Ar C's), 70.2, 69.8, 66.6, 66.5 (C-1,2,4,5), 21.6 (Ts-Me), 20.5 (CH_3C=O). High-resolution FAB-MS: calcd for $C_{21}H_{23}N_2O_7S$ $(M + H)^+$ 447.1226, found 447.1195.

4-*O*-Acetyl-1,5-anhydro-2-*O*-benzoyl-3-deoxy-3-[2-(*p*-tolylsulfonyl)hydrazino]-L-*lyxo*-pentitol (70) and 4-*O*-Acetyl-1,5-anhydro-2-*O*-benzoyl-3-deoxy-3-[2-(*p*-tolylsulfonyl)hydrazino]-L-*arabino*-pentitol (71). Reduction of **55** with $NaBH_3CN$ was accomplished by the method described in the general procedures. Two products, **70** and **71**, were isolated by flash chromatography (5% EtOAc/$CHCl_3$) with a total yield of 70%. ^{1}H NMR ($CDCl_3$) of **70**: δ 8.02 (2 H, d, J = 7.3, ortho H's), 7.59 (1 H, t, J = 7.4, para H), 7.44 (2 H, dd, J = 7.4, 7.3, meta H's), 7.73, 7.25 (2 H each, d, J = 8.1, Ts H's), 6.41 (1 H, b s, NH), 5.46 (1 H, b t, J = 3.0, 2-H), 4.92 (1 H, ddd, J = 10.8, 9.7, 5.0, 4-H), 4.05 (1 H, dd, J = 10.8, 5.0, 5-H), 3.59 (1 H, d, J = 11.9, 1-H), 3.52 (1 H, buried, NH), 3.50 (1 H, dd, J = 11.9, 3.0, 1-H), 3.38 (1 H, ddd, J = 9.7, 7.4, 3.0, 3-H), 3.30 (1 H, t, J = 10.8, 5-H), 2.40 (3 H, s, Ts-Me), 2.11 (3 H, s, CH_3C=O). ^{1}H NMR ($CDCl_3$) of **71**: δ 8.08 (2 H, d, J = 7.1, ortho H's), 7.65 (1 H, t, J = 7.4, para H), 7.51 (2 H, dd, J = 7.4, 7.1, meta H's), 7.53, 6.99 (2 H each, d, J = 8.1, Ts H's), 6.27 (1 H, d, J = 2.7, NH), 5.29 (1 H, b s, 4-H), 5.10 (1 H, ddd, J = 9.6, 9.5, 5.0, 2-H), 4.09 (1 H, dd, J = 11.1, 5.0, 1-H), 3.98 (1 H, dd, J = 12.7, 2.7, 5-H), 3.57 (1 H, dd, J = 12.7, 1.6, 5-H), 3.55 (1 H, b d, J = 3.0, NH), 3.49 (1 H, dd, J = 9.6, 3.0, 3-H), 3.48-3.45 (1 H, m, NH), 3.40 (1 H, dd, J = 11.1, 9.5, 1-H), 2.31 (3 H, s, Ts-Me), 2.13 (3 H, s, CH_3C=O). ^{13}C NMR ($CDCl_3$) of **71**: δ 171.3 (CH_3C=O), 166.3 (PhC=O), 133.7-128.1 (Ar C's), 68.4, 67.8, 66.8, 63.0, 55.9 (C-1,2,3,4,5), 21.6 (Ts-Me), 21.0 (CH_3C=O). High-resolution FAB-MS: calcd for $C_{21}H_{25}N_2O_7S$ $(M + H)^+$ 449.1382, found 449.1346.

When the reduction was carried out with $NaBD_3CN$, the intensity of the 3-H peak of both **70** and **71** was diminished by 45%. This corresponds to a 45% deuterium incorporation at the imino carbon C-3.

Acknowledgment. Financial support from the National Institute of Health (Grant GM 35906) and the donors of the Petroleum Research Fund, administered by the American Chemical Society, is greatly acknowledged. H.W.L. also thanks the Camille and Henry Dreyfus Foundation for a grant awarded to Distinguished New Faculty in Chemistry and the American Cancer Society for a Junior Faculty Research Award.

Supplementary Material Available: Experimental data for **1-12, 14-25, 28-43, 51-53, 65-68,** and **106-108** (17 pages). Ordering information is given on any current masthead page.

Preparation and Absorption Spectra of Arylhydrazones from α,β-Unsaturated Carbonyl Compounds

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Substituted arylhydrazones **2-17, 19,** and **23-29** were prepared from several α,β-unsaturated carbonyl compounds and their absorption spectra examined. The dependence on concentration of certain near-infrared bands of the spectra has been associated with aggregation and appears to correlate with structural elements of the compounds in a way suggesting significant intermolecular effects, either hydrogen bonding or charge transfer or both.

