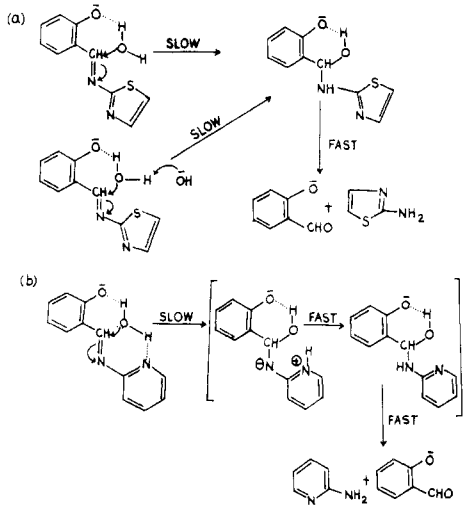
Scheme IV[a]

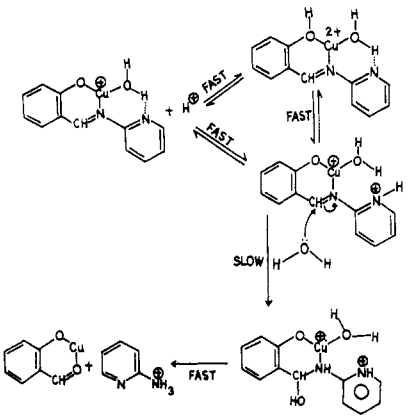


[a] Intramolecular general base catalysis: (a) $CH^-$-independent and $OH^-$-dependent paths of Tzim and (b) $OH^-$-independent path of Pyin.

$k_2^M$ cannot be compared with $k_2$. If it is assumed that the imine anions are positioned in the Stern layer of the micelle of CTAB, the estimated volume of which is taken to be 0.14 L,[13] then the second-order rate constant ($k_2^{(m)}$ = 0.14 $k_2^M$) in the micellar pseudophase for Tzim turned out to be $(2.2 \pm 0.3) \times 10^{-4}$ dm$^3$ mol$^{-1}$ s$^{-1}$. This is at least 200 times lower than the analogous data for Tzim in the aqueous phase (see Table V). For direct nucleophilic attack of $OH^-$ at the aldimine carbon micellar binding of both $OH^-$ and the imine anion would have resulted in the rate acceleration. This contrasting feature along with complete lack of [$OH^-$] dependence in the hydrolysis of the anion of Pyim in both the aqueous and micellar pseudophases strongly supports our earlier suggestion[10,11] that the hydrolysis of the phenoxide form of both the imines via both $OH^-$-independent and $OH^-$-dependent paths (the latter path for Tzim) involves intramolecular general base catalysis of the phenoxide group of Tzim and of the phenoxide group and pyridyl nitrogen of Pyim (Scheme IV).

The pseudo-first-order rate constant of hydrolysis of the neutral form of Tzim in the micellar phase ($k_{HL}^M$) of CTAB is not significantly different from the corresponding rate constant in the aqueous phase (see Table V). This is in contrast with the reported marked inhibitory effect of CTAB on the rate of apparently neutral hydrolysis of benzilidene imines which involves rate-determining attack of $OH^-$ on their protonated form.[18] The observed order of reactivity of the imines is $k_{HL}^M$(SDS) > $k_{HL}^M$(CTAB). The neutral form of the imines undergoes hydrolysis in the micellar pseudophase of SDS twice as fast as in the aqueous phase (see Table V). The observed kinetic effects as well as the low value of the micellar binding constant ($K_{HL}^M$) point to the fact that the imines, like their anionic forms, are presumably positioned in the Stern layer of the micelles rather than in the hydrophobic interior of the latter.

Scheme V



The second-order acid-catalyzed hydrolysis rate constant of the complex in the micellar pseudophase ($k^M_{CuL^+}$) of SDS is 5 times higher than the corresponding rate constant in the aqueous phase (see Talbe V). The relatively stronger acid catalysis of hydrolysis of $CuL^+$ in the anionic micelle may be attributed to the micelle-enhanced basicity of the unbound pyridyl nitrogen and the coordinated phenoxide moiety of the imine complex, which may undergo fast protonation preequilibrium preceding the rate determining hydration of the imine linkage (Scheme V). The validity of eq 10, however, suggests that the micelle-bound species $CuL^+$ is not appreciably protonated in the range of pH studied.

**Registry No.** *N*-Salicylidene-2-aminothiazole, 21151-43-9; *N*-salicylidene-2-aminopyridine, 1823-47-8; cupric perchlorate, 13770-18-8.

**Supplementary Material Available:** Two figures showing isosbestic points in the base hydrolysis of *N*-salicylidene-2-aminothiazole in the absence and presence of CTAB (3 pages). Ordering information is given on any current masthead page.

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# *N*-Methylpiperidine *N*-Oxide as a Source of Nonstabilized Ylide: A New and Efficient Route to Octahydroindolizine Derivatives

J. Chastanet and G. Roussi*

*Institut de Chimie des Substances Naturelles, C.N.R.S., 91190 Gif-sur-Yvette, France*

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*N*-Methylpiperidine *N*-oxide in the presence of LDA reacts with various nonactivated olefins to give high yields of the corresponding octahydroindolizines. The structure of the nonstabilized ylide intermediate allows the study of the *regiochemistry* and *stereochemistry* of this new cycloaddition reaction.

