Synthesis of 1,4,2-Dioxazolidines by the Reaction of Keto Aldehydes with *N*-Phenylhydroxylamine. Intramolecular [3 + 2] Cycloaddition between the Nitrone and Carbonyl Moieties

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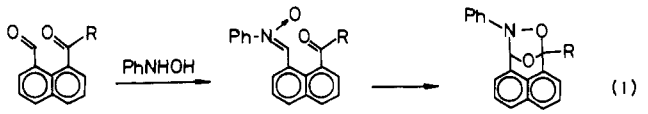
During our continuing interest in the chemistry of carbonyl oxides,[1] we noticed an apparent difference in reactivity between this intermediate and other 1,3-dipoles, for example, the nitrone; the former is well known to favor addition to carbonyl[2,3] In contrast, C–C double bonds are much more reactive than C–O double bonds toward nitrones, as the reaction with α,β-unsaturated carbonyl compounds illustrates.[4] Perhaps in accordance with this, only a few examples are known for the intermolecular cycloaddition of nitrones with carbonyl compounds leading to 1,4,2-dioxazolidines.[5,6] The similar stabilities between a nitrone/carbonyl pair and the adduct would be, however, an alternative reason. In reality, *C-tert*-butyl-*N*-phenylnitrone adds reversibly to pivalaldehyde to give the corresponding adduct.[5a] We undertook the reaction of keto aldehydes **1a–f** with *N*-phenylhydroxylamine (**2**), expecting that in the keto nitrone intermediates **3a–f** the nitrone and carbonyl groups are suitably arranged and, therefore, the intramolecular cycloaddition would occur very efficiently.

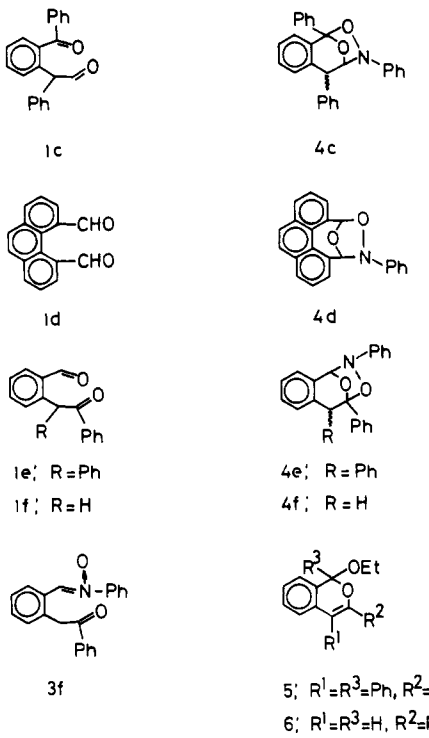
Treatment of a keto aldehyde **1a** with *N*-phenylhydroxylamine (**2**) in ethanol at room temperature for 15 h gave the corresponding 1,4,2-dioxazolidine **4a** (57% yield) as the sole isolable product. Thus, intramolecular [3 + 2] cycloaddition in the keto nitrone **3a** seems to be a very facile process (eq 1).[7] The same trend was observed for the keto aldehydes **1b,c** and dialdehyde **1d** (Table I).



(1)

1a; R = Ph 3a; R = Ph 4a; R = Ph
1b; R = Me 3b; R = Me 4b; R = Me

A remarkably different behavior was observed between *o*-(phenylbenzoylmethyl)benzaldehyde (**1e**) and *o*-(benzoylmethyl)benzaldehyde (**1f**). The reaction of **1e** with **2** gave an exo–endo mixture of the 1,4,2-dioxazolidine **4e** (exo:endo ratio = ca. 7:3). In the case of the keto aldehyde **1f**, however, the ^{1}H NMR spectra of the crude products showed the formation of both the keto nitrone **3f** and the keto ozonide **4f** (the **3f**:**4f** ratio = ca. 2:1 in $CDCl_3$ and 1:1 in CD_3COCD_3). These products, **3f** and **4f**, could not be separated from each other by column chromatography on silica gel, although the polarity of **3f** was expected to be significantly different from that of **4f** (in the thin-layer chromatography a broad band was observed). Although the crystallized material showed a fairly narrow range in the melting point (mp 174–178 °C), the IR spectra in the solid state (KBr) was much the same as those in solution ($CHCl_3$). These results would imply that the interconversion between **3f** and **4f** is very fast at least in solution. Probably, the phenyl substituent in **1e** accelerates the formation of the cycloadduct **4e**, and the stability of the keto nitrone **3f** is very similar to that of the corresponding 1,4,2-dioxazolidine **4f**.