Arylhydrazones are important intermediates for a number of synthetically useful transformations of carbonyl compounds,[1] such as the Fischer indole synthesis,[2] and are valuable derivatives of long-recognized merit for the characterization of aldehydes and ketones.[3] Recent work[4] has emphasized the sensitivity of these materials toward the conditions of their preparation and the importance of obtaining a better understanding of their properties; this work has further pointed out the somewhat surprising fact that much remains unknown in their chemistry. For example, some aromatic hydrazines display a high degree of

(1) Kamitori, Y.; Hojo, M.; Masuda, R.; Yoshida, T.; Ohara, S.; Yamada, K.; Yoshikawa, N. *J. Org. Chem.* **1988**, *53*, 519. See also: Kamitori, Y.; Hojo, M.; Masuda, R.; Fujitani, T.; Ohara, S.; Yokoyama, T. *J. Org. Chem.* **1988**, *53*, 129.

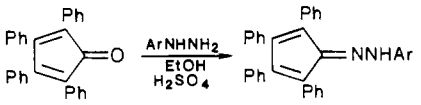
(2) Smith, P. A. S. *Derivatives of Hydrazine and Other Hydronitrogens Having N-N Bonds*; The Benjamin-Cummings Publishing Co.: Reading, MA, 1983; pp 47ff.

(3) Ault, A. *Techniques and Experiments for Organic Chemistry*, 4th ed.; Allyn and Bacon: Boston, 1983; passim.

(4) Behforouz, M.; Bolan, J.; Flynt, M. *J. Org. Chem.* **1985**, *50*, 1186.

0022-3263/89/1954-4188$01.50/0

Table I. Preparation of Tetracyclone Arylhydrazones[a]



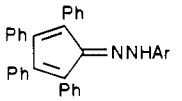
compd	Ar	yield, %	mp, °C
2	2,4-$(NO_2)_2$Ph	92	270–272
3	4-NO_2Ph	18	247–248
4	2-NO_2Ph	94	247–248
5	Ph	42	255–257
6	4-CH_3Ph	67	209–211
7	4-CH_3OPh	18	203–205

[a] All new compounds gave satisfactory elemental analyses. In each case characteristic IR bands near 1595, 1560, and 1520 cm^{-1} were observed. No attempt was made to optimize yields.

chemospecificity in their reactions with carbonyl groups,[5] condensing either with aldehydes or with ketones but not with both, although the origin of this effect is not completely clear. As part of our ongoing exploration of the controlled functionalization of hydrazines,[6] we would like to report here our results on the preparation of arylhydrazones from several α,β-unsaturated carbonyl compounds and comment on certain striking features of their absorption spectra.

Tetraphenylcyclopentadienone (tetracyclone, 1) was originally prepared by early workers for investigation as a structurally complex substrate for Diels–Alder reactions,[7] and initial reports indicated the frustrations associated with forming its arylhydrazones for characterization purposes.[8] Although precipitation of tetracyclone 2,4-dinitrophenylhydrazone **2** (Table I) in useful quantities was facilitated by an appropriate choice of solvent,[9] other members of this series have to date remained elusive. We have now developed a generally successful procedure (see the Experimental Section) for their preparation, the results of which are summarized in Tables I and II. We found that in each case the formation of the product could be conveniently monitored by noting the appearance of a new trio of characteristic infrared peaks near 1595, 1560, and 1520 cm^{-1} associated with the hydrazone moiety. The addition of aqueous sodium hydroxide to ethanolic solutions of either **2** or tetracyclone 4-nitrophenylhydrazone **3** caused major changes in the colors of the samples (**2**, yellow to blue; **3**, orange to green) with concomitant production of very strong new bands in the absorption spectra

Table II. Absorption Data for Tetracyclone Arylhydrazones



compd	Ar	UV/vis/NIR, nm
2	2,4-$(NO_2)_2$Ph	245, 393, 423, 785, 848[a]
3	4-NO_2Ph	254, 421, 805, 881[b]
4	2-NO_2Ph	250, 270, 373, 431, 765, 872[c]
5	Ph	267, 418, 773, 841
6	4-CH_3Ph	261, 428, 762, 851
7	4-CH_3OPh	264, 431, 765, 872

[a] Addition of NaOH solution caused the sample to turn from golden yellow to deep blue, with production of a very strong new band at 604 nm. Acidification or exposure to air returned the solution to its original color. [b] Addition of NaOH solution caused the sample to turn from brownish orange to deep green, with production of a very strong new band at 627 nm. Acidification or exposure to air returned the sample to its original color. [c] No change with NaOH.

(**2**, 604 nm; **3**, 627 nm). Acidification with hydrochloric acid or prolonged exposure to air returned the solutions to their original colors and the spectra to their former conditions. This effect may be associated with deprotonation–reprotonation of the hydrazone nitrogen, labilized through π resonance interaction with powerfully electron-withdrawing nitro groups and has some precedent in the case of 2,4-dinitrophenylhydrazones.[10] Of particular interest to us was the observation that tetracyclone 2-nitrophenylhydrazone **4** experienced changes in neither color nor spectrum when similarly treated with base. It appears that at least one *p*-nitro group is required for activation of the N–H bond toward base.

