(m, 9 H, 2 C_5-H), 4.9–5.3 (m, 9 H, 2 C_5-H, 2 CH_2 of pNB, 3 vinyllic and allyllic H), 5.68 (m, 2 H, 2 dd of C_6-H's), 6.9–7.6 (m, 18 aromatic H and 2 NH); IR ($CHCl_3$) 1785, 1742, 1692, 1680 cm^{-1}.

Anal. Calcd for $C_{46}H_{44}N_6O_{16}S_2$: C, 55.19; H, 4.43; N, 8.46; O, 25.57; S, 6.41. Found: C, 54.92; H, 4.67; N, 8.64; O, 25.82; S, 6.19.

Preparation of *p*-Nitrobenzyl 7-(Phenoxyacetamido)-3-methyl-3-cepham-4-carboxylate (9). A 260-mg sample of fraction II was refluxed in 3 mL of dimethylformamide for 45 min, and while the solution was hot, about half of the solvent was evaporated under reduced pressure. The remaining half was dissolved in 20 mL of ethyl acetate and washed with 1 N HCl (3 × 10 mL), a saturated solution of sodium bicarbonate, and brine. After being dried the solvent was evaporated, and the residue was chromatographed on a preparative silica gel plate by using a 7:3 mixture of ethyl acetate–hexane. The major component was extracted with acetone and the NMR of the isolated material was consistent with that of the title compound.

A similar reaction was repeated with cephams **7** and **8**, and the title compound was isolated by preparative thin-layer chromatography.

Preparation of *p*-Nitrobenzyl 1-Oxo-7-(phenoxyacetamido)-3-methylenecepham-4-carboxylate (4). A 815-mg sample of fraction III (containing 1:1 mixture of penam **5** and cepham **7**) was stirred in 4.8 mL of methanesulfonic acid for 35 min at room temperature. A solution was slowly poured onto 7.5 g of $NaHCO_3$ in 75 mL of water and 50 mL of ethyl acetate. The organic layer was separated, washed with brine, and dried and the solvent evaporated. The residue was dissolved in 2.0 mL of ethyl acetate, and the title compound crystallized out after scratching and keeping the solution in a refrigerator overnight. The isolated product is identical (NMR, IR, TLC) with an authentic sample.[3]

Oxidation of the Penam Sulfur in 5 to the Sulfoxide. A mixture of 636 mg of the penam **5** and 200 mg of *m*-chloroperbenzoic acid in 20 mL of dichloromethane was kept at room temperature for 45 min. The solution was washed with an aqueous solution of sodium bisulfite and brine. After the mixture was dried over $MgSO_4$, the solvent was evaporated to give 530 mg of the crude product which was purified by chromatography over silica gel (ethyl acetate–hexane, 7:3). Fractions 14–24 contained 170 mg of the pure penam sulfoxide isolated as a colorless foam: NMR ($CDCl_3$) δ 1.25 (s, 3 H, CH_3), 1.96 (s, 3 H, CH_3), 4.48 (s, 2 H, CH_2O), 4.52 (s, 4 H, $PhOCH_2$), 4.59 (s, 1 H, C_3-H), 4.85 (d, J = 4.5 Hz, 1 H, C_5-H), 5.02–5.5 (m, d, C_5-H, 2 CH_2 of pNB, 3 allyllic H), 5.98–6.17 (2 dd, J = 4.5 and 9 Hz, 2 H, C_6-H's), 6.8–7.52 (m, 18 aromatic H), 8.13–8.23 (2 d, J = 9.0 Hz, 2 NH); IR ($CHCl_3$) 1790, 1745, 1695, cm^{-1}.

Anal. Calcd for $C_{46}H_{44}N_6O_{17}S_2$: C, 54.33; H, 4.36; N, 8.26; S, 6.31; O, 26.74. Found: C, 54.08; H, 4.56; N, 8.08; S, 6.07; O, 27.00.