Experimental Section

Preparation of Keto Aldehydes. Keto aldehydes **1a–f** were prepared by treating the corresponding ozonides with triphenylphosphine in benzene at 20 °C for 15 h, followed by column chromatography on silica gel. **1a**: mp 89.5–90.5 °C (from ethyl acetate); ^{1}H NMR (CCl_4) δ 7.1–8.2 (m, 11 H), 9.97 (s, 1 H); IR 1690, 1660 cm^{-1}. Anal. Calcd for $C_{18}H_{12}O_2$: C, 83.06; H, 4.65. Found: C, 83.13; H, 4.63. **1b**: mp 120–123 °C (from ethyl acetate); ^{1}H NMR ($CDCl_3$) δ 2.77 (s, 3 H), 7.2–8.2 (m, 6 H), 10.06 (s, 1 H); IR 1690, 1685 cm^{-1}. Anal. Calcd for $C_{13}H_{10}O_2$: C, 78.77; H, 5.08. Found: C, 78.85; H, 5.07. **1c**: an oil; ^{1}H NMR (CCl_4) δ 5.52 (s, 1 H), 6.7–7.8 (m, 14 H), 9.70 (s, 1 H); IR 1725, 1660 cm^{-1}. **1d**: mp 166–169 °C (from ethyl acetate); ^{1}H NMR ($CDCl_3$) δ 7.2–8.3 (m, 8 H), 9.97 (s, 2 H); IR 1690 cm^{-1}.[8] **1e**: mp 119–120 °C (from ethyl acetate–hexane); ^{1}H NMR ($CDCl_3$) δ 7.8–8.0 (m, 15 H), 10.04 (s, 1 H); IR 1695, 1690 cm^{-1}. Anal. Calcd for $C_{21}H_{16}O_2$: C, 83.98; H, 5.37. Found: C, 84.37; H, 5.35. **1f**: mp 93–95 °C (from ethyl acetate–hexane); ^{1}H NMR ($CDCl_3$) δ 4.76 (s, 2 H), 7.2–8.1 (m, 9 H), 10.01 (s, 1 H); IR 1695, 1685 cm^{-1}. Anal. Calcd for $C_{15}H_{12}O_2$: C, 80.34; H, 5.39. Found: C, 80.39; H, 5.35.

(1) Mori, M.; Sugiyama, T.; Nojima, M.; Kusabayashi, S.; McCullough, K. J. *J. Am. Chem. Soc.* **1989**, *111*, 6884. (b) Nakamura, N.; Fujisaka, T.; Nojima, M.; Kusabayashi, S.; McCullough, K. J. *Ibid.* **1989**, *111*, 1799.

(2) Kuczkowski, R. L. *1,3-Dipolar Cycloaddition Chemistry*; Padwa, A., Ed.; Wiley: New York, 1984; Vol. 2, Chapter 11.

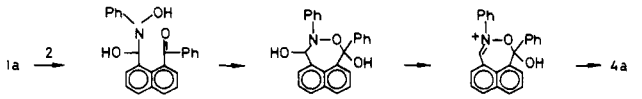
(3) Recently, Kuczkowski and co-workers found, however, that a carbonyl oxide can cycloadd to a vinyl ether giving the corresponding 1,2-dioxolane: Wojciechowski, B. J.; Pearson, W. H.; Kuczkowski, R. L. *J. Org. Chem.* **1989**, *54*, 115 and the references therein.

(4) Tufariello, J. J. *1,3-Dipolar Cycloaddition Chemistry*; Padwa, A., Ed.; Wiley: New York, 1984; Vol. 2, Chapter 9.

(5) (a) De Sarlo, F.; Brandi, A. *J. Chem. Res. Synop.* **1980**, 122. (b) Moderhack, D.; Stolz, K. *J. Org. Chem.* **1986**, *51*, 732.

(6) Synthesis of 1,4,2-dioxazolidines by other methods. (a) Lam, W. Y.; Des Marteau, D. D. *J. Am. Chem. Soc.* **1982**, *104*, 4034. (b) Taylor, E. C.; Tseng, C.; Rampal, J. B. *J. Org. Chem.* **1982**, *47*, 552. (c) Del'tsova, D. P.; Gambaryan, N. P.; Lur'e, E. P. *Izv. Akad. Nauk SSSR, Ser. Khim.* **1979**, 1788; *Chem. Abstr.* **1980**, *92*, 6475e. (d) Varwig, J.; Mews, R. *Angew. Chem., Int. Ed. Engl.* **1977**, *16*, 882.

(7) Alternatively, the dioxazolidine **4** would be produced by a stepwise process shown below.



(8) Sturrock, M. G.; Duncan, R. A. *J. Org. Chem.* **1968**, *33*, 2149.