In preparing the hydrazones (**8**-**17**) of furanacrolein and cinnamaldehyde, several approaches were taken (see the Experimental Section), depending on the state of the starting substituted phenylhydrazines, as these were generally available commercially either as the neutral solids or as solid hydrochlorides. In either event, clean products (Tables III and IV; Experimental Section) could be very readily obtained in minutes at room temperature where care was taken to insure the complete solubilization of the reactants, either by choice of solvent or by neutralization with base or a combination of both. Thus virtually quantitative formation of **8** was observed when 2,4-dinitrophenylhydrazine reagent, prepared according to Vogel,[11] was added to furanacrolein dissolved in absolute ethanol.

In principle, the reaction of the heteroaromatic hydrazine *N*-aminophthalimide **18** with cinnamaldehyde could lead to any of three compounds: the enal hydrazone **19**, the product of Michael addition **20**, or the pyrazoline **21**. In the event, enal hydrazones **19** and **23**–**25** were isolated in generally good yields (Table V; Experimental Section) from cinnamaldehyde and its derivatives. Steric and electronic factors appeared to have determined the outcome. Thus substitution of a simple carbon-containing group at the α-position of the enal was sufficient to render the starting materials unreactive (Table V, compound **22**), although the presence of an electron-withdrawing chlorine atom (Table V, compound **23**) in the same position had

(5) Under specified conditions, *N*-aminophthalimide reacts with a variety of aldehydes but not at all with ketones. For a fuller description of the patterns of reactivity of *N*-aminophthalimide, see: Hearn, M. J.; Lucero, E. R. *J. Heterocycl. Chem.* **1982**, *19*, 1537. For a related example in which are discussed the selective reactions of ketones with *p*-hydrazinobenzenesulfonic acid in the presence of aldehydes, see: Treibs, W.; Roehnert, H. *Chem. Ber.* **1951**, *84*, 433. *N*-Aminophthalimide is acylated readily with carboxylic acid anhydrides to produce crystalline triacylhydrazines but either does not react with other standard acylating agents, such as esters, or gives an oily mixture of products, as in the case with acids and acid chlorides. See Hearn, M. J.; Prisch, S. B. *Org. Prep. Proced. Int.* **1981**, *13*, 421.

(6) Hearn, M. J.; Campbell, M. L.; Hoppe, M.; Rosenberg, J.; Sinha, A. *J. Chem. Eng. Data* **1986**, *31*, 155. Hearn, M. J.; Magee, D. J.; Alhart, R.; Gleva, M.; Goldstein, S.; Levy, F.; Muenzen, C.; Neuringer, I.; Racin, M.; Rosenberg, J.; Silva, H.; Williams, P. *J. Chem. Eng. Data* **1985**, *22*, 1405 and references cited therein for controlled functionalization reactions of hydrazines.

(7) Ziegler, K.; Schnell, B. *Liebigs Ann. Chem.* **1925**, *445*, 266. Dilthey, W.; Quint, F. *J. Prakt. Chem.* **1930**, *128*, 139.

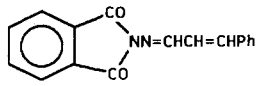
(8) Josten, W. *Ber. Dtsch. Chem. Ges.* **1938**, *71*, 2230. Josten reported that under his conditions neat phenylhydrazine gave reduction of the diene unit rather than hydrazone formation, such that the only isolated product was tetraphenylcyclopentenone, mp 162–163 °C.

(9) Sonntag, N.; Linder, S.; Becker, E.; Spoerri, P. *J. Am. Chem. Soc.* **1953**, *75*, 2283. Ogliaruso, M.; Romanelli, M.; Becker, E. *Chem. Rev.* **1965**, *65*, 261.

(10) Sawicki, E. *Photometric Organic Analysis*; Wiley-Interscience: New York, 1970; passim. Jones, L. A.; Holmes, J. C.; Seligman, R. B. *Anal. Chem.* 1956, *28*, 191.

(11) Vogel, A. I. *A Text-book of Practical Organic Chemistry*; John Wiley and Sons: New York, 1966; p 1061.

(12) *Beilstein's Handbuch der Organische Chemie*; Supplement 3/4, Volume 17, p 4699.



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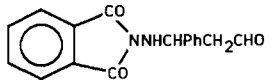

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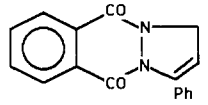

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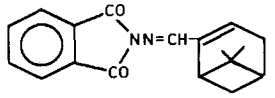
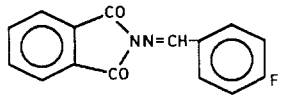
a contrary effect, leading to hydrazone formation in good yield. We propose that the lack of reactivity in the former case may be due to steric crowding and that the result in the latter case is tied to activation of the carbonyl group by the electronegative element. Our observations are consistent with the unusual sensitivity toward substrate structure previously noted for 18.[13] Both α- and β-hydrocinnamaldehydes reacted with 18 without complication to cleanly produce hydrazones 26 and 27 (Table VI); similarly straightforward condensations were observed with myrtenal and 4-fluorobenzaldehyde to yield 28 and 29, respectively (see the Experimental Section).