Acknowledgment. We are grateful to Dr. G. M. Maciak and associates for miroanalyses, J. L. Occolowitz for mass spectra, and T. K. Elzey for NMR measurements.

Registry No. 1, 29707-62-8; 2, 76665-50-4; 4, 61375-82-4; 5, 76739-44-1; 5 *S*-oxide, 76665-51-5; 6, 76665-52-6; 7, 76665-53-7; 8, 76738-30-2; 9, 28974-31-4.

o-Phenylenediamine from Sulfur, Ammonia, and Cyclohexane†

F. J. Weigert

Central Research and Development Department, E. I. du Pont de Nemours and Company, Wilmington, Delaware 19898

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Nazady[1] reported the synthesis of aniline from sulfur, ammonia, and cyclohexane in modest yield. During our investigation of this reaction, we discovered that a second nitrogen-containing product is produced under his conditions, *o*-phenylenediamine (OPD), the subject of this note.

Table I. *o*-Phenylenediamine Synthesis[a]

sulfur, mg	cyclohexane, μL	PhH, mL	NH_3, g	$PhNH_2$, mg	OPD, mg
100	200	2.5	0.5	25	3
100	200	2.5	1.0	10	11
400	800	1.5	1.0	76	18
400	800	1.5	2.0	109	109
400	1500	1.0	2.0	86	95
400	1500	0	2.0	83	95
800	2500	0	2.0	145	103
500	2500	0	1.0	94	29

[a] 1 h, 330 °C.

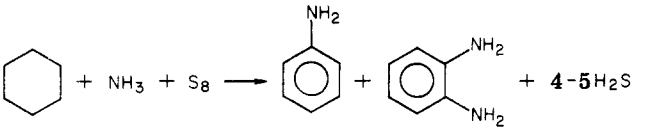
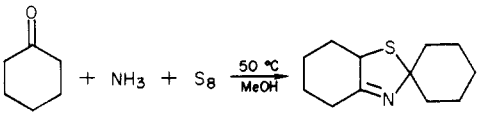
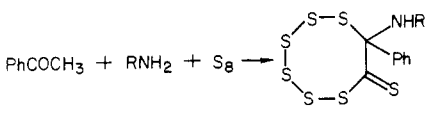


Table I gives the yield of aniline and OPD from the three ingredients at various reactant concentrations. In previous work[1] benzene was used as solvent; we find that it is merely an unnecessary diluent and reactor productivity is increased by replacing the benzene with additional cyclohexane. OPD is favored by high ammonia pressures and is less sensitive to other variables. GC analyses revealed that the regioselectivity to OPD was greater than 99%. Aniline is not the precursor of OPD not only because its amination is significantly slower than the formation of OPD under these conditions but also because *m*-phenylenediamine, the thermodynamically most stable isomer, is the major isomer produced, rather than the observed OPD from cyclohexane. Very little benzene is produced; excess cyclohexane is recovered unchanged.

The ortho selectivity has precedent in reactions of sulfur and amines with substituted organic compounds under milder conditions. Cyclohexanone reacts with sulfur and ammonia at 50 °C to give the spiro compound **2** in high yield.[2] Acetophenones react with sulfur and primary amines[3] to give hexathiocanes **3**. In both these examples



2



3

replacement of the carbonyl oxygen by a nitrogen substitutent is accompanied by sulfur functionalization of the adjacent carbon.

Methylcyclohexane gives a mixture of products including a methyl-OPD, but also containing toluidines (*o*:*m*:*p* = 5:83:13) and an aminobenzonitrile.

These reactions may proceed via alternating dehydrogenations by sulfur and nucleophilic attacks by ammonia. The isomer distribution of the toluidines suggests that at

† Contribution no. 2864.

(1) Nazady, J. G. Can. Patent 815064, 1969; *Chem. Abstr.* **1969**, *71*, 101508.

