A comprehensive investigation of variations in melting ranges and NMR data of 2,4-dinitrophenylhydrazine derivatives

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The well-known characterization method of aldehydes and ketones utilizing their 2,4-dinitrophenylhydrazones (DNPs) often gives variable melting ranges and conflicting results for a single derivative. We have found that the DNPs melting point discrepancies and the irreproducibility of the method are mainly due to *syn–anti* (*E–Z*) isomerization caused by traces of acids which remain in the products when prepared by the conventional methods. A bicarbonate washing of the DNPs removes the acid, stabilizes the melting range and reproducibly gives higher-melting derivatives. In the DNP preparations of aldehydes and some unsymmetrical ketones only the kinetically favored (and also thermodynamically more stable) *syn* (*E*) isomer is formed. The six different melting ranges of acetaldehyde DNP (AA-DNP) previously reported by other investigators are correlated with the amounts of acid present in their DNP crystals. Derivatives with higher concentrations of acid(s) give lower melting ranges. In the presence of small amounts of acid, *E–Z* isomerization occurs in most solvents but not in methanol or dimethyl sulfoxide (DMSO). Larger amounts of acid cause the isomerization in all solvents, but the process is much slower in the aforementioned solvents. Alcohols, but not chlorinated solvents, are suitable for the DNPs recrystallization. *E–Z* isomerization of AA-DNP also occurs thermally by first order kinetics when its pure *E* isomer is heated at its melted state. An equilibrium ratio of 2:1 (*E*:*Z*) is reached after 10 minutes. A substantial decrease (up to 2.05 ppm) is observed for the NMR chemical shifts of the AA-DNPs protons in benzene and electron rich aromatic solvents compared to those obtained in chloroform, acetonitrile, acetone, methanol, DMSO or even cyclohexane and electron deficient nitrobenzene. An explanation is given for the drastic chemical shift changes.

Introduction

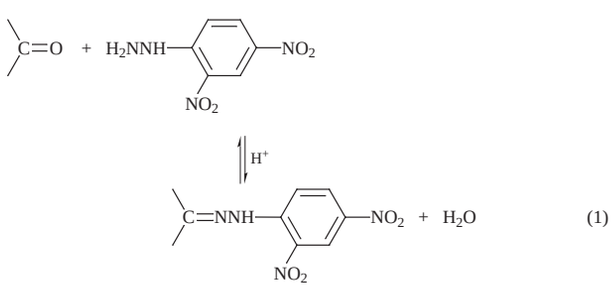
For over sixty years carbonyl compounds have been characterized through their 2,4-dinitrophenylhydrazones (DNPs).[1,2] Although one of the most important organic qualitative methods, this technique has often given various melting ranges for a single derivative (*e.g.* six for AA-DNP)[3–5] and consequently has generated conflicting results.[4,5] We previously reported a modified method[5] by which nearly pure DNPs are obtained after only one recrystallization of the derivatives. In contrast, several recrystallizations were required to achieve equal purity by the conventional method.[1,2,6] We have previously reported that the melting range discrepancies are mainly due to *syn–anti* (*E–Z*) isomerization which occurs during the melting point or NMR determinations and are caused by traces of acids present in the crystals.[5]

Results and discussion

The objective of this work is to answer the following remaining questions and possibly clarify the previously reported conflicting results. 1. Upon treatment of an aldehyde or an unsymmetrical ketone with the acidic solution of 2,4-dinitrophenylhydrazine, which DNP geometric isomer is formed? 2. If the *syn* (*E*) isomer is the only or the predominant product, then how can we explain the various reported melting ranges for a single product? 3. Does the initial presence of the *anti* (*Z*) isomer or the passage of time affect the extent of *E–Z* isomerization in solutions? 4. Does the solvent play a role in the DNP isomerization, and if so, what are the appropriate solvents of recrystallization for these products? 5. Do different solvents affect the chemical shifts of the DNP protons differently? 6. Do pure *syn* (*E*) DNPs isomerize thermally and, if so, what are the kinetics? 7. What is the kinetic/thermodynamic control of the isomerization in the presence of acid?