The 1,3-dipolar cycloaddition is one of the most useful reactions for the synthesis of five-membered heterocyclic compounds.[1] However, the vast majority of syntheses reported involve electron withdrawing group activated

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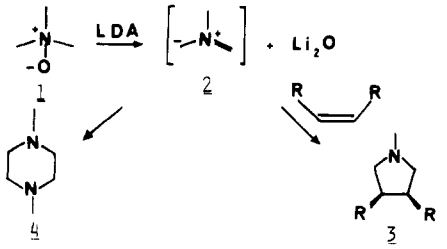
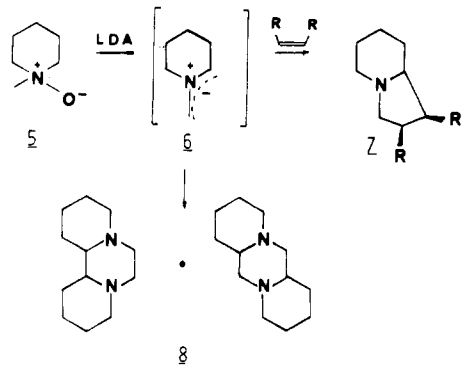
**Scheme I**



**Scheme II**



double bonds and classical dipoles such as nitrones,[2] nitrile oxides,[3] and stabilized azomethine ylides.[4]

Analogous unsubstituted ylides without stabilization of the carbanionic center were unknown prior to 1979, when the desilylation of α-trimethylsilyl iminium salts with subsequent trapping by activated double bonds was reported.[5] In contrast to their *intermolecular* counterparts, *intramolecular* additions of nonstabilized azomethine ylides have been reported to proceed efficiently with unactivated olefins.[6]

We have recently shown[7] that the nonstabilized ylide **2** can be generated by treating trimethylamine *N*-oxide (**1**) with LDA (Scheme I). This intermediate is highly reactive as demonstrated by its intermolecular addition to simple alkenes to give high yields of the corresponding pyrrolidines **3**, while in the absence of olefinic compound it dimerizes to the piperazine **4** (Scheme I).

To examine the *regioselectivity* and *stereoselectivity* of this reaction we decided to study the variation of the starting *N*-oxide and the extension of the method to the construction of the indolizidine skeleton **7** from *N*-methylpiperidine *N*-oxide (**5**) and various simple alkenes (Scheme II). The wide range of biological activities represented by alkaloids incorporating the indolizidine skeleton makes this a particularly attractive target.[8] In addition, the study could be of interest in the general question of the regioselectivity of the cycloaddition reactions.[4c,9]

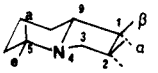


**Figure 1.** Trans ring junction indolizidine representation.

## Structural Elucidation of Indolizidines

The assignment of trans configuration to the different octahydroindolizines studied and the preference of the pyrrolidine ring to adopt an envelope conformation was made by analysis of $^1$H NMR (400 MHz) spectra[10] and on the basis of the presence of Bohlmann bands in the infrared spectra,[11] attributed to vibration of hydrogens oriented trans antiperiplanar to the nitrogen lone pair. In these puckered structures C-1, C-2, C-3, and C-9 are almost coplanar, while the nitrogen atom is situated out of the plane. Protons at positions 3 and 9 can be approximated to axial (ax) or equatorial (eq) whereas 1 and 2 bisect the plane. For simplicity we use α and β terminology for pyrrolidine substituents, α substituents being on the side of the nitrogen lone electron pair (Figure 1).

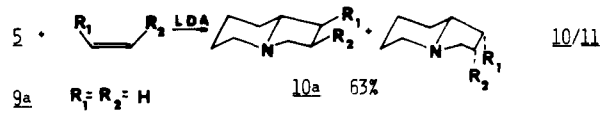
## Results

We report our results concerning the behavior of the ylide **6** generated from *N*-methylpiperidine *N*-oxide (**5**) (1 equiv) by treatment with LDA (3.5 equiv) in the presence or absence of various olefins (1.1 equiv). In both cases the reaction is followed by GLC. After 3 h, usual workup provides the expected indolizidine products, whose structures were determined by physical methods.

As with trimethylamine *N*-oxide[7] (**1**), treatment of compound **5** with LDA in the absence of an olefinic compound provides high yields (70%) of a mixture of piperazines **8** in a 0.05/0.4/1/0.12 ratio. The structures of the different isomers have not yet been elucidated.

When the reaction between ylide **6** and an olefin is unfavorable, competitive dimerization is observed. Thus in the presence of the unreactive olefins 1-methylcyclopentene and 1,2-dihydropyran, formation of piperazines **8** is the only reaction observed.