(2) Asinger, F.; Thiel, M.; Kaltwasser, H. *Justus Liebigs Ann. Chem.* **1957**, *606*, 67–74.

(3) Asinger, F. J.; Saus, A.; Offermanns, H.; Dagga, F. A. *Justus Liebigs Ann. Chem.* **1969**, *723*, 119–128.

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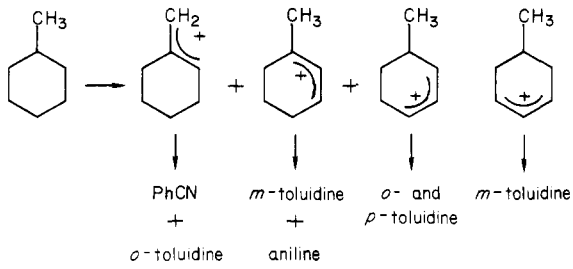
least one ammonia attack occurs at the oxidation level of an allylic carbenium ion, as the toluidine isomer distribution is that expected from attack at the most accessible position of the most stable isomer of these ions.



Experimental Section

Cyclohexane or methylcyclohexane and sulfur were loaded into a 10-cm^3 shaker tube and cooled to −78 °C. After evacuation, ammonia was distilled into the tube, and the sealed tube was heated and shaken for the desired time behind a barricade. The tube was cooled to −78 °C, and any noncondensable gases such as nitrogen or hydrogen from ammonia decomposition were vented. Solid ammonium polysulfide can plug the reactor vent opening so to ensure safe discharge of the reaction product, a hole must be made in the solid to allow the warming gases to escape. The tube was inverted over a receiver and allowed to warm to room temperature. The solid ammonium polysulfides present sublimed and decomposed, liberating H_2S and ammonia. The liquid which remained was analyzed for high-boiling amines by gas chromatography, using an SE-30 column. Products were isolated by distillation and characterized by standard methods in large-scale runs.

Registry No. *o*-Phenylenediamine, 95-54-5; cyclohexane, 110-82-7; sulfur, 10544-50-0; ammonia, 7664-41-7.

A Facile Biomimetic Method for Oxidative Deamination of Primary Amines to Aldehydes via Transposition of an Imine Functionality

James H. Babler* and Benedict J. Invergo

Department of Chemistry, Loyola University of Chicago, Chicago, Illinois 60626

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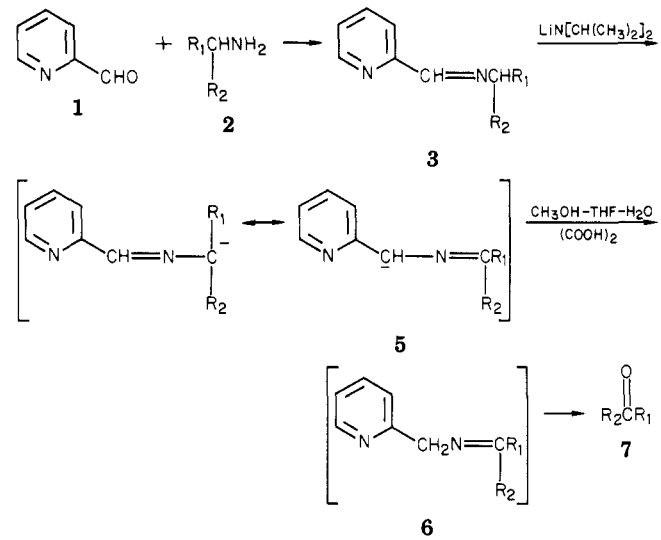
Considerable attention has been given by various research groups to developing methods for the oxidation of primary amines possessing the general structure **2** to the corresponding carbonyl compounds (**7**).[1] Prior to 1978 the synthetic methodology[2] available for effecting this transformation afforded good yields of ketones from primary amines containing secondary alkyl groups (i.e., **2**, R_1, R_2 = alkyl or aryl); however, similar attempts to prepare aldehydes from primary amines containing *primary alkyl* groups (i.e., **2**, R_1 or R_2 = H) generally gave poor yields (less than 40%). Although several methods[2,3] are available for conversion of substituted benzylamines to the corresponding aromatic aldehydes, they are less satisfactory for the preparation of aliphatic aldehydes. Recently a solution to this latter problem has been reported.[4] The new methodology effects the oxidation of primary alkyl amines to aldehydes by use of the heterocyclic reagent 5-bromo-3-(methylthio)-1,4-diphenyl-1,2,4-triazolium bromide, followed by oxidation of the corresponding derivatives with diethyl azodicarboxylate and subsequent acid-catalyzed hydrolysis.