28



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We would like to comment on the near-infrared absorption bands of some of our compounds (Tables II and III). Although the application of near-infrared spectrometry to structural problems in organic chemistry is still in its nascent stage, the technique may have potential for the determination of intermolecular effects.[18] In spite of the early experiments of Wulf and Liddel[14] suggesting the absorptive richness of the near-infrared (NIR) spectra of arylhydrazines, not much work has subsequently been done to explore these materials and their derivatives. For saturated solutions in ethanol, we have now found that each of our compounds displays a strong broad peak in the 800-nm region (log ϵ ca. 5), in line with our preliminary observation of such bands in the spectra of certain other heterocyclic hydrazones.[6] Several facts lead us to associate the broad 800-nm peak with significant intermolecular effects, either hydrogen bonding or charge transfer or both. The absorption appears to be a function of the nature of substituent groups, especially where the latter are capable of inducing considerable polarization of the molecule by interaction through π bonds. This is particularly pronounced for the nitro compounds. Thus, among the cinnamaldehyde derivatives, compound 11 (X = Ph, Y = H, Z = H) absorbs near 760 nm, whereas 13 (X = Ph, Y = H, Z = NO_2) has a peak at 829 nm, a substantial difference which we ascribe to the polarizing influence of the strong electron-withdrawing nitro group acting through the π-bonding system. Experimentalists have long sought correlations between chemical constitution and absorption spectra. These attempts have been exemplified by Nietzki's Rule[15] and its latter-day modifications, which have generally stated that the sequential introduction of more chromophoric and auxochromic groups into a structure will increase the wavelength of absorption bands. In regard to the interesting violation of Nietzki's Rule represented by 9 (X = Ph, Y = NO_2, Zn = NO_2; λ = 788 nm) within the series of cinnamaldehyde hydrazones, the ortho substituent may hinder coplanarity of the arylhydrazino unit with the rest of the π system, reducing the polarizing influence of the nitro group overall and thereby the value of the wavelength maximum.

Reference to a simpler hydrazine model system may also be useful in understanding our spectra. We have found that the absorption spectrum of 4-nitrophenylhydrazine in ethanol has a maximum in the 800-nm region. In dilute solutions (10^{-4} M), the peak is bell-shaped and occurs near 801 nm, but at increasing concentrations (10^{-3} M or higher) the peak becomes asymmetric, and the maximum is progressively shifted to longer wavelengths, indicating the incremental dependence of the position of the wavelength maximum on concentration (see the Experimental Section for further data). Such behavior may well be a consequence of interactions allowing for aggregation, and one possible highly simplified depiction of these would have individual molecules stacked in solution, permitting intermolecular charge transfer,[16] as well as hydrogen bonding. It would be expected that as the concentration was increased, donor-acceptor interactions would be more effectively realized and the transition would move to longer wavelengths.[17]

Continuing this theme among the present arylhydrazones, we have sought other relationships between structures and spectra. Although originally used to express chemical reactivity of para-substituted benzoic acids, Hammett σ constants have also been applied to spectroscopic data with very useful outcome.[21] We have now found that the absorption maxima of discrete sets of our para-substituted compounds seem to correlate with Hammett σ values in a second-order fit (Tables II and III). In this way, compounds 10, 12, 14, and 16 in the furanacrolein family have NIR wavelength maxima as a function of σ in a curvilinear fit of order 2 with correlation coefficient of 0.99 (see the Experimental Section for regression method), consistent with intermolecular aggregation. Compounds 11, 13, 15, and 17 within the cinnamaldehyde series

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(14) Wulf, O.; Liddel, U. *J. Am. Chem. Soc.* **1933**, *55*, 3574. Wulf, O.; Liddel, U. *J. Am. Chem. Soc.* **1935**, *57*, 1464.

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(16) Rohatgi, K. K.; Mukhopadhyay, A. K. *J. Phys. Chem.* **1972**, *76*, 3970. Despite much impressive work by numerous researchers, the literature seems to lack an agreed-upon overall explanation of the relationship between aggregation and charge transfer. For an extremely useful summary of aggregation effects on the spectra of such cationic xanthene dyes as Rose Bengal, see: Neckers, D. C.; Gupta, S. N. *J. Org. Chem.* **1987**, *52*, 936.

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(18) Symposium on Spectroscopy in Agricultural Chemistry, Session in NIR Spectroscopy in Agriculture, 40th Southeast Regional Meeting of the American Chemical Society, Atlanta, GA, November 9–11, 1988. McClure, W. F., Abstract No. 60. Carreira, L. A., Abstract No. 61; Barton, F. E., II, Abstract No. 62. Wetzel, D. L., Abstract No. 63. Murray, I., Abstract No. 64.

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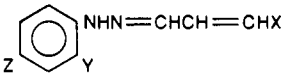
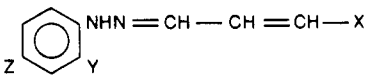
Table III. Arylhydrazones of Furanacrolein and Cinnamaldehyde[a]



compd	X	Y	Z	mp, °C	UV/vis/NIR, nm
8	2-furyl	NO_2	NO_2	218[b]	251, 318, 400, 803
9	phenyl	NO_2	NO_2	255–256[c]	245, 266, 305, 391, 788
10	2-furyl	H	H	125–127[d]	258, 303, 370, 764
11	phenyl	H	H	167–169[e]	258, 286, 368, 760
12	2-furyl	H	NO_2	181–183	309, 332, 421, 839
13	phenyl	H	NO_2	191–193[f]	243, 296, 340, 414, 829
14	2-furyl	H	CH_3	124	261, 304, 375, 766
15	phenyl	H	CH_3	144–147	262, 277, 374, 765
16	2-furyl	H	Cl	120–122	264, 320, 372, 761
17	phenyl	H	Cl	130–132	262, 281, 368, 758

[a] All new compounds gave satisfactory elemental analyses. [b] Literature mp [ref 25] 215 °C. [c] Literature mp [ref 26] 255 °C. [d] Literature mp [ref 22] 125–126 °C. [e] Literature mp [ref 26] 168 °C. [f] Literature mp [ref 26] 195 °C.