Indolizidine **10a** ($R_1 = R_2 = H$) is obtained in good yield (63%) by the reaction of **5** and ethylene. Use of cyclopentene **9b** leads to the formation in high yield of a product **10b**, which has exo stereochemistry,[12] while 2-



| | | | | | | |
|---|---|---|---|---|---|---|
| 9a | $R_1 = R_2 = H$ | 10a | 63% | | | 10/11 |
| 9b | $R_1, R_2 = (CH_2)_3$ | 10b | 92% | 11b | - | 100/1 |
| 9c | $R_1 = R_2 = Ph$ | 10c | 50% | 11c | | 100/1 |

(1) Huisgen, R.; Grashey, R.; Sauer, J. In "The Chemistry of Alkenes"; Patai, S., Ed.; Interscience: London, 1964; pp 806–878. Huisgen, R. *Angew. Chem., Int. Ed. Engl.* **1963**, *2*, 565, 633.

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(10) Ringdahl, B.; Pinder, A. R.; Pereira, W. E.; Oppenheimer, N. J.; Craig, J. C. *J. Chem. Soc., Perkin Trans. 1* **1984**, 1.

(11) Bohlmann, F. *Chem. Ber* **1958**, *91*, 2157.

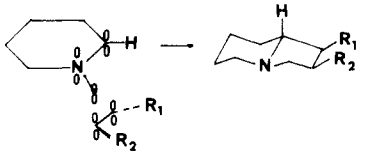
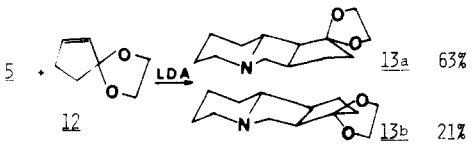
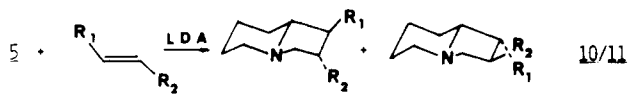


**Figure 2.** Exo transition state leading to β-substituted indolizidines.

cyclopenten-1-one ethylene ketal (**12**) leads to the two exo regioisomers **13a,b** in 84% overall yield.



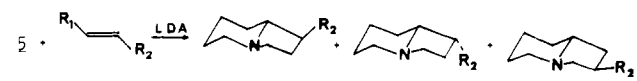
*exo*-Diphenylindolizidine (**10c**) is formed stereospecifically from *cis*-stilbene (**9c**) (50%), while *trans*-stilbene (**9d**) and *trans*-β-methoxystyrene (**9e**) give a mixture of the isomers **10d** and **11d** (71%) and **10e** and **11e** (61%), respectively, the major isomer having the 1-



| | | | | | |
|---|---|---|---|---|---|
| 9d | $R_1 = R_2 = Ph$ | 10d 24% | 11d 47% | | 1/2 |
| 9e | $R_1 = Ph$ $R_2 = OMe$ | 10e 3% | 11e 58% | | 1/19 |

phenyl substituent in the endo position.[13] It is noteworthy that the reaction with β-methoxystyrene (**9e**) is *regiospecific* and leads to 1-phenyl-2-methoxyindolizidine.

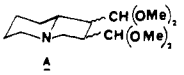
In the interesting case of monosubstituted olefins, a mixture of stereo- and regioisomers is obtained. Styrene (**9f**) and *p*-methoxystyrene (**9g**) lead respectively to the corresponding 1- and 2-substituted indolizidines, the ratio [(**14** + **15**)/**16**] being equal to 3.6 and 5.2, respectively. The formation of the 1-β compound is favored to a greater extent in the case of β-methoxystyrene (**14g**/**15g** = 1) than in that of styrene (**14f**/**15f** = 2). The 2-α-substituted compounds were formed in too low a yield to be characterized in the mixture.[14]



| | | | | |
|---|---|---|---|---|
| 9f | $R_1 = H$, $R_2 = Ph$ | 14f 39% | 15f 19% | 16f 16% |
| 9g | $R_1 = H$, $R_2 = PhOMe$ | 14g 47% | 15g 5% | 16g 10% |

(12) We have observed that cyclohexene gave slowly 40% of a mixture of *exo*- and *endo*-dodecahydrobenz[*a*]indolizine in a 1.9/1 ratio. The low reactivity of this olefin was shown by the exclusive formation of indolizidine **10b** in a competitive reaction with cyclopentene. Analyses were performed on the isomeric mixture: IR 2760 (strong band), 2720, 2650 (shoulder) $cm^{-1}$; MS, *m/e* 179, 97; $^1H$ NMR (400 MHz) (of the major exo isomer) δ 1.90 (m, 1 H, $H_{3\beta}$), 2.10 (m, 2 H, $H_{5ax}$, $H_{1\alpha}$), 2.8 (b d, 1 H, $H_{2\alpha}$), 3.10 (b d, 1 H, $H_{5eq}$), 3.35 (dd, 1 H, $H_{3\alpha}$); picrate of the mixture. Anal. Calcd for $C_{18}H_{24}N_4O_7$: C, 52.94; H, 5.88; N, 13.73; O, 27.45. Found: C, 52.64; H, 5.99; N, 13.55; O, 27.46.