Table I. Reaction of Keto Aldehydes 1 with *N*-Phenylhydroxylamine (2)[a]

keto aldehyde	products (% yield)	recovered 1 (%)
1a	4a (57)	1a (35)
1b	4b (56)	1b (32)
1c	4c (65),[b] 5 (30)	1c (3)
1d	4d (36)	1d (50)
1e	4e (47)[c]	1e (30)
1f	3f + 4f (46), 6 (12)	1f (25)

[a] A mixture of a keto aldehyde 1 (2 mmol) and 2 (2 mmol) in ethanol (20 mL) was kept with stirring at room temperature for 15 h. [b] The exo:endo ratio = 68:32. [c] The exo:endo ratio = 67:33.

Reaction of Keto Aldehydes 1a-e with *N*-Phenylhydroxylamine (2). An equimolar mixture of **1a** (2 mmol) and **2** (2 mmol) in ethanol (20 mL) was kept with stirring at room temperature for 15 h. The mixture was poured into water and extracted with ether. Then, the crude products were column chromatographed on silica gel. Elution with benzene–hexane (1:1 v/v) yielded the 1,4,2-dioxazolidine **4a** (57% yield): mp 147–148 °C (from ether–hexane); ^{1}H NMR ($CDCl_3$) δ 6.26 (s, 1 H), 6.4–8.0 (m, 16 H); ^{13}C NMR ($CDCl_3$) δ 97.63 (1 C), 108.17 (1 C), 118.82–137.07 (21 C), 151.12 (1 C); IR 1600, 1490, 1450, 1070, 960, 780, 725, 700 cm^{-1}. Anal. Calcd for $C_{24}H_{17}NO_2$: C, 82.03; H, 4.88; N, 3.99. Found: C, 82.26; H, 4.95; N, 3.76.

The reactions of **1b–e** were undertaken under similar conditions. **4b**: mp 145–146 °C (from ether–hexane); ^{1}H NMR ($CDCl_3$) δ 2.35 (s, 3 H), 6.41 (s, 1 H), 7.0–7.9 (m, 11 H); ^{13}C NMR ($CDCl_3$) δ 19.06 (1 C), 96.83 (1 C), 106.56 (1 C), 117.71–135.96 (17 C), 151.27 (1 C); IR 1595, 1485, 1310, 1090, 960, 810, 775 cm^{-1}. Anal. Calcd for $C_{19}H_{15}NO_2$: C, 78.87; H, 5.23; N, 4.84. Found: C, 78.83; H, 5.15; N, 4.80. **4c**: a 2:1 mixture of the exo and endo isomer; mp 129–131 °C (from ether–hexane); ^{1}H NMR ($CDCl_3$) δ 4.54 (s, exo), 4.94 (d, J = 4 Hz, endo), 5.56 (d, J = 4 Hz, endo), 5.62 (s, exo), 6.5–7.9 (19 H);[9] IR 1600, 1490, 1450, 985, 750, 695 cm^{-1}. Anal. Calcd for $C_{27}H_{21}NO_2$: C, 82.84; H, 5.41; N, 3.58. Found: C, 82.77; H, 5.30; N, 3.44. **4d**: mp 197–198 °C (from methylene chloride–hexane); ^{1}H NMR ($CDCl_3$) δ 6.67 (s, 1 H), 6.69 (s, 1 H), 7.1–8.0 (m, 13 H); ^{13}C NMR ($CDCl_3$) δ 100.39 (1 C), 105.48 (1 C), 116.33–136.44 (19 C), 149.92 (1 C); IR 1595, 1485, 1440, 1300, 1060, 825, 760 cm^{-1}. Anal. Calcd for $C_{22}H_{15}NO_2$: C, 81.21; H, 4.65; N, 4.31. Found: C, 81.21; H, 4.61; N, 4.28. **4e**: a 2:1 mixture of the exo and endo isomer: mp 155–156 °C (from ethanol); ^{1}H NMR ($CDCl_3$) δ 4.51 (s, 1 H), 6.18 (s, endo), 6.32 (s, exo), 7.1–8.0 (m, 19 H); ^{13}C NMR ($CDCl_3$) δ 55.14 (exo), 57.61 (endo), 96.49 (exo), 96.54 (endo), 109.48 (endo), 110.03 (exo), 118.07–140.19 (complex signals exo + endo), 150.59 (exo), 150.88 (endo); IR 1595, 1485, 1450 cm^{-1}. Anal. Calcd for $C_{27}H_{21}NO_2$: C, 82.84; H, 5.41; N, 3.58. Found: C, 83.07; H, 5.36; N, 3.57. A vinyl ether **5**: an oil; ^{1}H NMR ($CDCl_3$) δ 1.21 (t, J = 7 Hz, 3 H), 3.6–4.2 (m, 2 H), 6.66 (s, 1 H), 6.8–7.6 (m, 14 H).