Although Karabatsos and his co-workers,[4a,7–9] through extensive NMR studies of the hydrazone derivatives, have answered some of the above questions, their results are far from conclusive due to the complications caused by traces of acids present in the crystals. Also, the reports of other investigators on the effects of acid,[4a,10–14] heat[14–18] and solvents[4a,9,16,19,20] on the *E–Z* isomerization of the C=N containing compounds do not fully answer the above questions.

To answer question 1, five independent experiments were performed. In Experiment 1, the DNPs of a number of aldehydes and unsymmetrical ketones were prepared (reaction 1)



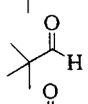
(1)

by the conventional method[2,6] as well as by the modified method.[5]

The melting ranges and the NMR data on the crude and the recrystallized DNPs were recorded and the *E*:*Z* ratios were calculated. The results are shown in Table 1.

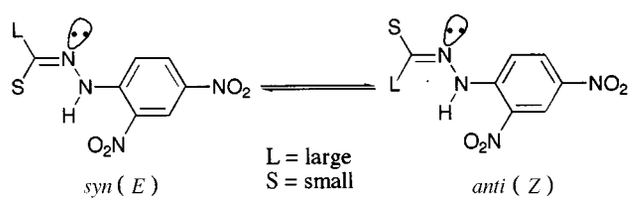
As shown in Table 1, it appears that the crude samples obtained by the conventional method, except for entry 3, either are formed as, or become isomeric mixtures (Scheme 1). However, upon washing with a sodium bicarbonate solution (modified method) except for entry 4, these same samples gave substantially higher melting ranges and were shown by NMR ($CDCl_3$) to be pure *E* isomers.

Table 1 Melting ranges of DNPs and *syn*:*anti* (*E*:*Z*) ratios of $CDCl_3$ solutions

		Mp/°C (*E*:*Z*)[a]			
		Lit. method		Modified method	
Entry	Compound	Crude	Recryst.	Crude	Recryst.
1		120–127 (2:1)	142–143(2:1)	157–163 (1:0)	165–166 (1:0)
2		168–171 (95:5)	180–181 (1:0)	179–181 (1:0)	183–184 (1:0)
3		209–210 (1:0)	209–210 (1:0)	209–210 (1:0)	210–211 (1:0)
4		104–106 (4:1)	109–110 (83:17)	107–109 (7:1)	112–114 (9:1)
5		117–118 (24:1)	119–120 (1:0)	120–122.5 (1:0)	122–123 (1:0)
6		124–125 (49:1)	124–125 (1:0)	124–125 (1:0)	124–125 (1:0)

[a] Ratios reported as 1:0 have less than 0.5% of the *anti* isomer.

The percentage composition (Table 1) of the DNPs *E*:*Z* isomers are based on the relative signal areas of the H of the aldehyde-DNPs and the α-methyl protons of the ketone-DNPs (Scheme 1). In the DNPs of aldehydes, the *cis*-H to the NH



Scheme 1 DNP *syn–anti* (*E–Z* isomerization) (see ref. 21). S = H for aldehyde-DNPs and CH_3 for methyl ketone-DNPs

group (*E*) always appears at lower fields (~7.5 ppm) and the *trans*-H (*Z*) appears at higher fields (~7.0 ppm) and in the DNPs of methyl ketones, the α-CH_3 (~2–2.15 ppm) protons appear at lower fields (about 0.1 ppm) when they are *cis* to the NH groups compared to when they are *trans*.[9]

In Experiments 2, 3, 4 and 5 the isomerization of the AA-DNP, samples (mp 142–143 and 165–166 °C) in solutions as well as in the melted states were studied.

