[1,3] Alkyl Migration as a Third Type of \(N,N\)-Dialkanoylindigo Photochemistry

Bradley D. Smith,* David E. Alonso,** Jeffrey T. Bien, John D. Zielinski, Sheridan L. Smith,* and Kenneth J. Haller

Department of Chemistry and Biochemistry, University of Notre Dame, Notre Dame, Indiana 46556 and Department of Chemistry, Andrews University, Berrien Springs, Michigan 49104

Received June 18, 1993

The cis/trans photoisomerization of \(N,N\)-dialkylindigo dyes (Scheme I) is a textbook example of photochromism.\(^1,2\) The trans isomer of \(N,N\)-dialkylindigo (1a), for example, absorbs at 562 nm and is observed as a pink color, whereas the cis isomer absorbs at 430 nm and is yellow. In aprotic solvents, the photoisomerization is clean and reversible over many cycles. At one time these compounds were considered as potential solar energy conversion and storage systems.\(^3\) In the presence of electron donors such as tertiary amines and in the absence of oxygen, single electron transfer photochemistry predominates producing the corresponding reduced leucoindigo derivatives.\(^4\) Here we report our discovery of a third type of \(N,N\)-dialkanoylindigo photochemistry, namely, a photochemical [1,3] alkyl migration reaction (Scheme I).

The \(N,N\)-dialkylindigo derivatives 1a–i were prepared from indigo and the appropriate acid chloride by known methods.\(^5\) Their room temperature benzene solutions were irradiated with light selective for the \(\Delta\) absorption band (\(\lambda > 530 \text{ nm}\)) and the resulting photochemistry monitored by TLC and absorption spectroscopy. Compounds 1a–d behaved like typical \(N,N\)-dialkylindigo dyes.\(^2\) They displayed the expected clean trans to cis photoisomerization, and no side products were observed even after extensive irradiation periods (48 h). Upon standing in the dark the cis isomers of 1a–d reverted back completely to the trans configuration at rates consistent with previous studies.\(^2\) Compounds 1e–i also underwent trans to cis photoisomerization but concomitant with this, irreversible photobleaching occurred and eventually the starting materials were consumed. In each case after photobleaching, TLC and NMR indicated the appearance of a major colorless product in 40–65% yield.\(^5\) \(\text{I}^\text{H} NMR\) spectra of the isolated colorless products showed they were analogous to one another. The mass spectra indicated they were isomeric with their starting compounds and the combined spectral data suggested their identity as 2e–i. Of significance was the abundant ion observed at \(m/z = 289\) in the EI mass spectra, suggestive of the fragment 3.

In the case of 2e, the structural assignment was confirmed with an X-ray crystal structure.\(^6\)

The rearrangement of 1e–i to produce 2e–i, respectively, can be classified as a photochemical [1,3] alkyl migration, an uncommon but documented reaction.\(^7\) Although the mechanism is not firmly established, a number of points can be noted. We have solved the X-ray structures of a number of \(N,N\)-dialkanoylindigo compounds, including the published structure of 1d.\(^8\) In each of these \(X\)-ray structures, the \(N\)-acyl groups adopt a conformation placing the \(R\) group in a position proximate to the central \(C=C\) bond of the indigo chromophore as represented in Scheme I. NMR studies have shown these \(N\)-acyl conformations are strongly preferred.\(^8\)

*Andrews University.


\(5\) Two minor products were also observed, one was the respective purple-colored \(N\)-alkanoylindigo derivative (5–15% yield) and the other, a labile yellow material (10–20% yield), has yet to be identified.

\(6\) The authors have deposited atomic coordinates for 2e with the Cambridge Crystallographic Data Centre. The coordinates can be obtained, on request, from the Director, Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge, CB2 1EZ, UK. An ORTEP representation is included in the supplementary material.