Reaction of a Keto Aldehyde 1f with *N*-Phenylhydroxylamine. An equimolar mixture of **1f** (2 mmol) and **2** (2 mmol) in ethanol (20 mL) was kept with stirring at 20 °C for 15 h. After evaporation of the solvent, the ^{1}H NMR spectra of the crude products were measured, which showed the existence of both the nitrone **3f** and the 1,4,2-dioxazolidine **4f**. Column chromatography of the crude products on silica gel (elution with benzene–hexane, 1:1, v/v) gave the vinyl ether **6**: an oil; ^{1}H NMR (CCl_4) δ 1.20 (t, J = 7 Hz, 3 H), 3.3–3.7 (m, 2 H), 6.66 (s, 1 H), 6.8–7.6 (m, 14 H). From the second fraction (elution with ether–benzene, 1:1, v/v) was obtained a mixture of the keto nitrone **3f** and the dioxazolidine **4f**, the **3f**:**4f** ratio in $CDCl_3$ being ca. 2:1: mp 174–178 °C (from ethanol); IR 1680, 1595, 1550, 1345, 1210, 1070, 750, 685 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 3.23 (d, J = 18 Hz, **4f**), 3.50 (d, J = 18 Hz, **4f**), 4.41 (s, **3f**), 6.23 (s, **4f**), 7.0–8.1 (m), 8.13 (s, **3f**), 9.18–9.33 (m); ^{13}C NMR ($CDCl_3$) δ 40.51 (**4f**), 44.21 (**3f**), 96.12 (**4f**), 108.02 (**4f**), 118.06–138.28 (complex signals, **3f** + **4f**), 149.47 (**3f**), 150.84 (**4f**), 197.34 (**3f**). Anal. Calcd for $C_{21}H_{17}NO_2$: C, 79.98; H, 5.43; N, 4.44. Found: C, 80.08; H, 5.33; N, 4.32.

(9) The assignment of the stereochemistry was based on the fact that for the relevant exo-endo 1,3-diphenylindene ozonide and exo–endo 2,3-diphenylindene ozonide the same relation holds for the chemical shift and coupling constant between the exo and endo protons attached to the phenyl substituent in ^{1}H NMR spectra: Miura, M.; Nojima, M.; Kusabayashi, S.; McCullough, K. J. *J. Am. Chem. Soc.* **1984**, *106*, 2932.

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Synthesis of Aryl-Substituted Sulfonium Salts by the P_2O_5–Methanesulfonic Acid Promoted Condensation of Sulfoxides with Aromatic Compounds

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Interest in aryl-substituted sulfonium salts in this laboratory has stemmed from the observation that such compounds are highly photosensitive and can be used as efficient photochemical sources of strong Brønsted acids.[1,2] This discovery has led to extensive use of triarylsulfonium salts as photoinitiators in cationic vinyl and ring-opening polymerizations and in the design of novel microelectronic photoresists. More recently, we have been exploring the relationship between the structure of various sulfonium salts and their photosensitivity and spectral response. These efforts have prompted a number of attempts from this and other laboratories to discover new methods for the synthesis of photoactive aryl-substituted sulfonium salts.

A considerable number of synthetic routes have been derived for the preparation of symmetric and asymmetric aryl-substituted sulfonium salts. Several excellent reviews of the subject reflect the current state of activity in this field.[3-6] Of particular note is the recent report by Julia and co-workers[7] of the facile synthesis of alkyldiarylsulfonium salts by the acid-catalyzed alkylation of diphenyl sulfide with alcohols and ethers. In previous communications from this laboratory, we described the preparation of triarylsulfonium salts in high yields by the copper-catalyzed condensation of diaryliodonium salts with diaryl sulfides[8] and with aryl thiols.[9] In general, currently available synthetic methods for the preparation of aryl-substituted sulfonium salts suffer from low yields, utilize unavailable starting materials, or involve complex multistep procedures. Because of the ready availability of diaryl sulfides and diaryl sulfoxides, most syntheses of aryl-substituted sulfonium salts rely on the use of these compounds as substrates. For example, unsymmetrical aryl-substituted sulfonium salts in moderate yields can be prepared by the condensation of diaryl sulfoxides with aryl and alkyl Grignard reagents in the presence of trialkylsilyl triflates.[10] Triarylsulfonium salts can also be synthesized by the condensation of diaryl sulfoxides with aromatic hydrocarbons in the presence of aluminum chloride or sulfuric acid.[11-14] However, the low yields and restrictions placed on substrates due to the harsh reaction conditions employed severely restrict the generality of this method.

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