*Carbohydrate Research*, 228 (1992) 451–454
Elsevier Science Publishers B.V., Amsterdam



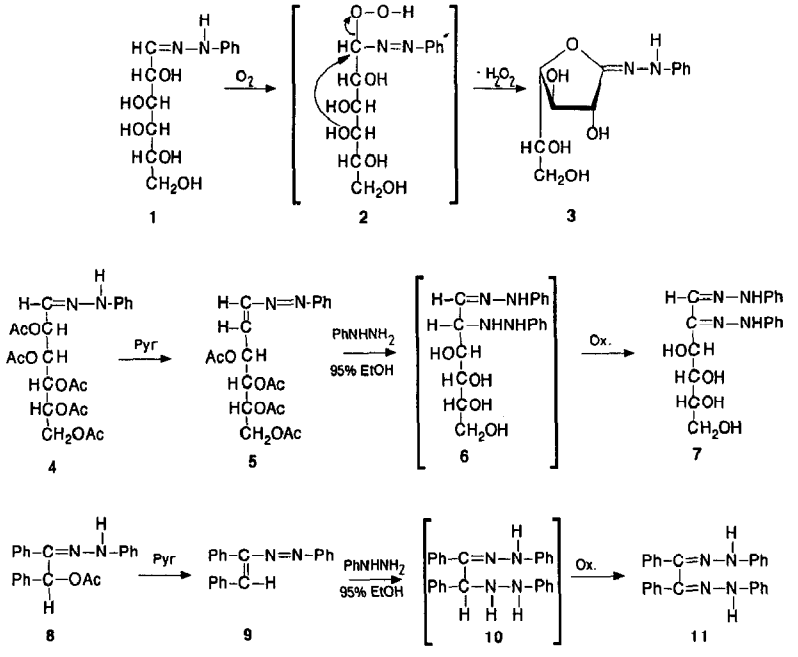
# Note

## Oxidation and elimination reactions of phenylhydrazones in bases

H. S. El Khadem and Arthur Crossman, Jr.
*Department of Chemistry, The American University, 4400 Massachusetts Ave. N.W., Washington D.C. 20016 (U.S.A.)*

(Received July 5th, 1991; accepted October 18th, 1991)

The reactions of aldose phenylhydrazones in basic media contrast markedly with those of aldoses and glycosylamines. The last two undergo degradative oxidations in basic media to afford lower aldonic acids and formic acid[1–8], whereas such aldose phenylhydrazones as **1** undergo peroxidation without degradation to yield aldonohydrazono-1,4-lactones[9] (**3**). Phenylhydrazones having good leaving-groups attached to α carbon atoms are known to undergo elimination in basic media to give azoalkenes[10–12]. Some azoalkenes have been shown to undergo conjugate additions with nucleophiles[13,14]. We have added phenylhydrazine to azoalkenes **5** and **9** and in both




Scheme 1

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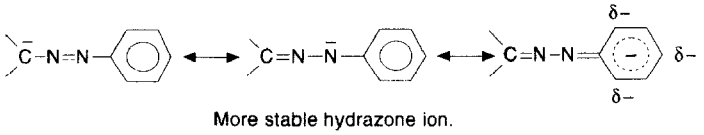
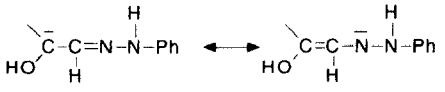
cases obtained bis(phenylhydrazones) (**7** and **11**). This denoted that the two additions were accompanied by oxidations of the phenylhydrazinohydrazones (**6** and **10**) formed. This oxidation is analogous to the oxidations that occur when aldoses and ketoses are converted to osazones[15]. Noteworthy is the fact that during the formation of osazone **7**, the excess phenylhydrazine used caused deacetylation by transamidation.

To determine whether similar differences existed between such α-hydroxy carbonyl derivatives, as benzoin and their phenylhydrazones, ethanolic KOH solutions of benzoin, α-anilinodeoxybenzoin, and benzoin phenylhydrazone were shaken with oxygen, at room temperature, and the products analyzed. The first two compounds underwent rapid degradative oxidations and afforded two mol of benzoic acid, whereas benzoin phenylhydrazone was largely unaffected. This was attributed to the inability of aldose phenylhydrazones and benzoin phenylhydrazone to form enolhydrazines analogous to enediols and enolamines that usually undergo degradative oxidation[3,8]. Another difference between aldoses and aldosamines on one hand and aldose phenylhydrazones on the other, is that the first two compounds isomerize[1-4] in the presence of base whereas aldose phenylhydrazones do not isomerize to any appreciable extent[16]. This behavior also can be attributed to the inability of aldose phenylhydrazones to enolize in basic media. The reason for this is probably because the NH protons of phenylhydrazones are markedly more acidic than their α-hydrogens because of the added resonance stabilization of the hydrazone anions. The latter are hybrids of three resonance forms whereas the enolhydrazinate anions, produced by ionization of the α-hydrogen, are hybrids of two forms. Preferential ionization of the NH protons of phenylhydrazones suppresses enolization and slows epimerization and degradative oxidation of aldose phenylhydrazones.



More stable hydrazone ion.



Less stable enolhydrazine ion.

