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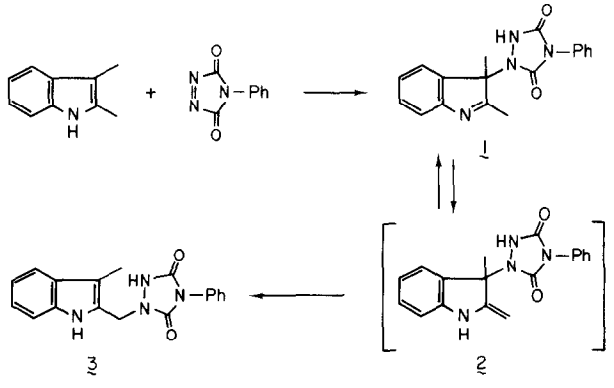
# THE CHEMISTRY OF AN AZOMETHINE IMINE DERIVED FROM 2,3-DIMETHYLINDOLE AND N-PHENYL TRIAZOLINEDIONE: A NEW AND FACILE CONDENSATION METHOD

R. Marshall Wilson* and Alvan Hengge
Department of Chemistry, University of Cincinnati
Cincinnati, Ohio 45221

**Abstract:** The urazole **3** derived from 2,3-dimethylindole and PTAD has been found to be converted readily to the unusually stable azomethine imine **5** with t-butylhypochlorite followed by elimination of HCl. This azomethine imine has been shown to serve as a carbonyl-equivalent in a number of aldol-type condensations under mild conditions.

Triazolinediones are highly reactive compounds that readily undergo cycloadditions and ene reactions with olefins. It occurred to us that the N-substituted urazoles that are the products of these commonly encountered ene reactions might be manipulated easily to provide a variety of allylically modified olefins. Our interest in finding novel and mild methods to functionalize the indole system[1] led us to explore this approach using 2,3-dimethylindole and N-phenyl triazolinedione (PTAD).

Addition of 1 eq. of PTAD to a benzene solution of 2,3-dimethylindole leads to the immediate discharge of the red PTAD color and to the quantitative formation of indolenine **1** (Scheme I), a moderately stable red oil:[2] $^1$H-NMR (80 MHz, $CDCl_3$) $\delta$1.64 (s, 3H), 2.34 (s, 3H), 7.0-7.5 (m, 9H), 8.69 (br s, 1H); IR ($CHCl_3$, $cm^{-1}$) 1780, 1720, 1596, 1500, 1420; UV (MeCN, nm) $\lambda_{max}$ 210 ($\varepsilon$=35,000), 216 (36,000), 223 (29,000). If **1** is not isolated but heated at 60°C for 20 hours, the rearranged crystalline urazole **3** can be isolated in 56% yield: m.p. 202.3-203.0°C; $^1$H-NMR (80 MHz, $CDCl_3$/DMSO-$D_6$ 10:1) $\delta$ 2.36 (s, 3H), 4.88 (s, 2H), 7.07-7.53 (m, 10H), 9.53 (s, 1H); IR (KBr, $cm^{-1}$) 3490, 1785, 1725, 1500; UV (MeCN, nm) $\lambda_{max}$ 226 ($\varepsilon$=38,000), 274 (7900). This rearrangement can be rationalized as proceeding through **2** by a pathway which is consistent with other known indole oxidation processes.[3]