(13) It is noteworthy that *trans*-1,1,4,4-tetramethoxy-2-butene generates a high yield (90%) of a mixture of the two indolizidines A. Preparative TLC ($CH_2Cl_2$–MeOH 80/20) allows the separation of the two isomers which possess identical MS (*m/e* 273, 272, 258, 242, 235, 228, 198,



A

179, 98, 97, 75, 57) and HRMS (calcd for $C_{14}H_{27}NO_4$ 273.1940, found 273.1949). Only one $^1H$ NMR spectrum could be obtained, which does not allow definitive stereochemistry attribution: $^1H$ NMR (400 MHz) δ 2.10 (m, 1 H), 2.20 (m, 1 H, $H_{5ax}$) 2.40 (dd, 1 H), 3.15 (m, 2 H, $H_{3\alpha}$, $H_{5eq}$), 3.45 (m, 12 H, OMe), 4.4 (d, 1 H, CH–O), 4.55 (d, 1 H, CHO).

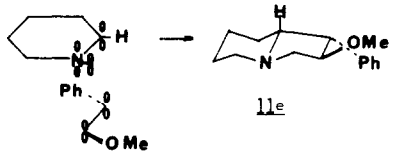


**Figure 3.** Transition state leading to indolizidine **11e**.

## Discussion

The reactions between the ylide **6** generated from *N*-methylpiperidine *N*-oxide (**5**) and various olefinic compounds are of the 1,3-dipolar cycloaddition type, as shown by the *stereospecificity* observed with cis and trans dipolarophiles and by the *nonpolymerization* of styrene.[4c] All the olefins used afford the trans ring junction indolizidines, which have been calculated to be more stable by 2–4 kcal $mol^{-1}$.[10]

The lack of data concerning the orbital coefficients of olefinic and ylide carbons excludes, here any quantitative interpretation of the regioselectivities observed in the course of our work. However, it is noteworthy that additions are less selective than with other ylides such as nitrones[15] or diazoalkanes.[9e] One interpretation may be that there is little difference in the atomic orbital coefficients of the termini of the 1,3-dipole **6**. The *stereospecific* formation of 1-phenyl-2-methoxyindolizidines (**10e**, **11e**) from β-methoxystyrene (**9e**) may be justified by the presence of the methoxy group, which allows a better differentiation of the two olefinic carbons.

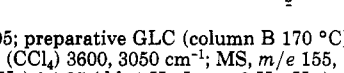
The reaction between ylide **6** and *cis*-stilbene (**9c**) or monosubstituted or cyclic olefins provides selectively β-substituted indolizidines via an exo transition state (Figure 2).

The reaction is *stereospecific* with cyclopentene (**9b**), *cis*-stilbene (**9c**), and 2-cyclopenten-1-one ethylene ketal (**12**) but *stereoselective* with cyclohexene,[12] styrene (**9f**), vinylanisole (**9g**), and 2-propen-1-ol.[14] Steric factors in the endo transition state are certainly responsible in part for such selectivity. *trans*-β-Methoxystyrene (**9e**) adds selectively via a transition state in which the phenyl group is endo (Figure 3), owing to secondary orbital interaction that favors this approach over its exo counterpart.[9f]

## Conclusion

We have shown that it is possible to generate the nonstabilized cyclic ylide **6** by treating *N*-methylpiperidine *N*-oxide with LDA. When trapped with various simple olefins this ylide readily provides the corresponding indolizidines by a cycloaddition reaction with synthetically interesting yields.

(14) A preliminary result obtained with 2-propen-1-ol shows that the reaction provides 66% of a mixture of isomers containing 2β-(1-hydroxymethyl)octahydroindolizine B (17%), 2α-isomer B′ (38%), and traces of 1-substituted isomer: HRMS, calcd for $C_9H_{17}NO$ 155.1300,



B B′

found 155.1305; preparative GLC (column B 170 °C) allows their separation. B: IR ($CCl_4$) 3600, 3050 $cm^{-1}$; MS, *m/e* 155, 154, 115, 98, 60; $^1H$ NMR (400 MHz) δ 1.95 (dd, 1 H, $J_{gem}$ = 9 Hz, $H_{3\beta}$), 2.0 (dt, 1 H, $J_{gem}$ = 12 Hz, $H_{5ax}$), 2.4 (m, b s, 2 H, $H_{2\alpha}$, OH), 3.10 (b d, 1 H, $J_{gem}$ = 12 Hz, $H_{5eq}$), 3.25 (dd, 1 H, $J_{gem}$ = 9 Hz, $J_{3\alpha,2\alpha}$ = 7.5 Hz, $H_{3\alpha}$), 3.6 (m, 2 H, $J_{gem}$ = 13 Hz, $CH_2OH$). B′: IR ($CCl_4$) 3600–3050, 2750, 2675, 2600 (shoulder), 1020; MS, *m/e* 155, 154, 98; $^1H$ NMR (400 MHz) δ 2.0 (m, 2 H, $H_{5ax}$, $H_{2\beta}$), 2.2 (dd, 1 H, $H_{3\beta}$), 2.6 (b s, 1 H, OH), 3.05 (m, 2 H, $J_{3\alpha,3\beta}$ = 9 Hz, $H_{5eq}$, $H_{3\alpha}$), 3.7 (m, 2 H, $CH_2OH$).