Based on these data and the previously reported results,[4a,5] it is concluded that: a) in ketones (RC(O)R′) where R is much bulkier than R′ and in aldehydes both conventional and modified methods give the *E* isomer only (Experiments 1 and 2 and Table 1); b) the low melting range and the presence of the *Z* isomer in the DNP product prepared by the conventional method is not due to the existence of the *anti* isomer in the initial sample but rather it is due to the formation of this isomer during the melting point determination (Experiments 3 and 5) and NMR measurements (Experiment 2); c) traces of acid remaining in the DNP samples prepared by the conventional method are the causes for the observed *syn–anti* (*E–Z*) isomerization during the measurements (Experiments 2, 3 and 5); d) isomerization occurs in the sample's liquid phase and not in its solid phase during melting (Experiments 3 and 4).

To answer question 2 of why various melting ranges have been reported for the DNP derivative of a single compound (*e.g.* six for acetaldehyde DNP),[3–5] Experiments 6 and 7 were carried out. In Experiment 6, AA-DNPs with various melting ranges similar to the values reported by the previous investigators[4] were prepared, the acid contents of the samples were determined by titration and the results are shown in Fig. 1. As is

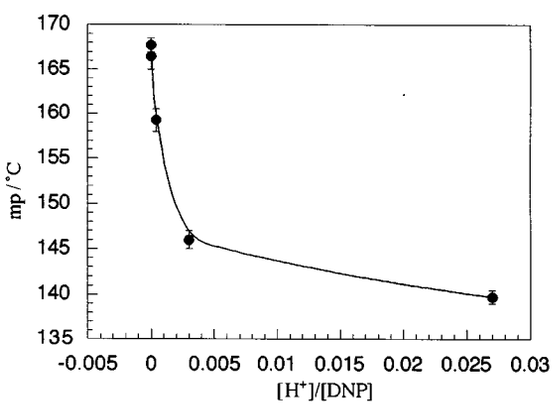


Fig. 1 Melting ranges of acetaldehyde DNP derivatives *vs.* acid content in the crystals as measured by titration

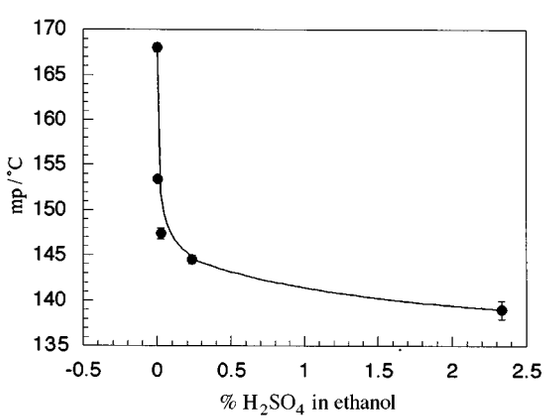
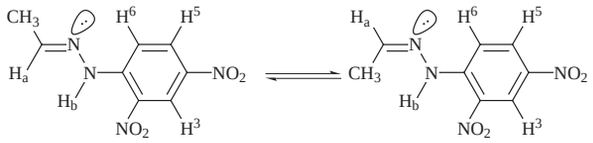


Fig. 2 Melting ranges of acetaldehyde DNP crystals *vs.* the percentage (g vol^{-1}) of H_2SO_4 in ethanol used for recrystalization of pure (mp 168–168.5 °C) DNP

shown, the sample with the lowest melting range (139–140.5 °C) contains a substantial amount of acid and the sample with the highest melting range (167–168.5 °C) does not contain any measurable amount of acid.

In Experiment 7, pure acetaldehyde DNP was recrystallized from ethanol containing various concentrations of H_2SO_4 and the melting ranges were determined. Fig. 2 shows that the DNP samples recrystallized from the more acidic ethanolic solutions

Table 2 Chemical shifts (δ) and equilibrium percentages of acetaldehyde DNP isomers in solvents in the presence of acid ([CF_3CO_2H]/[DNP] = 1/15)[a]



syn (*E*) *anti* (*Z*)