tures shows the rearrangement requires a relatively small movement of nuclei and mainly involves a reorganization of the bonding electrons. Direct irradiation of the trans absorption band of an \(N,N'\)-dicyanindigo is known to produce an excited singlet state which is thought to mediate trans to cis isomerization. Molecular orbital calculations indicate the excited singlet state has more zwitterionic character than the ground state due to increased delocalization of the nitrogen lone pairs toward the indigo carbonyl oxygens. The rearrangement described here has only been observed for \(\alpha\)-substituted-\(N,N'\)-dialkanyldigio derivatives with \(\alpha\)-substituents known to stabilize reactive centers via resonance delocalization, especially resonance donation. This suggests the rearrangement mechanism involves development of either cationic or radical character at the \(\alpha\)-carbon of the reacting \(N\)-alkanoyl group. The fact that the rearrangement was observed for 11, where \(R = 4\)-nitrobenzyl, is evidence against a polar mechanism; the overall substituent effects are more in line with a radical mechanism. The observation that the rearrangement is not inhibited by the radical scavengers 2,6-di-tert-butyl-4-methylphenol, ethyl acrylate, or oxygen is evidence against a radical chain mechanism. Furthermore, the absence of "out-of-cage" coupling products is evidence against a radical pair such as 4. Thus, a solvent-caged, radical mechanism is postulated, via the biradical intermediate 5, as described in Scheme II. The overall photochemical scheme is rationalized as follows. Trans to cis photoisomerization occurs when the excited singlet state, obtained upon direct irradiation, twists to form an excited \(\pi^*\) state which relaxes via a twisted \(\pi\) configuration to the cis-1 ground state. The cis-1 configuration is unaffected by the irradiation (\(\lambda > 530 \text{ nm}\)) but is unstable and thermally isomerizes back to the trans-1 form. Competing with the photoisomerization is the photochemical [1,3] alkyl migration pathway via biradical 5 (of unknown multiplicity). Substituents with high migratory aptitudes (i.e. 1e−1 with low \(CO-\text{CH}_2R\) bond dissociation energies) facilitate the migration and allow it to compete at room temperature. The migration is apparently irreversible, whereas the isomerization is a reversible cycle, hence the system drives toward migration as the eventual product (Scheme I). In the case of substituents with poor migratory aptitudes (1a–d), the biradical 5 may form, but the \(CO-\text{CH}_2R\) bond dissociation energy for the migration step is too high for it to compete with reversion to the trans-1 ground state (Scheme II).}

**Experimental Section**

**General Methods.** Anhydrous THF was obtained by distilling from sodium/benzophenone. All other solvents were purchased as reagent grade and were used without further purification. Flash chromatography was conducted with silica gel (60–200 mesh) as the solid support and preparative TLC with 20 × 20 cm plates of silica gel (500 μm thickness). NMR spectra were acquired on a GE GN 300 MHz instrument. Coupling constants (\(J\)) are quoted in hertz and are accurate to ±0.3 Hz.

**Synthesis of \(N,N'\)-Dicyanindigos 1a–i.** These compounds were prepared by either of the two general methods described by Setaune. Method A. Indigo was stirred with the appropriate acid chloride and 2,6-lutidine in butyl acetate at 100 °C for 2 h. The solvent was removed under vacuum and the crude product purified by flash chromatography (eluent, 1:1 hexane/ethyl acetate) to give the following compounds. 

\[N,N'-\text{Diacylindigo}(1a): \text{recrystallized repeatedly from acetonitrile, mp } 257–258 ^\circ C \text{ (lit. } 256 ^\circ C).\]

\[N,N'-\text{Dibenzyloindigo}(1b): \text{recrystallized from methylene chloride/hexane, mp } 267–268 ^\circ C \text{ (lit. } 256 ^\circ C).\]

\[N,N'-\text{Bis(3-methoxypropionyl)indigo}(1c): \text{purified by flash chromatography (eluent, 1:1, ethyl acetate/hexane) and then recrystallized from hexane/methylene chloride, mp } 158–159 ^\circ C \text{ (lit. } 158–160 ^\circ C).\]

\[N,N'-\text{Bis(chloroacetyl)indigo}(1d): \text{purified by flash chromatography (eluent, 1:1, ethyl acetate/hexane) and then recrystallized from methylene chloride/hexane, mp } 157–158 ^\circ C \text{ (lit. } 158–160 ^\circ C).\]

\[N,N'-\text{Bis(methoxyacetyl)indigo}(1e): \text{purified by flash chromatography (eluent, 1:1, ethyl acetate/hexane) and recrystallized from hexane/methylene chloride: mp } 185–186 ^\circ C \text{ (lit. } 185–186 ^\circ C).\]

\[N,N'-\text{Bis(4-hydroxyacetyl)indigo}(1f): \text{purified by flash chromatography (eluent, 1:1, ethyl acetate/hexane) and recrystallized from hexane/methylene chloride: mp } 178–179 ^\circ C \text{ (lit. } 178–179 ^\circ C).\]

\[N,N'-\text{Bis(4-methoxyacetyl)indigo}(1g): \text{purified by flash chromatography (eluent, 1:4, ethyl acetate/hexane): mp } 192–193 ^\circ C \text{ (lit. } 192–193 ^\circ C).\]

\[N,N'-\text{Bis(4-methoxyphenylacetyl)indigo}(1h): \text{purified by flash chromatography (eluent, 1:1, ethyl acetate/hexane) and recrystallized from hexane/methylene chloride: mp } 169–170 ^\circ C \text{ (lit. } 169–170 ^\circ C).\]

\[N,N'-\text{Bis(4-methoxyphenyl)indigo}(1i): \text{purified by flash chromatography (eluent, 1:1, ethyl acetate/hexane) and recrystallized from hexane/methylene chloride: mp } 174–175 ^\circ C \text{ (lit. } 174–175 ^\circ C).\]