Table IV. IR Data for Arylhydrazones of Furanacrolein and Cinnamaldehyde



compd	X	Y	Z	infrared bands, cm^{-1}
8	2-furyl	NO_2	NO_2	3282, 1732, 1617, 1312
9	phenyl	NO_2	NO_2	3292, 1710, 1594, 1307
10	2-furyl	H	H	3305, 1598, 1306
11	phenyl	H	H	3308, 1602, 1310
12	2-furyl	H	NO_2	3315, 1603, 1310
13	phenyl	H	NO_2	3318, 1595, 1305
14	2-furyl	H	CH_3	3305, 1616, 1303
15	phenyl	H	CH_3	3296, 1615, 1306
16	2-furyl	H	Cl	3319, 1602, 1290
17	phenyl	H	Cl	3308, 1601, 1296

have maxima appearing to correlate with σ in a second-order fit, with a correlation coefficient of 0.99.

Among the tetracyclone derivatives, two NIR maxima are typically apparent. Compounds **3**, **5**, **6**, and **7** have broad NIR maxima at longer wavelengths correlating with σ in a second-order fit (coefficient 0.99). On the other hand, the same tetracyclone phenylhydrazones have sharp NIR maxima at shorter wavelengths correlating with σ in a fit which is first order (coefficient 0.99). One interpretation of the latter results is that two entities may be responsible for the observed maxima: one at shorter wavelength corresponding to an absorption by an aggregate of comparatively low order, possibly unimolecular, and a second concentration-dependent absorption, substantially shifted to longer wavelengths and due to a higher order polymolecular aggregate.

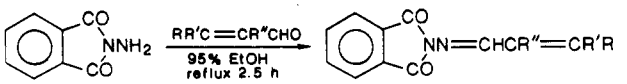
In summary, our results indicate that the preparation of arylhydrazones from several α,β-unsaturated carbonyl compounds is dependent to a significant degree on the structural characteristics of the parent compounds and the experimental conditions which these characteristics dictate. The dependence on concentration of the near-infrared bands of the absorption spectra of the hydrazones has been associated with aggregation and appears to correlate with structural elements of the compounds in a way suggesting significant intermolecular effects, either charge transfer or hydrogen bonding or both.

Experimental Section

Combustion analyses were performed by Galbraith Laboratories, Knoxville, TN. Analyses were obtained for all new compounds and were submitted for examination by editors and reviewers. Melting points were taken in open capillary tubes using a Mel-Temp apparatus and are uncorrected. Infrared spectra were recorded on a Perkin-Elmer 1310 spectrophotometer as Nujol mulls. Ultraviolet–visible–near-infrared spectra were run on saturated solutions in ethanol using standard 10-mm cuvettes (International Crystal Laboratories) on a GCA-McPherson 707 UV–vis–NIR instrument fitted with a Cyborg data collection system. Aldehydes and arylhydrazines from Aldrich Chemical Co. were used as received, as was *N*-aminophthalimide from Fluka A.-G. The latter material was also prepared by the artful method of Drew and Hatt.[19] As a rule, prolonged reaction times, viz., more than 3 h, were avoided for *N*-aminophthalimide, since this material experiences skeletal rearrangement under such conditions, the consequences of which have been previously related.[5] Tetracyclone was freshly prepared[20] by the efficient base-catalyzed aldol condensation of diphenylacetone and benzil. Representative procedures are given below for the different kinds of arylhydrazones prepared; any exceptions or modifications for individual compounds are noted. In all cases filtration by gravity was the preferred method for isolation of crystalline samples, as this led to substantially less entrainment of reagents and solvents and thus considerably purer materials. **Safety Notes:** Gloves were worn. In general, any scale-up of small-scale preparations of compounds with relatively high proportions of nitrogen was done with due caution. No specific safety problems were associated with the methods given below.

Preparation of Arylhydrazones of Tetracyclone. Representative Procedure (Compound 5, Tetracyclone Phe-

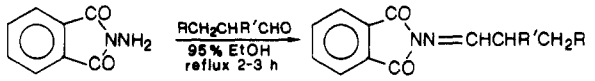
Table V. Preparation of Cinnamaldehyde Phthaloylhydrazones



compd	R	R′	R″	yield, %	mp, °C
19	Ph	H	H	78	199–200[a]
22	Ph	H	Me	no reaction	
23	Ph	H	Cl	81	193–194
24	Ph	Ph	H	50	180–182
25	2-NO_2Ph	H	H	54	255–256

[a] Literature mp [ref 5] 199–200 °C. All new compounds gave satisfactory elemental analyses and displayed the expected "signature" bands in the infrared spectrum near 1770 and 1720 cm^{-1} corresponding to the phthalimide moiety.