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## Experimental Section

**Instrumentation and Solvents.** Melting points (mp) are not corrected. Infrared spectra (IR) were recorded neat on a Perkin-Elmer 257 spectrophotometer. Mass spectra (MS) were obtained with a MS.50 spectrograph or with a Hewlett-Packard 5992 A equipped with a gas–liquid chromatograph. High-resolution mass spectrometry (HRMS) for exact mass measurements was conducted with a Kratos MS 80 RF instrument. Proton magnetic resonance spectra ($^1$H NMR) were measured either with a Bruker WM 400 (400 MHz) or through I.E.F. (Institut d'Electronique Fondamentale, Université de Paris-Sud, 91405 Orsay, France). Routine spectra (60 MHz) were obtained on a Perkin-Elmer R12 type while carbon magnetic resonance spectra ($^{13}$C NMR) were recorded on a Bruker HX 90E. Chemical shifts are reported in units of $\delta$ downfield of internal $Me_4Si$; chloroform-*d* was used as the solvent. Splitting patterns are designated with s (singlet), d (doublet), t (triplet), m (multiplet), and b (broad). Analytical and preparative gas–liquid chromatography (GLC) was executed on a Girdel 75H chromatograph. The following columns were used: (A) OV1 5% and (B) Carbowax 10%. Analytical and preparative thin-layer chromatography (TLC) was done on silica gel Merck HF 254 + 366 precoated plates. Column chromatography was done on silica gel Merck 60 (70–230 mesh ASTM) (S) or on neutral (A) or basic (AA) alumina.

Anhydrous tetrahydrofuran (THF) was distilled from sodium benzophenone ketyl immediately before use and stored under nitrogen. Lithium diisopropylamide in THF (LDA) was prepared from diisopropylamine distilled from $CaH_2$ and commercially available butyllithium.

All the experiments were carried out under a nitrogen atmosphere arranged with a mercury bubbler so that the system could be left under a slight pressure. Syringes and reaction flasks were dried in an oven prior to use.

Elemental analyses were performed by the Service Central de Microanalyse du C.N.R.S.

**General Procedure.** In a typical experiment, a suspension in THF (50 mL) of the *N*-oxide (**5**) (1 equiv), dried under vacuum (50 °C) in a reaction flask sealed with a rubber septum, and the olefin (1.1 equiv) is cooled to −78 °C. LDA (3.5 equiv) is then added via syringe over a period of a few minutes, and the reaction mixture turns homogeneous. After the solution has been stirred for a period of 1 h, the reaction progress is followed by GLC observing the ratio product formed/olefin and by TLC observing the disappearance of the *N*-oxide, after sample hydrolysis with a drop of methanol.

Most reactions are complete in 3 h. Hydrolysis, extraction with $CH_2Cl_2$, drying over $Na_2SO_4$, and chromatography provide the product (procedure A).

In some cases extraction was avoided by the addition of a stoichiometric quantity of water and filtration over alumina of the crude residue obtained after vacuum distillation of solvent and diisopropylamine (procedure B).

Picrates were chosen as characteristic crystalline derivatives.

***N*-Methylpiperidine *N*-Oxide (5).**[16] *N*-Methylpiperidine (6 g, 60 mmol) is treated with 30% $H_2O_2$ (20 mL) at room temperature for 24 h. The excess hydrogen peroxide is destroyed by addition of $MnO_2$, until the filtrate proved negative to KI paper. The solution is evaporated to dryness under reduced pressure at 60 °C to prevent decomposition. Flash chromatography (AA) ($CH_2Cl_2$) affords *N*-oxide **5** (5.5 g, 48 mmol, 79%): MS, *m/e* 115, 99, 98; $^1$H NMR (60 MHz) $\delta$ 1.2–2.6 (m, 6 H), 3.15 (s in m, 7 H).

**Piperazines 8.** *N*-Oxide **5** (320 mg, 2.78 mmol) is treated with LDA (9.73 mmol) for 4 h. GLC analysis (column A) shows the presence of four peaks in a 0.04/0.4/1/0.1 ratio. MS spectra of these four compounds analyzed on a spectrometer equipped with a GLC apparatus are identical (*m/e* 194, 98, 97, 96). Chromatography on alumina (hexane–$CH_2Cl_2$ 50/50) provides piperazines **8** (190 mg, 1 mmol, 70%).

**Octahydroindolizine (10a).** A suspension of *N*-oxide **5** (160 mg, 1.39 mmol) in THF (50 mL) is cooled to −78 °C. Dried ethylene is then bubbled through the mixture, and LDA (4.87 mmol) is added.

After 2 h, procedure B provides **10a** (110 mg, 0.88 mmol, 63%): picrate mp (MeOH) 228 °C (lit.[17] mp 227 °C).