**Notes**


14. With the evidence in hand, the alternative mechanisms mentioned, as well as others, such as a concerted rearrangement, cannot be completely discounted. Biradical 5, however, does provide a nice rationalization for the small amount of \(N\)-alkanoylindigo observed (ref 8), namely, a-flavion of the \(N-C\) bond in 5 followed by hydrolysis of the resulting \(O\)-acylated product during chromatographic purification.
**Scheme II**

\[
\begin{array}{c}
\text{[\(\text{OAO}\) \text{L}_4]} \\
\text{[1,3] alkyl shift} \\
\end{array}
\]

**Irradiation Experiments. Photorearrangement.** A stirring, room temperature solution of the appropriate \(N,N'\)-diacylindigo 1a–i in benzene (10 mL, 1 mM, no attempt was made to exclude oxygen) was irradiated with a Xe 150-W arc lamp equipped with a housing unit to collimate the beam and an Oriel 51272 filter to allow \(\lambda \geq 530\) nm. When TLC indicated consumption of the starting material (6–12 h), the solvent was evaporated and the extent of conversion to the major rearranged product determined by \(^1\)H NMR. The major product was then isolated by preparative silica TLC to give in each case the following compounds.

**2e** (65% conversion): TLC (eluent, 1:1, ethyl acetate/hexane) \(R_f = 0.80\); \(^1\)H NMR (acetone-\(d_6\)) 8.21 (1H, d, \(J = 8.0\)), 7.73 (2H, t, \(J = 9.0\)), 7.62 (1H, d, \(J = 8.0\)), 7.42 (1H, t, \(J = 7.5\)), 7.36–7.30 (2H, m), 4.90 (1H, A of ABq, \(J = 17.0\)), 4.76 (1H, B of ABq, \(J = 17.0\)), 4.43 (1H, d, \(J = 10.0\)), 3.94 (1H, d, \(J = 10.0\)), 3.49 (3H, s), 3.27 (3H, s) ppm; \(^{13}\)C NMR (CDCl\(_3\)) 193.1 s, 172.0 s, 150.6 s, 146.4 s, 139.2 s, 137.8 d, 134.7 s, 128.5 d, 125.0 s, 124.5 d, 123.7 d, 122.4 s, 119.7 s, 118.1 d, 117.1 d, 114.0 d, 113.5 s, 76.4 d, 73.9 d, 72.5 s, 60.0 d, 59.6 d ppm; MS (EI) m/z 406 (M), 361, 335, 289; HRMS calcd for \(C_{22}H_{14}N_6O_4\) 406.1165, found 406.1176; UV \(\lambda_{	ext{max}} = 305\) nm.

**2f** (60% conversion): TLC (eluent, 2:1, ethyl acetate/hexane) \(R_f = 0.10\); \(^1\)H NMR (acetone-\(d_6\)) 8.29 (1H, d, \(J = 8.0\)), 7.82–7.50 (4H, m), 7.40 (1H, t, \(J = 8.0\)), 7.36 (1H, t, \(J = 8.0\)), 7.28 (1H, d, \(J = 8.0\)), 4.96 (1H, A of ABq, \(J = 16.5\)), 4.84 (1H, B of ABq, \(J = 16.5\)), 4.63 (1H, d, \(J = 10.0\)), 4.03 (1H, d, \(J = 10.0\)), 3.99–3.92 (1H, m), 3.87–3.80 (1H, m), 3.60–3.52 (4H, m), 3.33 (3H, s), 3.21 (3H, s) ppm; MS (EI) m/z 494 (M), 406, 378, 368, 350, 289, 283, 269; HRMS calcd for \(C_{22}H_{16}N_6O_4\) 494.1689, found 494.1708; UV \(\lambda_{	ext{max}} = 305\) nm.

