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PHOTOINDUCED PARA-CYCLOADDITION OF PHTHALIMIDES

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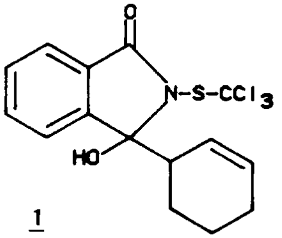
SUMMARY: N-Substituted phthalimides (R= $-SCCl_3$, $-CH_3$, phenyl) reacted with cyclohexene on irradiation at $\lambda > 280$ nm by way of para-cycloaddition, yielding N-substituted tricyclo(4.2.2.0)dodeca-8,11-diene-9,10-dicarboximides. The N-(trichloromethylthio)phthalimide gave the cycloadduct as by-product, while for N-methyl- and N-phenylphthalimide the para-cycloaddition predominated.

Many examples of inter- and intramolecular photoadditions of N-substituted phthalimides with alkenes have been published, yielding carbinols (3-alkenyl-3-hydroxyphthalimidines) by allylic attack of the carbonyl group, preferably benzazepinedione derivatives by insertion of the olefin into the C-N bond followed by imide ring enlargement.$^{1)}$ In this paper a ($4\pi + 2\pi$) para-cycloaddition of the benzene moiety of phthalimides to cyclohexene is described which was observed during photoinduced addition of pesticides to biomolecules$^{2)}$.

During irradiation ($\lambda > 280$ nm)$^{3)}$ of N-(trichloromethylthio)phthalimide, used as a fungicide in plant protection, it is mainly added to cyclohexene by allylic attack of the excited carbonyl group, yielding the corresponding carbinol $\underline{1}^{4)}$(80%). The expected oxetane $\underline{2}^{5)}$ was observed as by-product (6%).$^{6)}$



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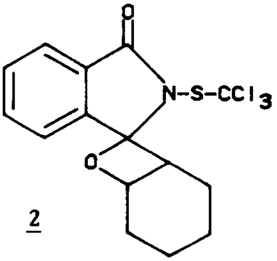
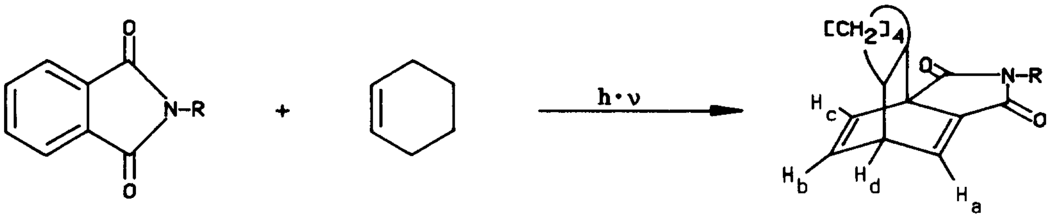


2

As second but unexpected by-product, $\underline{3}$ (11%$^{6)}$), was formed and identified on on the basis of its spectra$^{8)}$.Instead of the phthalimide AA′BB′ pattern in the aromatic region there are signals of three olefinic protons in the ^{1}H-NMR spectrum, i.e δ 7.2 (d,J=6 Hz, H_a), 6.82 (dd, J=7 Hz,J=6 Hz, H_b) and 6.15 (dt, J=7 Hz, J=1 Hz, H_c). From decoupling experiments, two of these are vicinal (H_b and H_c) and the third (H_a) is separated by H_d at δ 3.81 (t, J=6 Hz).



a: R= $-SCCl_3$
b: R= $-CH_3$
c: R= phenyl

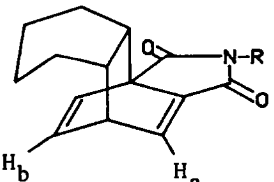
3: R= $-SCCl_3$
4: R= $-CH_3$
5: R= phenyl

From the three possible 1.2-,1.3-,1.4-additions[7],only the 1.4-(para)-adduct 3 is consistent with the observed pattern of three olefinic protons, providing support for the structure of 3. On GC and HPLC analyses 3 eluted as a sharp peak, establishing its isomeric purity.

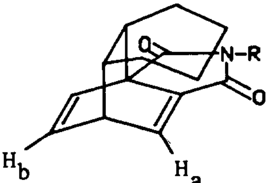
Irradiation of N-methylphthalimide in the presence of cyclohexene under the same conditions afforded the para-cycloadduct 4 as main product (44%[6]),but as a mixture of three isomers as was evident from the GC and HPLC analyses.[9] In the ^{1}H-NMR spectrum of the isomer mixture of 4, two of the isomers gave the same characteristic olefin signals[10] as 3. The third isomer showed an ABX-pattern for the H_c, H_b, and H_d protons and a doublet for H_a[10]. By means of integration the isomer ratio was found to be 10:8:2.

As third example of this type of cycloaddition, the N-phenylphthalimide was irradiated in the presence of cyclohexene, yielding the para-cycloadduct 5[11] as main product (>90%[6]).5 was also obtained in form of three isomers in nearly the same ratio as 4.