**1$\beta$,2$\beta$-Cyclopentanooctahydroindolizine (10b).** A suspension of *N*-oxide **5** (240 mg, 2.09 mmol) in THF (50 mL) and cyclopentene **9b** (157 mg, 2.3 mmol) is cooled to −78 °C. LDA (7.35 mmol) is added dropwise. After 3 h, procedure B gives pure **10b** (318 mg, 1.92 mmol, 92%): GLC column A; MS, *m/e* 165, 164, 136, 97; IR 2780, 2700, 2600 cm$^{-1}$; $^1$H NMR (400 MHz) $\delta$ 1.65 (dd, 1 H, $J_{gem}$ = 9 Hz, $H_{3\beta}$), 1.90 (dt, 1 H, $J_{gem}$ = 12 Hz, $J_{5ax,6eq}$ = 3 Hz, $H_{5ax}$), 2.20 (m, 1 H, $H_{1\alpha}$), 2.65 (m, 1 H, $J_{2\alpha,3\beta}$ = 7.5 Hz, $H_{2\alpha}$), 3.10 (b d, 1 H, $J_{gem}$ = 12 Hz, $H_{5eq}$), 3.30 (dd, 1 H, $J_{gem}$ = 9 Hz, $J_{3\alpha,2\alpha}$ = 9 Hz, $H_{3\alpha}$); picrate (EtOH) mp 172–173 °C. Anal. Calcd for $C_{17}H_{22}N_4O_7$: C, 51.78; H, 5.58; N, 14.21; O, 28.43. Found: C, 51.86; H, 5.67; N, 13.97; O, 28.49.

***cis*-1$\beta$,2$\beta$-Diphenyloctahydroindolizine (10c).** *N*-Oxide **5** (140 mg, 1.22 mmol) and *cis*-stilbene (**9c**) (248 mg, 1.37 mmol) are treated with LDA (4.27 mmol). After 3 h, procedure A gives the crude product (346 mg) purified by chromatography on silica gel (hexane–$CH_2Cl_2$ 50/50) (170 mg, 0.61 mmol, 50%): mp (ether–hexane) 88 °C; GLC column A; IR 3080–3030, 2780, 2750, 2650 (shoulder), 1600, 1500, 1450, 700 cm$^{-1}$; MS, *m/e* 277, 194, 97; $^1$H NMR (400 MHz) $\delta$ 2.10 (dt, 1 H, $J_{gem}$ = 11.5 Hz, $J_{5ax,6ax}$ = 11.5 Hz, $J_{5ax,6eq}$ = 3 Hz, $H_{5ax}$), 2.30 (m, 1 H, $J_{9ax,1\alpha}$ = 11 Hz, $H_{9ax}$), 2.65 (dd, 1 H, $J_{2\alpha,3\beta}$ = 9 Hz, $H_{3\beta}$), 3.10 (b d, 1 H, $J_{gem}$ = 11.5 Hz, $H_{5eq}$), 3.25 (dd, 1 H, $J_{1\alpha,2\alpha}$ = 11 Hz, $J_{1\alpha,9ax}$ = 11 Hz, $H_{1\alpha}$), 3.45 (dd, 1 H, $J_{gem}$ = 9 Hz, $H_{3\alpha}$), 3.70 (dd, 1 H, $H_{2\alpha}$), 6.85 (d, 2 H), 6.95 (m, 8 H); picrate (EtOH) mp 219 °C; Anal. Calcd for $C_{26}H_{26}N_4O_7$: C, 61.65; H, 5.18; N, 11.08; O, 22.11. Found: C, 61.47; H, 5.18; N, 11.21; O, 22.02.

**1$\beta$,2$\beta$-Cyclopentano-1′-spiro-2″-dioxolane and -3′-spiro-2″-dioxolane (13a,b).** *N*-Oxide **5** (240 mg, 2.09 mmol) and 2-cyclopenten-1-one ethylene ketal (**12**) (305 mg, 2.4 mmol) are treated with LDA (7.35 mmol) for 3 h. Procedure B gives 467 mg of crude mixture. GLC analysis (column A) shows two isomers **13a,b** formed in a 1/0.33 ratio. Chromatography on silica gel ($CH_2Cl_2$–MeOH 98/2 to 10/90) gives variously enriched fractions (392 mg, 1.76 mmol, 84%). The first one (268 mg) contains less than 15% of the **13b** isomer and the most polar more than 60%. Each fraction presents the same MS (*m/e* 224, 223, 179, 98). **13a**: IR 2770, 2710, 2670, 1320, 1100 cm$^{-1}$; $^1$H NMR (400 MHz) $\delta$ 2.05 (dd, 1 H, $J_{1\alpha,2\alpha}$ = 9 Hz, $J_{1\alpha,9ax}$ = 9 Hz, $H_{1\alpha}$), 2.8 (m, 1 H, $J_{2\alpha,3\alpha}$ = 9 Hz, $H_{2\alpha}$), 3.20 (b d, 1 H, $H_{5eq}$), 3.25 (dd, 1 H, $J_{gem}$ = 9 Hz, $J_{2\alpha,3\alpha}$ = 9 Hz, $H_{3\alpha}$), 3.9 (m, 4 H, $CH_2$–O); picrate mp (EtOH) 173–174 °C. Anal. Calcd. for $C_{19}H_{24}N_4O_9$: C, 50.44; H, 5.31; N, 12.39; O, 31.86. Found: C, 50.69; H, 5.45; N, 12.65; O, 31.68.

***trans*-1,2-Diphenyloctahydroindolizines (10d and 11d).** *N*-Oxide **5** (280 mg, 2.43 mmol) and *trans*-stilbene (**9d**) (488 mg, 2.67 mmol) are treated with LDA (8.5 mmol). After 3 h, procedure B gives the starting olefin (168 mg, 0.9 mmol) and a mixture of **10d** and **11d** (479 mg, 1.73 mmol, 71%) in a 1/2 ratio determined by GLC (column A): IR 3030, 2780, 2730, 2650 (shoulder), 1600, 1500, 1450, 760, 750, 700 cm$^{-1}$; MS, *m/e* 277, 97; picrate of the mixture (EtOH mp 88–90 °C. Anal. Calcd for $C_{26}H_{26}N_4O_7$: C, 61.65; H, 5.18; N, 11.08; O, 22.11. Found: C, 61.40; H, 5.21; N, 11.27; O, 22.29.