The reason why aldoses isomerize to give two epimeric aldoses and a ketose, whereas glycosylamines yield mainly one isomer (1-amino-1-deoxyketoses), may be attributed to the ionization of enediols and enolamines in basic media. Enediols formed from aldoses possess two OH protons of comparable acidity. Ionization of one OH group affords on protonation two epimeric aldoses and ionization of the other OH, a ketose. In basic media, glycosylamines afford enolamines, which possess one OH and one NH group. Because the OH group is much more acidic, it preferentially ionizes to give 1-amino-1-deoxyketoses (Amadori compounds).

EXPERIMENTAL

*General methods.* — Melting points were measured on Kofler blocks and are uncorrected; i.r. spectra with a BIO RAD FTS-7. F.t.-i.r. spectrophotometer, and mass spectra on a Hewlett Packard 5995A EI-GC/MS. $^1$H-N.m.r. and $^{13}$C-n.m.r. spectra were recorded at 300 MHz with a Bruker or a Varian 300-MHz instrument. Thin-layer chromatograms were performed on Eastman Kodak silica gel 60 plastic sheets precoated with fluorescence indicator $F_{254}$ purchased from Thomas Scientific Co., and were viewed with a Chromato-Vue u.v. illumination chamber. Combustion analyses were performed by Spang Microanalytical Laboratories, Eagle Harbor, Michigan.

*Addition of phenylhydrazine to 1-phenylazo-*D-arabino-*3,4,5,6-tetraacetoxyhexene* (**5**). — 1-Phenylazo-D-*arabino*-3,4,5,6-tetraacetoxyhexene[10] (**5**) (1.0 g, 2.4 mmol) was dissolved in 20 mL of EtOH and refluxed with 2.57 g of phenylhydrazine for 2 days. D-*arabino*-Hexulose phenylosazone (**7**) crystallized out in characteristic needle clusters and was recrystallized from 95% EtOH. It had m.p. 198–201° alone or admixed with an authentic D-*arabino*-hexulose phenylosazone. The i.r. and mass spectra of the two products matched and the latter showed major ions at *m/z* 358 ($M^+$), 322 (loss of $H_2O$), 267 (loss of PhN), 93 ($PhNH_2$), and 77 (Ph).

*1,2-Diphenyl-1-phenylazoethene* (**9**). — Benzoin phenylhydrazone (2.2 g, 7.3 mmol) was acetylated with $Ac_2O$ (13.0 mL) and dry pyridine (36.0 mL) for 2 days at room temperature. The mixture was then poured onto 200.0 mL of ice and left overnight. The oily acetate (**8**) that separated was washed several times with water, dried and warmed with pyridine in 95% EtOH. 1,2-Diphenyl-1-phenylazoethene (**9**) precipitated (yield 1.0 g; 48%) and was recrystallized from 95% EtOH as yellow needles m.p. 89° (lit.[13] m.p. 88–90°); g.l.c.–e.i.-m.s. *m/z* 284 ($M^+$); 108 ($PhNHNH_2$); 93 ($PhNH_2$), and 77 (Ph); *ν(KBρ)* 1600 (C = C) $cm^{-1}$.

*Anal.* Calc. for $C_{20}H_{16}N_2$: C, 84.48; H, 5.63; N, 9.86. Found: C, 84.38; H, 5.66; N, 9.70.

*Benzil bisphenylhydrazone* (**11**). — A solution of 1,2-diphenyl-1-phenylazoethene (**9** 0.2 g, 0.7 mmol) in 95% EtOH (15.0 mL) was treated with two drops of AcOH and phenylhydrazine (0.1 g, 0.9 mmol). The solution was refluxed for 30 min, concentrated, and the brown oil that separated treated with MeOH. The yellow solid obtained was recrystallized from EtOH as needles (0.2 g, 67%), m.p. 224–225° alone or mixed with an authentic sample of benzil bis(phenylhydrazone) (**11**); *ν*(KBr) 1601 (C = N) $cm^{-1}$ and g.l.c.–e.i.-m.s. *m/z* 390 ($M^+$) plus the following fragments, 108 ($PhNHNH_2$), 93 ($PhNH_2$), and 77 (Ph).

*Anal.* Calc. for $C_{26}H_{22}N_4$: C, 79.97; H, 5.67; N, 14.35. Found: C, 79.91; H, 5.64; N, 14.41.

*Action of KOH and oxygen on benzoin.* — Benzoin (10.0 g, 0.047 mol) was dissolved in 95% EtOH (100.0 mL) and treated with a concentrated solution of KOH to raise the pH above 12. Oxygen was bubbled through the solution for 2 days and upon acidification benzoic acid separated. The yield was 94% based on 2 mol of benzoic acid produced. The peroxidation product was recrystallized from dilute EtOH in plates, m.p.

120° alone or mixed with an authentic sample of benzoic acid. The i.r. and e.i.-m.s. spectra of the two matched.

*Action of KOH and oxygen on α-anilinodeoxybenzoin.* — A solution of α-anilinodeoxybenzoin (8.0 g) was dissolved in 95% EtOH (100.0 mL) and a concentrated solution of KOH was added to raise the pH above 12. Oxygen was bubbled through the solution for 2 days and upon acidification benzoic acid precipitated. It was identified in the same manner as already described. The yield was 95% based on 2 mol of benzoic acid formed.

*Action of base and oxygen on benzoin monophenylhydrazone.* — Benzoin monophenylhydrazone (5.0 g) was dissolved in 50.0 mL of 95% EtOH and treated with concentrated KOH to raise the pH to 12–14. After bubbling oxygen through the solution for 3 days, the only product isolated was the starting material which was identified by comparison of the m.p., i.r., and e.i.-m.s.

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