Table VI. Preparation of Hydrocinnamaldehyde Phthaloylhydrazones[a]



compd	R	R'	yield, %	mp, °C
26	Ph	H	39	108–109
27	H	Ph	56	93–95

[a] These new materials gave microanalytical and infrared data consistent with the proposed structures.

nylhydrazone). Tetracyclone (0.384 g, 1.00 mmol) and phenylhydrazine hydrochloride (0.448 g, 3.10 mmol) were combined in a 250-mL round bottom flask with absolute ethanol (70 mL). Concentrated sulfuric acid (4 mL) was then added dropwise, and the solution was stirred at reflux for 22.5 h. The mixture was permitted to cool and stand over night, and the resultant dark maroon crystals were filtered by gravity, dried on a watch glass, and then washed with hot ethanol to give the phenylhydrazone of tetraphenylcyclopentadienone (**5**). See Tables I and II. Compounds **2–4**, **6**, and **7** were similarly prepared, although in these cases reflux time was 4 h. Observations on the effects of added base on the spectra (vide supra) were obtained by preparing saturated solutions of the hydrazones in ethanol (20 mL) and recording the UV–vis–NIR spectra before and after the sequential addition of two increments (0.5 and 1.5 mL) of 0.099 M aqueous NaOH solution from a serum pipet. In cases where changes in color and spectra were noted, the first increment was generally sufficient to bring these about. The addition of more than the second increment did not result in further change. In cases where no changes in color and spectra were noted, not even a very large amount of base could induce change. In further exploration of the exchange reactions which hydrazones can experience with hydrazines, we treated compounds **3–7** with 2,4-dinitrophenylhydrazine reagent under conditions previously specified[13] to determine whether each would react and produce **2**. In the event, only **7** so exchanged its hydrazine unit, giving **2** in 85% yield.

Preparation of Arylhydrazones of Cinnamaldehyde and Furanacrolein. The choice of method depended on the state of starting arylhydrazine, as these were commercially available as neutral solids or as solid hydrochlorides. The procedures were well suited to a conveniently small scale and were usually carried out in small test tubes.

Representative Procedures for 2,4-Dinitrophenylhydrazones (Compound 8, 2-Furanacrolein 2,4-Dinitrophenylhydrazone). 2-Furanacrolein (1 mmol) was dissolved in absolute ethanol (5 mL), and 2,4-dinitrophenylhydrazine reagent (10 mL), prepared according to Vogel,[11] was added in one portion with stirring. The orange precipitate which formed immediately was filtered by gravity and recrystallized from hot absolute ethanol to give **8**: mp 218 °C (lit.[12] mp 215 °C); see Tables III and IV.

Representative Procedure for Arylhydrazones from Arylhydrazine Hydrochlorides (Compound 10, 2-Furanacrolein Phenylhydrazone). Phenylhydrazine hydrochloride (0.50 g, 3.5 mmol) and sodium acetate (0.80 g, 9.7 mmol) were dissolved in distilled water (5 mL), and this mixture was added in several portions with stirring to a solution of 2-furanacrolein (0.30 g, 2.5 mmol) in absolute ethanol (10 mL). A precipitate formed immediately, and it was filtered by gravity and then recrystallized from hot absolute ethanol to give **10**: mp 125–127 °C (lit.[22] mp 125–126 °C); see Tables III and IV.

Representative Procedure for Arylhydrazones from Neutral Solid Arylhydrazines (Compound 12, 2-Furanacrolein 4-Nitrophenylhydrazone). 4-Nitrophenylhydrazine (0.50 g, 3.3 mmol) was dissolved in distilled water (30 mL) with heating, and the hot solution was filtered by gravity directly into a solution of 2-furanacrolein (0.30 g, 2.5 mmol) in absolute ethanol (10 mL), immediately producing crystalline material. The latter was filtered by gravity and recrystallized from aqueous ethanol to give **12**, mp 181 °C. Anal. Calcd for $C_{13}H_{11}N_3O_3$: C, 60.70; H, 4.31. Found: C, 60.54; H, 4.47. See Tables III and IV.

Representative Procedure for Enal Phthaloylhydrazones (Compound 25, *o*-Nitrocinnamaldehyde Phthaloylhydrazone). *N*-Aminophthalimide (3 mmol) was mixed with absolute ethanol (40 mL), and to the mixture was added *o*-nitrocinnamaldehyde (4 mmol). The mixture was stirred at reflux for 2.5 h and allowed to cool. The crystalline product was collected by filtration by gravity; it represented the pure sample of **25**, mp 255 °C. Anal. Calcd for $C_{17}H_{11}N_3O_4$: C, 63.55; H, 3.45. Found: C, 63.13; H, 3.75. See Table V.