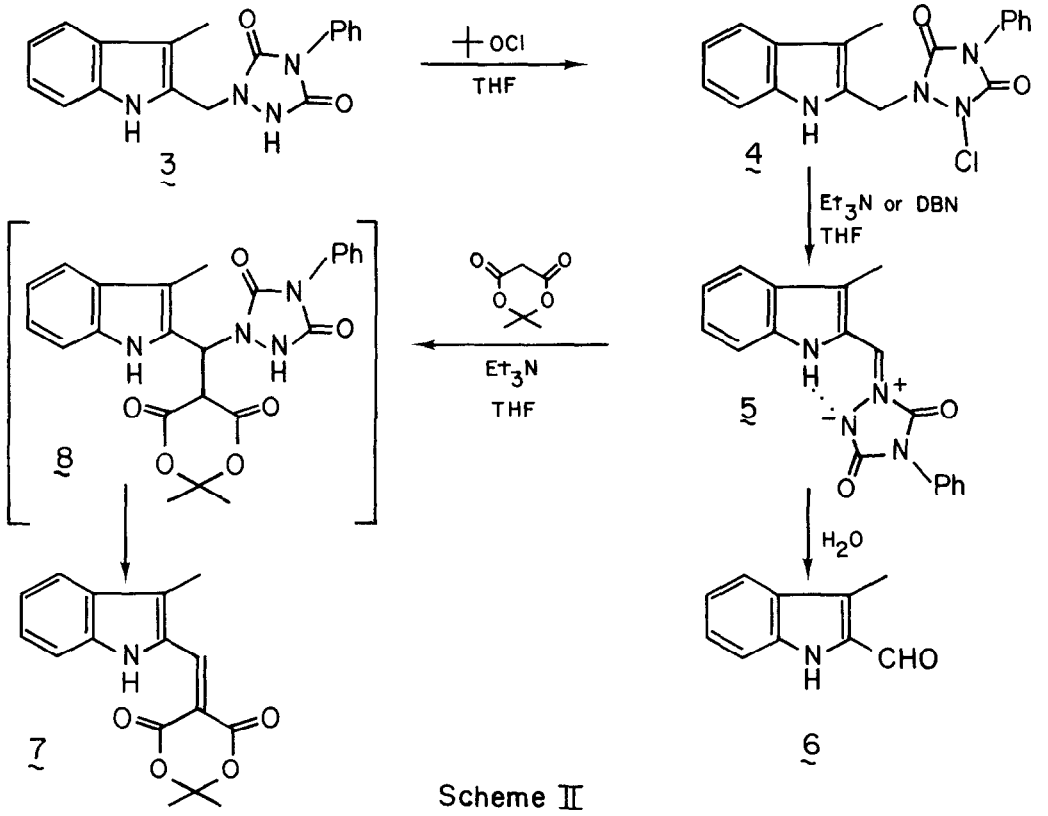



Scheme I

Treatment of **3** with 1 eq. of t-butylhypochlorite in dry THF results in the rapid disappearance of the N-H signal in the NMR at $\delta$ 9.5 ppm. Thus, chlorination seems to occur preferentially at the urazole nitrogen to form **4** (Scheme II) rather than at the indole moiety. That this is indeed the case was shown by the immediate formation of the red-orange azomethine imine **5** upon treatment of **4** (generated in situ) with 1 eq. of either triethylamine or DBN. This azomethine imine is stable enough to be isolated in about 80% yield by simply passing the reaction mixture through a short column of dried Florisil and evaporation of the solvent. The spectral properties of **5** are consistent with those of other PTAD-derived azomethine imines:[4] m.p. approx. 205°C (dec.); $^1$H-NMR (80 MHz, $CDCl_3$) $\delta$2.71 (s, 3H), 7.35-7.80 (m, 9H), 8.37 (s, 1H), 11.38 (br s, 1H); IR ($CHCl_3$, $cm^{-1}$) 1785, 1700, 1595, 1490, 1380; UV (MeCN, nm) $\lambda_{max}$ 220 ($\varepsilon$=15,000), 335 (3600), 470 (13,000); Partial $^{13}$C-NMR (300 MHz, $CDCl_3$): 154.5 (C=O), 150.7 (C=O), 141.2 (C=N).

The stability of **5** is probably due to a combination of factors. Judging from the extremely deshielded indole N-H proton ($\delta$ 11.38 ppm) the negative terminus of the azomethine imine seems to be stabilized by internal hydrogen bonding with the indole N-H as shown in Scheme II. On the other hand the positive terminus is probably stabilized by the electron-donating indole substituent.

These stabilizing interactions may account for the fact that **5** is unreactive toward a variety of dipolarophiles.[5] In contrast **5** is quite sensitive to traces of water and acids. Upon exposure to water **5** readily undergoes hydrolysis to the aldehyde **6** (Scheme II).