	CH_3		H_a		H_b		H3		H5		H6		(%)[b]
Solvent	*E*	*Z*	*E*	*Z*	*E*	*Z*	*E*	*Z*	*E*	*Z*	*E*	*Z*	*E*:*Z*
$CDCl_3$	2.14	2.08	7.56	7.11	11.04	11.17	9.12	9.14	8.30	8.34	7.94	7.97	66:33
CD_3CN	2.05	2.03	7.71	7.13	10.93	10.96	8.93	8.96	8.26	8.31	7.87	7.89	77:23
[$^2H_6$]Acetone	2.08	2.08	7.95	7.21	11.19	11.09	8.95	8.99	8.35	8.41	7.97	8.01	92:8
CD_3OD	2.07	2.07	7.75	7.14	—	—	9.02	9.06	8.32	8.38	7.97	7.98	82:18
[$^2H_6$]DMSO	2.02	2.04	8.00	7.23	11.32	10.90	8.82	8.86	8.31	8.38	7.84	7.84	86:14
C_6D_{12}	2.08	2.0	7.40	7.00	11.08	11.24	9.04	9.10	8.29	8.32	7.92	7.98	66:33
$C_6D_5NO_2$	2.05	2.01	7.60	7.08	10.96	10.96	8.91	8.93	8.24	8.26	7.80	7.75	75:25
$C_6D_5CD_3$	1.46	1.17	5.95	6.33	10.31	10.60	8.71	8.71	7.69	7.7	7.32	7.42	74:26
$C_6H_5OCD_3$	1.65	1.43	6.37	6.46	10.51	10.71	8.77	8.77	7.90	7.85	7.49	7.59	71:29
C_6D_6	1.40	1.08	5.84	6.30	10.31	10.60	8.80	8.80	7.70	7.76	7.34	7.45	71:29

[a] Chemical shifts are nearly the same in each solvent in the presence or absence of acids. [b] At equilibrium.

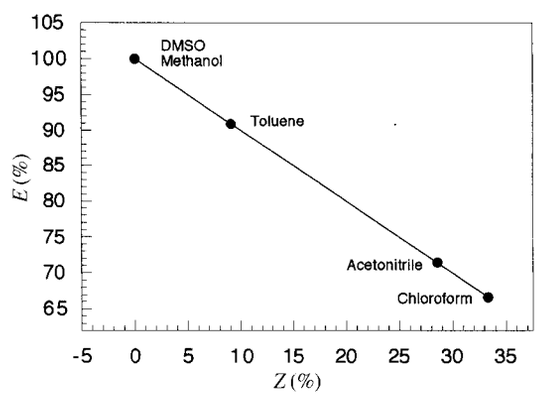


Fig. 3 *E*–*Z* Equilibration (96 h) of AA-DNP in the presence of acid ([H^+]/[DNP] = 1/1000) in deuterated solvents at ambient temperature

give lower melting ranges compared to those recrystallized from the less acidic ethanolic solutions.

These results clearly indicate that the various melting ranges reported by several investigators[4] do not point to the presence of impurities such as the *anti* (*Z*) form but rather correlate with the various amounts of acid present in the crystals. The results also indicate that the six different melting ranges reported for the acetaldehyde DNP are due to the extent that the acid has been removed from the crystals through washing before recrystallization by each investigator. Higher amounts of acid increase the rate of formation of the *Z* form during the melting point and NMR studies, and consequently affect these data.

To answer question 3 of whether the presence of the *anti* isomer or long standing of the DNP solution promotes the isomerization and shifts the equilibrium toward the higher concentration of the *anti* (*Z*) isomer (as has been suggested by Karabatsos[4a]), Experiment 8 was performed. The results indicate that neither time nor the presence of the *Z* isomer cause the isomerization, but rather that acid is needed for this transformation.

To study the effects of medium (questions 4 and 5) on the *E*–*Z* equilibria and on the DNP proton chemical shifts, pure samples of the AA-DNP *syn* (*E*) isomer in the presence or absence of acid in a number of solvents were studied (Experiments 9 and 10, Fig. 3 and Table 2).

The following observations and conclusions can be made based on the results.