Representative Procedure for α- and β-Hydrocinnamaldehyde Phthaloylhydrazones (Compound 26, α-Hydrocinnamaldehyde Phthaloylhydrazone). *N*-Aminophthalimide (3 mmol) was mixed with absolute ethanol (20 mL) and 2-phenylpropionaldehyde (4 mmol). The mixture was stirred at reflux for 2.5 h, cooled, and permitted to stand for 96 h, producing a large volume of product as white hairy needles. The mixture was filtered to give an analytically pure sample of **26**, mp 108–109 °C. Anal. Calcd for $C_{17}H_{14}N_2O_2$: C, 73.37; H, 5.07. Found: C, 73.28; H, 5.04. See Table VI.

Myrtenal Phthaloylhydrazone (Compound 28). *N*-Aminophthalimide (6 mmol) was mixed with 95% ethanol (25 mL) and myrtenal (7 mmol), and the mixture was refluxed for 2.5 h. The hot solution was then filtered by gravity to remove a small amount of an insoluble white microcrystalline material, identified (IR, melting point) as phthalhydrazide.[5] The filtered solution was allowed to cool and was then evaporated on a watchglass to give long yellow needles of **28**: 67%; mp 158 °C; IR ν (mull) 1720, 1660, 1610 cm^{-1}; NIR λ (ethanol) 761 nm. Anal. Calcd for $C_{18}H_{18}N_2O_2$: C, 73.45; H, 6.16. Found: C, 73.06; H, 6.50.

4-Fluorobenzaldehyde Phthaloylhydrazone (Compound 29). 4-Fluorobenzaldehyde (1.241 g, 10 mmol) and *N*-aminophthalimide (0.973 g, 6 mmol) were refluxed with stirring for 2 h in absolute ethanol (27 mL). At the end of this time, the hot solution was filtered by gravity. The product crystallized out of the reaction medium upon standing over night and was filtered off to give long white needles of **29**: 26%; mp 187 °C; IR ν (mull) 1800, 1780, 1730, 1650, and 1610 cm^{-1}. Anal. Calcd for $C_{15}H_9N_2O_2F$: C, 67.16; H, 3.38. Found: C, 67.25; H, 3.65.

Near-Infrared Spectra of Substituted Arylhydrazines. All of the materials examined displayed non Beer's Law behavior at higher concentrations, although the most pronounced effect was noted for the nitro compound. Spectra were recorded in absolute ethanol on freshly prepared solutions. For each compound, the concentration, wavelength maximum, and band shape are reported. 4-Nitrophenylhydrazine 10^{-4} M, 801 nm, Gaussian bell; 10^{-3} M, 862 nm, asymmetric; 10^{-2} M, 921 nm, asymmetric. 4-Tolylhydrazine 10^{-3} M, 770 nm, asymmetric. 4-Chlorophenylhydrazine 10^{-3} M, 755 nm, asymmetric. Phenylhydrazine 10^{-3} M, 707 nm, asymmetric.

Note on Polynomial Regression Analysis. Compounds bearing para-substituents were chosen. In the listings given below, Hammett σ values[23] for the appropriate substituent groups were employed as X coordinates, while the near-infrared absorption data for the individual compounds were used as the corresponding Y coordinates, in a statistical program adapted from J. C. Davis.[24] The format for the input data was: (entry number, para-substituent, *X*, *Y*). Major features for each of the computer runs were as follows.

Furanacrolein arylhydrazones: (1, H, 0, 764), (2, NO_2, 0.78, 839), (3, CH_3, –0.17, 766), (4, Cl, 0.23, 761). Input order of equation = 2. Parameters of the regression equation: A = 155.764, B = –20.516, C = 759.931. Total sums of squares = 4269.0000. Sums of squares due to regression = 4242.2500. Sums of squares due to deviation = 26.7500. Standard deviation of residuals = 3.657185. Correlation coefficient = 0.996862.

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Cinnamaldehyde arylhydrazones: (1, H, 0, 760), (2, NO_2, 0.78, 829), (3, CH_3, −0.17, 765), (4, Cl, 0.23, 758). Input order of equation = 2. Parameters of the regression equation: A = 150.173, B = −25.6864, C = 757.482. Total sums of squares = 3494.0000. Sums of squares due to regression : 3483.7500. Sums of squares due to deviation = 10.2500. Standard deviation of residuals = 2.263 846. Correlation coefficient = 0.998 532.

Tetracyclone arylhydrazones (major absorption): (1, NO_2, 0.78, 881), (2, H, 0, 841), (3, CH_3, −0.17, 851), (4, CH_3O, −0.27, 872). Input order of equation = 2. Parameters of the regression equation: A = 158.890, B = −69.9495, C = 838.985. Total sums of squares = 1020.7500. Sums of squares due to regression = 989.7500. Sums of squares due to deviation = 31.0000. Standard deviation of residuals = 3.937 004. Correlation coefficient = 0.984 698.

Tetracyclone arylhydrazones (minor absorption): (1, NO_2, 0.78, 805), (2, H, 0, 773), (3, CH_3, −0.17, 762), (4, CH_3O, −0.27, 765). Input order of equation = 1. Parameters of the regression equation: A = 40.9291, B = 772.771. Total sums of squares = 1166.7500. Sums of squares due to regression = 1141.2600. Sums of squares due to deviation = 25.25000. Standard deviation of residuals = 3.570 714. Correlation Coefficient = 0.989 012.