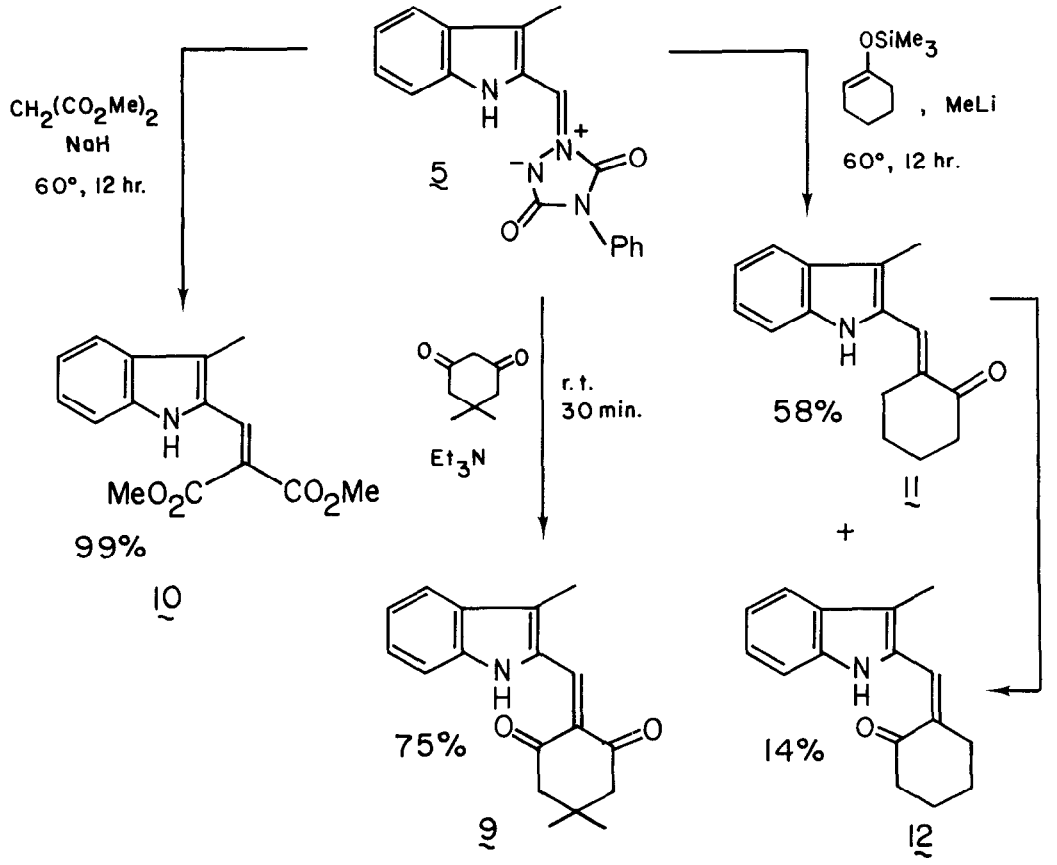



Scheme II

Of particular significance is the facile condensation of **5** with a number of enolate species.[6] For example treatment of **5** with Meldrum's acid and triethylamine in THF at room temperature for 30 minutes affords the alkylidene derivative **7** in quantitative yield. The same condensation may be affected in comparable yield directly from **3** when **5** is generated in situ as outlined in Scheme II.

The related condensations shown in Scheme III have also been achieved. The yields quoted in Scheme III are all for the isolated products, were obtained without isolating **5**, and are based on **3**. It can be seen from these examples that this type of condensation consistently proceed in good yields even with the enolates of simple ketones, and is successful when the enolate species are generated under a variety of conditions. It should be noted that in each case the addition of the enolate to **5** proceeds rapidly as judged by the disappearance of the red-orange color of **5** to form the adduct analogous to **8** in Scheme II. However, in the malonate and cyclohexanone cases heating is required to bring about the elimination of the urazole and form the final product. Intermediates related to **8** could be observed by NMR but attempted isolation was unsuccessful.

The extreme ease with which these condensations may be conducted is illustrated by the following typical experimental procedure. A solution of the urazole **3** in dry THF and under an atmosphere of argon is treated with 1 eq. of t-butylhypochlorite. After about 1 minute, 1 eq. of triethylamine is added. The




Scheme III

formation of the red-orange azomethine imine is complete in about 30 seconds at room temperature. To this red-orange azomethine imine solution is added a solution of 1 eq. of the enolate with stirring at room temperature and the resulting solution is stirred for 30 minutes at room temperature (**7** and **9**) or for 12 hours at 60°C (**10, 11** and **12**).

To the best of our knowledge these are the first examples of the use of an azomethine imine as a carbonyl-equivalent in aldol-type condensations. This may be all the more significant since the requisite urazole starting materials related to **3** are so readily available through ene reactions of PTAD with olefins. In order to better establish the utility of this method we currently are investigating the scope of this new condensation method.