1. Pure samples of AA-DNP in solvents listed in Table 2 did not show any isomerization in the absence of acid in 96 h.

2. It appears that the extent of *E*–*Z* isomerization in the presence of traces of acid ([H^+]/[DNP] = 1/1000) depends on the nature of the solvent and the length of time (Fig. 3). In methanol and dimethyl sulfoxide (DMSO) no isomerization occurred after 96 h even when the relative concentration of acid was increased to 1/100. It should be noted that *E*:*Z* ratios similar to those of Fig. 3 were obtained when NMR data of AA-DNP prepared by the conventional method (containing trace amounts of H_2SO_4 because of the method of preparation) were recorded in these solvents.

3. In contrast to other solvents, alcohols are suitable solvents to be used for the recrystallization of DNPs.

4. At higher concentrations of acids ([H^+]/[DNP] = 1/15) isomerization occurs in all solvents and the *E*:*Z* ratios are higher in H-bond acceptor solvents such as DMSO, methanol and acetone (Fig. 3 and Table 2).

Two explanations can be offered for the effects of acid concentration and media on the isomerization and *E*:*Z* equilibria ratios. (a) Acids in low concentrations will protonate solvents such as DMSO or methanol rather than the DNP molecule, while in the nonhydrogen bonding solvents such as chloroform or toluene the DNP molecule will be protonated and the isomerization will be facilitated. Acids in higher concentrations will protonate the solvent as well as the DNP molecules. (b) The weak hydrogen bonding of the NH proton and the H-bond acceptor solvents may be responsible for the higher *E*:*Z* ratios in these solvents. Hydrogen bonding may be more favorable in the less hindered *E* form compared to the *Z* form. The NH chemical shifts in Table 2 are consistent with this interpretation. In C_6D_{12}, where no interactions would be expected, H_b for the *Z* isomer has a larger δ (by 0.16) than H_b for the *E* isomer. This is reversed in H-bonding solvents up to DMSO where H_b for the *E* isomer has a significantly larger δ (0.42).

5. As Table 2 shows: (a) With small variations, the chemical shifts of the acetaldehyde DNP protons follow the molecular electronic effects in the first seven solvents. (b) There is a drastic shift in absorptions to higher fields for all the protons when the solvent is changed to benzene, toluene or anisole. This shift is especially pronounced for the CH_3 and H_a protons. For example, the signal for $CH_{3(anti)}$ appears at δ 1.17 in $C_6D_5CD_3$ compared to 2.04 in [$^2H_6$]DMSO ($\delta_{diff.} = 0.87$), and the signal for $H_{a(syn)}$ appears at δ 8.0 in [$^2H_6$]DMSO while in $C_6D_5CD_3$ it appears at δ 5.95 ($\delta_{diff.} = 2.05$). (c) In contrast to what has been previously reported,[9] $H_{a(syn)}$ does not always resonate at lower magnetic fields compared to $H_{a(anti)}$. This is true for the first seven solvents but it is reversed when toluene, anisole or

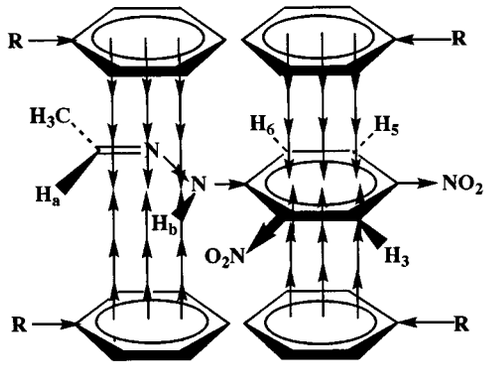
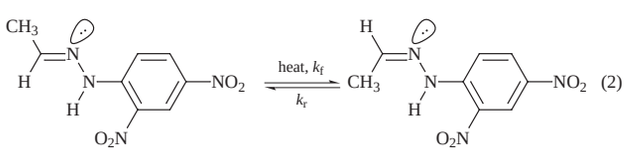


Fig. 4 A simplified cartoon depicting shielding of DNP protons by solvent molecules

benzene is used. (d) No correlation can be made between the chemical shift variations and the dipole moments or the dielectric constants of the solvents. The DNPs δ values are nearly the same whether obtained in nonpolar cyclohexane or in polar chloroform. (e) The chemical shifts in strongly hydrogen bonding solvents (*e.g.* methanol, DMSO) are nearly the same as in nonhydrogen bonding solvents (*e.g.* chloroform, cyclohexane) and consequently the δ value variations cannot be attributed to simple solvent–solute hydrogen bonding interactions.