The two isomers separated by preparative GLC (column A) give the same MS. Only the major one **11d**, was obtained in sufficient quantity to allow NMR analysis: $^1$H NMR (400 MHz) $\delta$ 2.10 (dt, 1 H, $H_{5ax}$), 2.4 (m, 2 H, $H_{3\beta}$, $H_{9ax}$), 3.25 (b d, 1 H, $H_{5eq}$), 3.30 (dd, 1 H, $J_{3\alpha,3\beta}$ = 9 Hz, $H_{3\alpha}$), 3.60 (m, 1 H, $H_{2\alpha}$), 7.2 (m, 10 H).

**1$\alpha$-Phenyl-2$\beta$-methoxyoctahydroindolizine (11e).** *N*-Oxide **5** (350 mg, 3 mmol) and $\beta$-methoxystyrene (**9e**) (500 mg, 3.6 mmol) are treated with LDA (10.5 mmol) for 3 h. Procedure A gives after chromatography on silica gel ($CH_2Cl_2$–MeOH 97/3) compound **11e** (429 mg, 1.85 mmol, 61%): IR 2780, 2750 and 2650 (shoulders), 1600, 1500, 1440, 1100, 800, 760, 700 cm$^{-1}$; MS, *m/e* 231, 200, 97; $^1$H NMR (400 MHz) $\delta$ 2.10 (dt, 1 H, $H_{5ax}$), 2.25 (dd, 1 H, $J_{3\beta,2\alpha}$ = 6 Hz, $H_{3\beta}$), 2.85 (s, 3 H, OMe), 2.88 (m, 1 H, $H_{1\beta}$), 3.10 (b d, 1 H, $H_{5eq}$), 3.65 (dd, 1 H, $J_{gem}$ = 10.5 Hz, $H_{3\alpha}$), 4.0 (dd, 1 H, $H_{2\alpha}$), 7.2 (m, 5 H); picrate mp (EtOH) 191–192 °C. Anal. Calcd for $C_{21}H_{24}H_4O_8$: C, 54.78; H, 5.21; N, 12.17; O, 27.82. Found: C, 54.85; H, 5.30; N, 11.92; O, 27.79.

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**1- and 2-Phenyloctahydroindolizines 14f, 15f, and 16f.** *N*-Oxide **5** (190 mg, 1.65 mmol) and styrene (**9f**) (189 mg, 1.82 mmol) are treated with LDA (5.78 mmol) for 3 h. Procedure B gives a crude mixture of three cycloaddition products **14f**, **15f**, and **16f** (246 mg, 1.22 mmol, 74%). GLC analysis (column A) shows the presence of three peaks in a 1/0.5/0.4 ratio. The MS of those three fractions analyzed on a spectrometer equipped with a GLC apparatus are identical (*m/e* 201, 196, 97). Chromatography on neutral alumina (hexane–$CH_2Cl_2$ 50/50) gives two fractions. The first one (163 mg, 0.82 mmol, 50%) is a mixture of the two diasteroisomers of 1-phenylindolizidine, **14f** and **15f**, containing 10% of **16f**: picrate mp (EtOH) 174 °C (lit.[18] mp 172–173 °C) for the isomeric mixture **14f** + **15f**. The second one (93 mg, 0.46 mmol, 28%) contains **14f** contaminated by 14% of **16f**. **14f**: IR 2780, 2750, 2650 (shoulder), 1440, 860, 700 $cm^{-1}$; $^1H$ NMR (400 MHz) $\delta$ 1.2 (b m, 3 H), 1.5–1.9 (b m, 5 H), 2.1 (dt, 1 H, $H_{5ax}$), 2.4 (b m, 2 H, $H_{2\alpha}$, $H_{3\beta}$), 2.85 (dd, 1 H, $H_{1\alpha}$), 3.15 (b d, 1 H, $H_{5eq}$), 3.25 (m, 1 H, $H_{3\alpha}$), 7.3 (m, 5 H).