Scheme I



1 2 3 5 6 7

a, $R_1 = CH_3(CH_2)_9$, R_2 = H; b, $R_1 = C_6H_5$, R_2 = H; c, R_1, $R_2 = -(CH_2)_7-$; d, $R_1 = C_6H_5$, $R_2 = CH_3$

In view of the fact that the known synthetic methodology for conversion of primary amines to aldehydes seems unnecessarily lengthy and often requires expensive reagents, we set out to develop a more convenient method that would closely mimic the biosynthetic equivalent of this process. It is known that enzyme-catalyzed oxidative deamination of α-amino acids to afford the corresponding α-keto acids involves reaction with pyridoxal phosphate to form a Schiff-base intermediate[5] and subsequent transposition of the carbon–nitrogen double bond. Our strategy therefore envisioned conversion of the primary amine substrate to a suitable imine derivative which could be isomerized via prototropic rearrangement. Subsequent hydrolysis would then effect the desired oxidative transformation.

On the basis of analogy with the biosynthetic process, 2-pyridinecarboxaldehyde (**1**)[6] seemed to be an attractive reagent to test our proposed methodology. By use of *n*-undecylamine (**2a**) as a representative aliphatic primary amine, its imine derivative (**3a**) with the latter aldehyde (**1**) was readily prepared. Subsequent conversion in essentially quantitative yield to the corresponding anion (**4a** ↔ **5a**) was accomplished in the presence of excess lithium diisopropylamide (LDA) in tetrahydrofuran at −70 °C. It was anticipated that kinetic protonation of the resulting anion might effect the desired prototropic rearrangement (i.e., conversion of **3a** to **6a**). Indeed, as expected, subsequent acidification of the reaction mixture and simultaneous hydrolysis using oxalic acid dihydrate in aqueous methanol afforded undecanal (**7a**) in 94% yield (Scheme I).

(1) For a survey of some of these methods, see: Harrison, I. T.; Harrison, S. (Vol. 1 and 2); Hegedus, L. S.; Wade, L., Jr. (Vol. 3) "Compendium of Organic Synthetic Methods"; Wiley: New York, 1971, 1974, 1977; Vol. I, pp 150–152, 404–406; Vol. 2, pp 60, 161–162; Vol. 3, pp 264–265. For a review, see: Baumgarten, R. J. *J. Chem. Educ.* **1966**, *43*, 398.

(2) For specific examples, see: Corey, E. J.; Achiwa, K. *J. Am. Chem. Soc.* **1969**, *91*, 1429; Calo, V.; Todesco, P. E. *J. Chem. Soc., Perkin Trans. 1* **1972**, 1652.

(3) Katritzky, A. R.; Cook, M. J.; Ikizler, A.; Millet, G. H. *J. Chem. Soc., Perkin Trans. 1* **1979**, 2500.

(4) Doleschall, G. *Tetrahedron Lett.* **1978**, 2131. Doleschall, G.; Toth, G. *Tetrahedron* **1980**, *36*, 1649.

(5) Stryer, L. "Biochemistry"; W. H. Freeman and Co.: San Francisco, 1975; pp 432–435.

(6) Available from Aldrich Chemical Co., Inc., Milwaukee, WI.

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