These observations can be explained by assuming preferential solvation of the electron-deficient regions of the DNP molecules by the π electron systems of electron-rich aromatic molecules, *e.g.* benzene, toluene and anisole (Fig. 4). The ring currents of these aromatic molecules then shield the DNP protons. This explanation is supported by the observation that nitrobenzene, with a relatively electron-poor electron system, behaves similarly to the non-aromatic solvents.

To answer question 6 concerning the thermal isomerization of the *E* isomer and its kinetics, Experiment 11 was carried out. The results show that the isomerization occurs (reaction 2) and



an equilibrium ratio of $E:Z = 2:1$ is reached after 10 min at 172 °C.

A plot of $\ln[Z_f(\%) - Z(\%)]$ *vs.* t (min) (Fig. 5) shows a first order kinetics with a slope of −0.413 and a forward rate constant of 0.204.

The kinetics of equilibrium between the *syn* (*E*) and the *anti* (*Z*) forms can be adequately described by assuming that both the forward and the reverse reactions are first order and do not depend on any species other than the two forms (*E* and *Z*). In this situation, the appearance of the *Z* form follows eqn (3),

$$\ln ([Z]_{eq} - [Z]) = -k_f (1/[Z]_{eq})t + \ln [Z]_{eq} \qquad (3)$$

where $[Z]$ = the relative fraction of *anti* present at any time and $[Z]_{eq} = [Z]$ when equilibrium is established, t = time since the reaction began, k_f = the rate constant for the forward reaction. The reverse reaction rate constant, k_r, can be found through the equilibrium conditions, as $k_r = k_f (1/[Z]_{eq} - 1)$. Both the forward and the reverse reactions are first order overall.

To answer question 7 concerning the kinetic or the thermodynamic control of the *E–Z* isomerization, Experiment 12 was performed. The results show that in an *E–Z* mixture in the presence of acid, isomer *Z* is converted to the more stable *E*

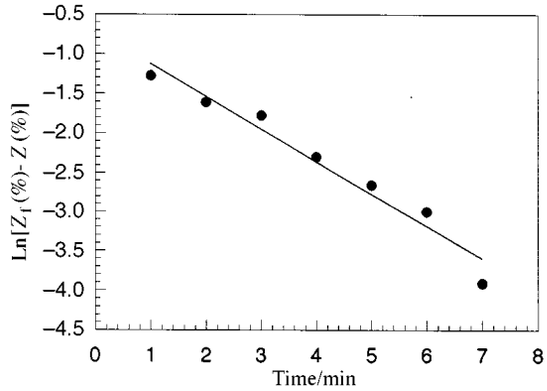


Fig. 5 First order thermal isomerization of pure AA-DNP (*E*) at 172 °C: $Z_f(\%)$ = final concentration of *anti*; $Z(\%)$ = concentration of *anti* at any time. Best fit slope −0.413.

form and hence the transformation appears to be thermodynamically controlled. These data are in agreement with the effect of heat on the isomerization of other C=N bonds previously reported by other investigators.[13,16,17]

Conclusions

1. Only the *syn* (*E*) isomer is formed in detectable amounts in the preparation of DNPs of aldehydes and of unsymmetrical ketones where the two groups are substantially different in size. Observation of the *anti* (*Z*) isomers in these samples is due to the acid catalyzed *syn–anti* (*E–Z*) isomerization process occurring during the NMR measurements. The formation of DNPs is thermodynamically controlled.

2. The reported melting point discrepancies for DNPs are mainly due to *syn–anti* (*E–Z*) isomerization caused by traces of acids during the melting process. There is an inverse correlation between the amounts of acids present in the samples and the melting ranges.