**1-(4-Methoxyphenyl)octahydroindolizine (14g).** *N*-Oxide **5** (390 mg, 3.39 mmol) and *p*-methoxystyrene (**9g**) (500 mg, 3.75 mmol) are treated with LDA (11.86 mmol) for 3 h. Procedure A gives a crude mixture (900 mg) containing unreactive olefin. GLC analysis (column A) shows the presence of three cycloadducts in 1/0.1/0.2 ratio. Chromatography on neutral alumina (hexane–$CH_2Cl_2$ 50/50) gives two major fractions. The first one is constituted by a mixture of **14g** (272 mg, 1.17 mmol, 34%) containing 15% of its $\alpha$ isomer **15g**; the second one is constituted by the same compound **14g** (220 mg, 0.95 mmol, 28%) containing 30% of the $2\beta$ isomer **16g**. **14g**: IR 2750, 2700, 2650 (shoulder), 1600, 1500, 1440, 1250, 830, 740; MS, *m/e* 231, 97; $^1H$ NMR (400 MHz) $\delta$ 2.10 (dt, 1 H, $H_{5ax}$), 2.20 (m, 1 H, $H_{2\alpha}$), 2.40 (m, 1 H, $H_{3\beta}$), 2.80 (dd, $H_{1\alpha}$), 3.10 (b d, 1 H, $H_{5eq}$), 3.20 (dd, 1 H, $H_{3\alpha}$), 3.8 (s, 3 H, OMe), 7.1–7.4 (AB system, 4 H, $J_{ortho}$ = 6 Hz); picrate mp (EtOH) 169–171 °C. Anal. Calcd for $C_{21}H_{24}N_4O_8$: C, 54.78; H, 5.21; N, 12.17; O, 27.82. Found: C, 54.21; H, 5.12; N, 11.97; O, 27.71.

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**Registry No.** **5**, 17206-00-7; **8** (isomer 1), 1771-52-4; **8** (isomer 2), 494-69-9; **9a**, 74-85-1; **9b**, 142-29-0; **9c**, 645-49-8; **9d**, 103-30-0; **9e**, 4747-15-3; **9f**, 100-42-5; **9g**, 637-69-4; **10a**, 13618-93-4; **10a**·picrate, 5210-66-2; **10b**, 96947-16-9; **10b**·picrate, 96996-79-1; **10c**, 96866-60-3; **10c**·picrate, 96947-19-2; **10d**, 96947-17-0; **10d**·picrate, 96996-80-4; **11d**, 96947-18-1; **11d**·picrate, 96996-81-5; **11e**, 96866-61-4; **11e**·picrate, 96947-21-6; **12**, 695-56-7; **13a**, 96866-67-0; **13a**·picrate, 96947-20-5; **13b**, 96866-68-1; **14f**, 96866-62-5; **14f**·picrate, 96866-69-2; **14g**, 96866-64-7; **14g**·picrate, 96866-71-6; **15f**, 96866-63-6; **15f**·picrate, 96866-70-5; **15g**, 96866-65-8; **16f**, 96896-97-8; **16g**, 96866-66-9; *N*-methylpiperidine, 626-67-5.

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# 1,1,6,6-Tetramethyldibenzo[*b*,*e*]phosphajulolidine

Chin H. Chen,* Jeffrey J. Doney, John L. Fox, and Henry R. Luss

*Research Laboratories, Eastman Kodak Company, Rochester, New York 14650*

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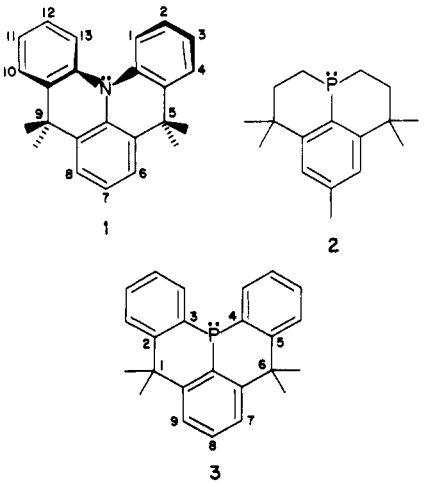
1,1,6,6-Tetramethyldibenzo[*b*,*e*]phosphajulolidine (**3**), the phosphorus analogue of 5,5,9,9-tetramethyl-5*H*,9*H*-quino[3,2,1-*d*,*e*]acridine, was synthesized. Single-crystal X-ray analysis of **3** showed that the molecule, because of the longer P–C bonds (1.820–1.836 Å) and the pyramidality of phosphorus, has approximately $C_s$ symmetry, whereas the nitrogen analogue has $C_2$ symmetry. The geometry about phosphorus is pyramidal, with the phosphorus atom 0.81 Å out of the plane of the three bonded carbon atoms. The corresponding C–P–C angles are 99.0°, 98.3°, and 108.5°.

The bridged triphenylamine 5,5,9,9-tetramethyl-5*H*,9*H*-quino[3,2,1-*d*,*e*]acridine (**1**) has been shown by variable-temperature $^1H$ NMR and X-ray analyses to have appproximate $C_2$ symmetry along the axis connecting C7 and the nitrogen.[1] To minimize the steric interaction between H1 and H13, the nitrogen in this conformation is flattened, lying only slightly outside the plane (0.03 Å) formed by the three N–C bonds linking the phenyl groups, with C–N–C bond angles of 117–124°.[2]

As part of a study of the n–$\pi$ interaction between the lone-pair electrons on the phosphorus and the adjacent aromatic $\pi$ system in a rigidized bicyclic framework, we recently reported the synthesis of the first phosphajulolidine **2**.[3] Its cyclic voltammetric and UV spectroscopic ($\lambda_{max}$ 255 nm) data suggest that **2** has no n–$\pi$ interaction between the lone-pair electrons on the phosphorus and the adjacent $\pi$ system.[4]



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Examination of a Dreiding stereo model of **2** reveals also a strain-free and somewhat flexible bonding framework around the *pyramidal* phosphorus. To confirm these and other findings from our earlier work[3,5] single-crystal X-ray

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