**2g** (42% conversion): TLC (eluent, 1:1, ethyl acetate/hexane) \(R_f = 0.80\); \(^1\)H NMR (CDCl\(_3\)) 8.28 (1H, d, \(J = 8.5\)), 7.76–7.70 (3H, m), 7.58 (1H, d, \(J = 8.5\)), 7.45 (1H, t, \(J = 8.5\)), 7.35 (1H, t, \(J = 8.5\)), 7.31 (1H, d, \(J = 8.5\)), 4.23 (1H, d, \(J = 14.5\)), 4.13 (1H, A of ABq, \(J = 15.5\)), 4.03 (1H, B of ABq, \(J = 15.5\)), 3.11 (1H, d, \(J = 14.5\)), 2.50 (3H, s), 2.00 (3H, s) ppm; MS (EI) m/z 438 (M), 410, 377, 350, 289, 61; HRMS calcd for \(C_{22}H_{16}N_6O_4\) 438.0708, found 438.0726; UV \(\lambda_{	ext{max}} = 308\) nm.

**2h** (45% conversion): TLC (eluent, 1:4, ethyl acetate/hexane) \(R_f = 0.80\); \(^1\)H NMR (acetone-\(d_6\)) 8.24 (1H, d, \(J = 8.0\)), 7.96 (1H, d, \(J = 8.5\)), 7.84 (1H, t, \(J = 8.0\)), 7.80 (1H, d, \(J = 8.0\)), 7.54 (1H, d, \(J = 8.0\)), 7.46 (2H, d, \(J = 8.0\)) ppm; MS (EI) m/z 494 (M), 406, 378, 368, 350, 289, 283, 269; HRMS calcd for \(C_{22}H_{16}N_6O_4\) 494.1689, found 494.1708; UV \(\lambda_{	ext{max}} = 305\) nm.

**Notes**

$J = 8.5$), 7.46-7.36 (3H, m), 7.28 (1H, t, $J = 7.5$), 7.00 (4H, t, $J = 8.5$), 6.70 (2H, d, $J = 8.5$), 4.76 (1H, A of ABq, $J = 17.5$), 4.61 (1H, B of ABq, $J = 17.5$), 4.13 (1H, d, $J = 15.0$), 3.82 (3H, s), 3.70 (3H, s), 3.12 (1H, d, $J = 13.0$) ppm; MS $m/z$ (EI) 558 (M), 530, 437, 410, 289, 121; HRMS calcd C$_{35}$H$_{40}$O$_2$N$_2$ 558.1791, found 558.1792; UV $\lambda_{\text{max}}$ = 305 nm.

2i (40% conversion): TLC (eluent, 1:4, ethyl acetate/hexane) $R_f$ = 0.75; $^1$H NMR (acetone-$d_6$) 8.26 (1H, d, $J = 8.0$), 7.96 (1H, d, $J = 8.0$), 7.82 (1H, t, $J = 8.0$), 7.80 (1H, d, $J = 8.0$), 7.64 (2H, d, $J = 8.0$), 7.44-7.10 (10H, m), 4.87 (1H, A of ABq, $J = 17.0$), 4.70 (1H, B of ABq, $J = 17.0$), 4.22 (1H, d, $J = 13.0$), 3.22 (1H, d, $J = 13.0$) ppm; MS $m/z$ (EI) 588 (M, not observed), 407, 380, 349, 289 (baseline), 133; HRMS of 289 fragment, calcd C$_{26}$H$_{24}$O$_2$N$_2$ 289.0613, found 289.06147; UV $\lambda_{\text{max}}$ = 302 nm.

**Attempted Radical Scavenging Experiments.** Oxygen gas was slowly bubbled through a benzene solution of 1e (1 mM) as it was irradiated with $\lambda > 530$ nm light. At regular periods the solution was analyzed by TLC which showed the same apparent rate of conversion to rearranged products as a control solution. Similarly, a solution of 1e (1 mM) and 2,6-di-tert-butyl-4-methylphenol or ethyl acrylate (5 mM) in benzene was irradiated with $\lambda > 530$ nm light. Again TLC showed no change in the rate of rearrangement compared to a control sample.

**Acknowledgment.** B.D.S. acknowledges the donors of the Petroleum Research Fund administered by the American Chemical Society for support of this research. J.D.Z. was an undergraduate NSF-REU summer scholar. Amanda E. Avellone and John M. Roosenburg, II, are acknowledged for their for assistance in the preparation of 1i. We are grateful to Professors X. Creary and P. Wagner for helpful discussions.

**Supplementary Material Available:** $^1$H NMR spectra of all compounds and the ORTEP structure of 2e (15 pages). This material is contained in libraries on microfiche, immediately follows this article in the microfilm version of the journal, and can be ordered from the ACS; see any current masthead page for ordering information.