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Registry No. **2**, 121597-12-4; **3**, 121597-13-5; **4**, 121597-14-6; **5**, 4828-86-8; **6**, 121597-15-7; **7**, 121597-16-8; **8**, 15056-71-0; **9**, 1237-69-0; **10**, 121597-17-9; **11**, 1216-15-5; **12**, 5584-21-4; **13**, 88254-45-9; **14**, 121597-18-0; **15**, 88254-47-1; **16**, 121597-19-1; **17**, 88254-46-0; **19**, 32387-09-0; **23**, 121597-20-4; **24**, 121597-21-5; **25**, 121597-22-6; **26**, 121597-23-7; **27**, 116594-85-5; **28**, 121597-24-8; **29**, 121597-25-9; PhCH=CHCHO, 104-55-2; PhCH=CClCHO, 18365-42-9; Ph_2C=CHCHO, 1210-39-5; tetracyclone, 479-33-4; myrtenal, 564-94-3; phthalhydrazide, 1445-69-8; *p*-fluorobenzaldehyde, 459-57-4; (2,4-dinitrophenyl)hydrazine, 119-26-6; (4-nitrophenyl)hydrazine, 100-16-3; (2-nitrophenyl)hydrazine, 3034-19-3; phenylhydrazine hydrochloride, 59-88-1; *p*-tolylhydrazine hydrochloride, 637-60-5; (4-methoxyphenyl)hydrazine hydrochloride, 19501-58-7; 2-furanacrolein, 623-30-3; (4-chlorophenyl)hydrazine hydrochloride, 1073-70-7; *o*-nitrocinnamaldehyde, 1466-88-2; 3-phenylpropanal, 104-53-0; 2-phenylpropanal, 93-53-8; *N*-aminophthalimide, 1875-48-5.

Kinetics and Mechanisms of Cyclization in Acidic Media of *N*-[(3,5-Dichloroanilino)carbonyl]-*N*-[(isopropylamino)carbonyl]glycine to Hydantoins: Iprodione and Its Isomer

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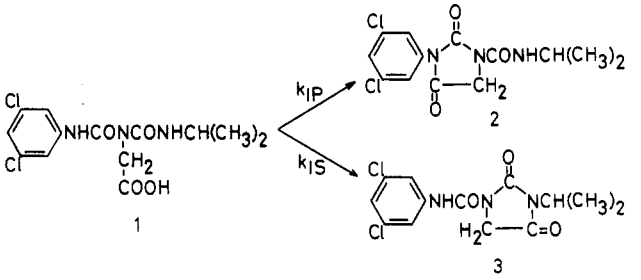
N-[(3,5-Dichloroanilino)carbonyl]-*N*-[(isopropylamino)carbonyl]glycine (**1**) cyclizes quantitatively and irreversibly at 50 °C in the pH range 0.5–6 by two parallel paths to give iprodione (**2**) and its isomer **3**. Formation of the antifungal agent **2** is characterized by a general base catalysis with carboxylate anions, water, and hydroxide ion (β = 0.38) and a solvent isotope effect of 2.90. These results are consistent with a specific base catalyzed addition of the enolate anion of the ureido group to the carboxylic function of hydantoic acid (pK_{a1} = 4.25) to give tetrahedral intermediate T^- whose general acid catalyzed decomposition is rate limiting. Formation of isomer **3** occurs by a specific base catalyzed cyclization of **1** compatible with a nucleophilic attack of the enolate anion of the ureido moiety on the carboxylic group in the pH range 2–6. Below pH 2 hydantoic acid undergoes a specific acid catalyzed and a spontaneous hydrolysis involving a nucleophilic attack of the ureido enol on the carboxylic function, protonated or not, respectively. Formation of iprodione is general base catalyzed while that of its isomer is not: this can be explained by the change in basicity of the leaving groups from the tetrahedral intermediate, i.e., the *N*-[(3,5-dichlorophenyl)ureido] (pK_{a2} = 11.7) and the *N*-isopropylureido ($pK_{a3} \simeq 18$) anions, respectively.

Iprodione [3-(3,5-dichlorophenyl)-*N*-isopropyl-2,4-dioxo-1-imidazolidinecarboxamide] (**2**) is a contact antifungal agent that is active with respect to phytopathogenic fungi.[2]

In ethanolic solution, iprodione is rearranged to its isomer [*N*-(3,5-dichlorophenyl)-3-isopropyl-2,4-dioxo-1-imidazolidinecarboxamide] (**3**), which is a much less effective fungicide.[3] This last reaction requires the intermediate formation of the 3-(isopropylcarbamoyl)-5-(3,5-dichlorophenyl)hydantoic acid (**1**). An industrial procedure of synthesis of iprodione involves the conversion in strongly alkaline media of the isomer to hydantoic acid, which is cyclized to iprodione in acidic solution.[4,5]



In this paper, we describe a kinetic study of the cyclization of the hydantoic acid **1**, undertaken in order to elucidate the mechanism of formation of iprodione and its isomer and to better understand the behavior of iprodione in its conditions of use.

(1) Present address: UFR of Pharmaceutical Sciences, Paul Sabatier University.

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