3. Removal of acid by a base wash stabilizes and increases the melting ranges.

4. In solutions, no isomerization occurs in the absence of acids, but thermal isomerization is observed when pure (neutralized) DNP samples are heated at the melting state for more than one minute. For acetaldehyde DNP *syn–anti* equilibration (2:1) is reached at 172 °C in 10 min. The isomerization is first order kinetics.

5. Traces of acid ([Acid]/[DNP] = 1/1000) facilitate the *syn–anti* isomerization in solvents such as chloroform, toluene or even acetonitrile and acetone but not in methanol or DMSO. However, isomerization occurs in all solvents in the presence of substantial amounts of acids although with much slower rates in methanol and DMSO. Alcohols, but not chlorinated solvents and acetonitrile are suitable recrystallization solvents.

6. A substantial decrease in the chemical shifts of all of the acetaldehyde DNP protons especially those of CH_3 and H_a is observed when benzene and electron-rich aromatic solvents are used in place of solvents such as chloroform, DMSO, cyclohexane or nitrobenzene. These drastic signal shifts may be attributed to the ring current effects of the electron rich aromatic solvent molecules on the DNP molecules.

Experimental

General methods

Melting ranges are uncorrected and were recorded on a Thomas-Hoover melting point apparatus, and they are in Celsius. ^{1}H NMR spectra were recorded on a Varian Gemini 200 spectrophotometer at 200 MHz. Aldehydes, ketones, 2,4-dinitrophenylhydrazine and deuterated solvents were purchased from Aldrich Chemical Company.

Experiment 1. 2,4-Dinitrophenylhydrazones

2,4-DNP derivatives of aldehydes and ketones listed in Table 1 were prepared by both the conventional and the modified methods according to the procedure below:

A solution of 1.0 g of the carbonyl compound in 40 mL of 95% ethanol was added to 35 mL of freshly prepared 2,4-dinitrophenylhydrazine solution.[6] The yellow-orange precipitate was filtered off on a fritted disk glass funnel. About half of the solid was removed and treated according to the literature method[6] by allowing part of the material to dry at room temperature (lit. crude) and part was recrystallized from 95% ethanol (lit. recryst., Table 1) the remainder of the material on the funnel was washed with 3 × 20 mL of a 5% aqueous sodium bicarbonate solution. A portion of this solid was air dried (modified crude) and the remainder was recrystallized from 95% ethanol (modified recryst., Table 1). To obtain pure samples of AA-DNP (mp 168–168.5 °C) free of traces of acid, the recrystallized sample (mp 165–166 °C, modified recryst., Table 1) was washed with a 5% aqueous sodium bicarbonate solution and then recrystallized twice with 95% ethanol.

Experiment 2

A small sample of AA-DNP, prepared as lit. recryst., above, (sample A, mp 142–143 °C; $E:Z$ of $CDCl_3$ solution = 2:1, Table 1) was thoroughly washed with a 5% aqueous sodium bicarbonate solution and then dried. No measurable loss of weight was observed and its mp rose to 165–167.5 °C. Its NMR ($CDCl_3$) showed the presence of the *E* isomer only.

Experiment 3

Sample A was allowed to melt and then washed with sodium bicarbonate solution and dried. Its NMR ($CDCl_3$) showed the $E:Z$ ratio to be 4:1.

Experiment 4

When sample A was heated to just below its melting range (141 °C) and then treated with a sodium bicarbonate solution, its NMR ($CDCl_3$) showed only the *syn* (*E*) DNP.

Experiment 5

Acetaldehyde DNP prepared by the modified method and recrystallized as above, (sample B, mp 165–166 °C, $E:Z$ of $CDCl_3$ solution = 1:0, Table 1) did not isomerize upon melting (subsequent NMR ($CDCl_3$) showed $E:Z$ = 1:0).