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**References and Notes**

1. Wilson, R. M.; Farr, R. A.; Burlett, D. J. J. Org. Chem. **1981**, 46, 3293.

2. The indolenine **1** is very prone to rearrangement unless stored below 10°C.

3. (a) Taylor, W. I. Proc. Chem. Soc. **1962**, 247. (b) Sundberg, R. J., "The Chemistry of Indoles", Academic Press, New York, N.Y., 1970.

4. (a) Greene, F.; Cheng, C. J. Org. Chem. **1984**, 49, 2917. (b) Jones, D. W. Chem. Commun. **1982**, 766.

5. Dipolarophiles which were tested and found not to react with **5** include cyclopentadiene, dimethyl acetylenedicarboxylate, acetaldehyde, $CO_2$, $CS_2$, styrene, acetonitrile, and acetone.

6. The spectroscopic properties of the condensation products of **5** are listed below:

**7:** Yellow crystals; m.p. 196.1-196.6°C; $^1$H-NMR (300 MHz, $CDCl_3$) δ 1.79 (s, 6H), 2.64 (s, 3H), 7.1-7.7 (m, 4H), 8.56 (s, 1H), 11.83 (br s, 1H); Partial $^{13}$C-NMR (300 MHz, $CDCl_3$) δ 141.22 (d) 163.76 (s), 164.04 (s); IR ($CHCl_3$, $cm^{-1}$) 3300, 1765, 1690, 1640; exact mass calc. for $M^+$, $C_{16}H_{15}NO_4$, 285.1001, found 285.1026.

**9:** Orange crystals; m.p. 147.1-147.3°C; $^1$H-NMR (300 MHz, $CDCl_3$) δ1.12 (s, 6H), 2.58 (s, 2), 2.65 (s, 5H), 7.07-7.65 (m, 4H), 8.40 (s, 1H), 12.40 (br s, 1H); Partial $^{13}$C-NMR (300 MHz, $CDCl_3$) δ 137.14 (d), 197.80 (s), 199.61 (s); IR ($CHCl_3$, $cm^{-1}$) 3220, 1720, 1680, 1630, 1620; exact mass calc. for $M^+$, $C_{18}H_{19}NO_2$, 281.1416, found 281.1387.

**10:** Yellow crystals; m.p. 95.6-96.4°C; $^1$H-NMR (300 MHz, $CDCl_3$) δ 2.51 (s, 3H), 3.87 (s, 3H), 3.94 (s, 3H), 7.09-7.65 (m, 4H), 7.96 (s, 1H), 10.39 (br s, 1H); Partial $^{13}$C-NMR (300 MHz, $CDCl_3$) δ 134.20 (d), 166.68 (s), 168.61 (s); IR ($CHCl_3$, $cm^{-1}$) 3380, 1715, 1590, 1435; exact mass calc. for $M^+$, $C_{15}H_{15}NO_4$, 273.1001, found 273.1016.

The relative yields quoted for **11** and **12** in Scheme III are somewhat variable, as **11** is converted **12**, possibly photochemically, in solution under ambient conditions or on silica gel.

**11:** Yellow crystals; m.p. 139.7-140.1°C; $^1$H-NMR (300 MHz, $CDCl_3$) δ 1.89 (m, 4H), 2.41 (s, 3H), 2.52 (t, J=6.5 Hz, 2H), 2.99 (m, 2H), 7.22-7.74 (m, 4H), 7.74 (s, 1H), 8.26 (br s, 1H); IR ($CHCl_3$, $cm^{-1}$) 3490, 1665, 1570; exact mass calc. for $M^+$, $C_{16}H_{17}NO$, 239.1310, found 239.1315.

**12:** Orange crystals; m.p. 114.9-115.5°C; $^1$H-NMR (300 MHz, $CDCl_3$) δ 1.84-1.95 (m, 4H), 2.43 (s, 3H), 2.56 (t, J=6.7 Hz, 2H), 2.74 (t, J=6 Hz, 2H), 6.72 (s, 1H), 7.06-7.56 (m, 4H), 11.44 (br s, 1H); IR ($CHCl_3$, $cm^{-1}$) 3300, 1660, 1560; exact mass calc. for $M^+$, $C_{16}H_{17}NO$, 239.1310, found 239.1329.

Satisfactory full $^{13}$C-NMR and UV-VIS spectra were obtained for all products.

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