Experiment 6

Acetaldehyde DNP was prepared by the conventional method and recrystallized five successive times to reach a constant melting range of 167–168.5 °C. After each recrystallization the melting range was determined and the amount of acid present in the crystals was measured by washing 0.5 g of the sample with 20 mL of 0.01 M NaOH followed by two successive washes with 2 × 15 mL of water and then titration with 0.01 M potassium hydrogen phthalate in the presence of phenolphthalein. Fig. 1 shows a plot of the amount of acid present relative to DNP ($[H^+]$/[DNP]) *vs*. the corresponding melting ranges.

Experiment 7

Five samples of pure AA-DNP (mp 168–168.5 °C) prepared by the modified method were recrystallized from 100 mL solution of 95% ethanol containing various amounts of sulfuric acid (2.33, 0.233, 0.0233, 0.002 33 and 0.00 g) and the melting ranges were determined. A plot of melting ranges *vs*. the concentration of sulfuric acid in ethanol is shown in Fig. 2.

Experiment 8

A $CDCl_3$ solution of a pure sample of acetaldehyde DNP prepared by the modified method did not show any isomerization (by NMR) after standing at room temperature for ten days. Also, a $CDCl_3$ solution of a base-washed sample of this DNP containing a 9:1 $E:Z$ mixture did not show any concentration change after 10 days at room temperature. However, a $CDCl_3$ solution of a derivative prepared by the literature method and recrystallized twice from ethanol (mp 145–148 °C) containing 2% of the *anti* isomer gave an equilibrium mixture (2:1) of the $E:Z$ forms upon standing at room temperature for four days.

Experiment 9

Pure samples (each 5.6 mg, 25 μmol) of the *E* isomer of AA-DNP prepared by the modified method (mp 168–168.5 °C) were dissolved in $CDCl_3$, $C_6D_5CD_3$, CD_3CN, [$^2H_6$]DMSO and CD_3OD, and their proton NMR spectra were recorded. No isomerization was observed in any one of these solvents over a period of 96 h.

Experiment 10

Pure samples (each 5.6 mg, 25 μmol) of AA-DNP prepared by the modified method were dissolved in deuterated solvents (1 mL) containing trifluoroacetic acid ($[H^+]$/[DNP] = 1/1000 or 1/100)[22] and their NMR spectra were recorded at several time intervals (0.1, 24, 48 and 96 h). In $CDCl_3$, equilibrium was reached immediately, in toluene, acetone, acetonitrile after 24 h, but in methanol and DMSO no isomerization occurred even with ($[H^+]$/[DNP] = 1/100). The results are shown in Fig. 3. In the presence of higher concentrations of acids (1/15) equilibrium was reached immediately. The results are presented in Table 2.

Experiment 11

Ten samples (each 100 mg) of pure AA-DNP (*E* isomer) were heated at 172 °C (melt) for 1 to 10 min and then cooled and washed with 3 × 1 mL of saturated aqueous $NaHCO_3$. NMR of 5.6 mg of these samples in $CDCl_3$ showed the presence of the *anti* (*Z*) isomer in 5, 13, 16, 23, 26, 28, 31, 33, 33 and 33% for 1, 2, 3, 4, 5, 6, 7, 8, 9 and 10 min respectively. A plot of $\ln[Z_f(\%) - Z(\%)]$ *vs*. time is shown in Fig. 5.

Experiment 12

A base washed and dried sample of AA-DNP (5.6 mg) prepared according to Experiment 11 containing a 2:1 mixture of $E:Z$ was dissolved in 1 mL of [$^2H_6$]DMSO. Addition of trifluoroacetic acid ($[H^+]$/[DNP] = 1/1000) to this solution did not cause any change in the $E:Z$ ratio, but when the acid concentration was increased to 1/15, the *Z* isomer was converted to the *E* isomer and an equilibrium ratio of $E:Z$ = 86:14, similar to that of Table 2 was established immediately.

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21 *Syn* and *anti* designate the relative positions of the larger group on carbon (L) and the lone electron pair of nitrogen in the C=N containing compounds. If the two are on the same side, the configuration is *syn* (*E*) and if they are on the opposite sides, it is *anti* (*Z*). See E. L. Eliel, *Stereochemistry of Carbon Compounds*, McGraw-Hill, New York, 1962, 321.
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