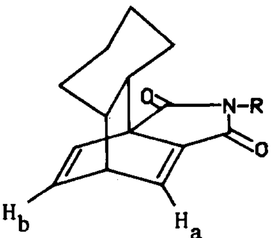
The differences between the observed isomers a, b, and c of 4 and 5 may be explained by the configuration of the brigding cyclohexane ring, taking the cis- (isomer a and b) or trans- (isomer c) arrangements. In the cis-isomer a the proton H_b should be shielded downfield due to steric effects. The same can be expected for H_a in the isomer b, while the trans-configuration (isomer c) leaves nearly the same effects on both sides. These estimated effects are consistent with the observed resonances in the ^{1}H-NMR spectra of 4 and 5, suggesting that the preferred isomer of 3 has the stereochemistry of structure a.



a



b



c

The reason for the stereoselective cycloadditon of cyclohexene to N-(trichloromethylthio)phthalimide is not clear, but appears to depend on the trichloromethylthio substituent.

The ^{13}C-NMR spectra of the isomer mixtures of 4 and 5 exhibit the same characteristic signals in the olefinic region as found for 3 $^{8)}$. However, these spectra can only be helpful for the stereochemical discussions once the pure isomers have been isolated.

The N-substituted tricyclo(4.2.2.0)dodeca-8,11-diene-9,10-dicarboximides 3, 4 and 5 were all obtained as colourless oils, which unfortunately precluded X-ray analyses of these cycloadducts; but their spectral and analytical data reported here leave no doubt about the assigned structures.

The author thanks Prof. W. Adam for helpful discussions.

REFERENCES AND NOTES

1) For recent reviews see: a) Kanaoka, Y., Acc. Chem. Res. **11**, 407 (1978); b) Mazzocchi, P.H., "Organic Photochemistry", vol. 5; Pawda, A. (editor), Marcel Dekker, New York, 1981, p. 421;
c) Maruyama, K., Kubo, Y., J. Org. Chem. **50**, 1426 (1985).
2) Schwack, W., Habilitationschrift, Würzburg (1986).
3) In a general procedure,100 mg of the N-substituted phthalimide,dissolved in 50 ml cyclohexene (dist. over P_2O_5), was irradiated in a quartz tube for 10 h, using a 150 W high pressure mercury lamp. A glass filter (WG 295, Schott) prevented irradiation with wavelengths shorter than 280 nm.For product isolation column chromatography (SiO_2) with benzene as eluant was used. Products were further purified by preparative TLC (SiO_2, 5% ethanol in n-hexane).
4) Compound 1. m.p. 170-172°C (benzene). IR (KBr): 3440, 3080, 2940, 2870, 1715 (C=O), 1615, 1600, 1360, 1225, 1080, 800 cm^{-1}. MS (15 eV): m/z= 378 (Cl_3, 5 %, M^++1), 296 (Cl_3, 29 %), 260 (Cl_2, 100 %), 243 (36 %), 210(23 %), 194 (14 %), 130 (48 %), 81 (21 %). ^{1}H-NMR (400 MHz, $CDCl_3$): δ 7.91 (1H, dt, J=7.5 Hz, J=1 Hz); 7.61-7.66 (2H, 2 td, J=7.5 Hz); 7.54-7.59 (1H,2 dd, J= 7.5 Hz, J=2.2 Hz); 6.20 (1H, d, J=10 Hz); 5.99 (1H, dq, J=10 Hz, J=2.5 Hz); 3.26 (1H, m); 3.06 (1H, s, OH). $C_{15}H_{14}Cl_3NO_2S$ (378.71), calc. % (found %): C 47.57 (47.26), H 3.73 (3.59), N 3.70 (4.06).
5) Compound 2. m.p. 135-136°C (ether). IR (KBr): 3080, 2950, 2870, 1740 (C=O), 1610, 1465, 1285, 1030, 960(oxetane), 800 cm^{-1}. MS (15 eV): m/z= 377 (Cl_3, 2 %, M^+), 306 (Cl_3, 4 %), 296 (Cl_3, 12 %), 260 (Cl_2, 100 %), 232 (80 %), 82 (95 %), 67 (30 %). ^{1}H-NMR (400 MHz, $CDCl_3$): δ 7.87-7.92 (2H, 2 dt, J=7.5 Hz, J=1 Hz); 7.77 (1H, td, J=7.5 Hz, J=1 Hz); 7.57 (1H, td, J=7.5 Hz, J=1 Hz); oxetane protons: 5.15 (1H, dt, J=7.8 Hz, J=6.4 Hz); 3.45 (1H, dt, J=7.8 Hz, J=9.6 Hz). $C_{15}H_{14}Cl_3NO_2S$ (378.71), calc. % (found %): C 47.57 (47.36), H 3.73 (3.60), N 3.70 (3.92).

6) Yields were calculated on the amount of converted starting material.

7) For recent reviews see: Bryce-Smith, D., Gilbert, A., Tetrahedron **32**, 1309 (1976) (Part I); Tetrahedron **33**, 2459 (1977) (Part II).

8) Compound **3**. IR (film): 3070, 2990, 2950, 2865, 1780, 1730 (C=O), 1660,1450, 1270, 1250, 1195, 1030 cm^{-1}. MS (15 eV): m/z= 377 (Cl_3, M^+,1 %), 342 (Cl_2, 21 %), 309 (Cl_3,23 %), 295 (Cl_3,5 %), 260(Cl_2,76 %), 82 (100 %), 67 (59 %). $C_{15}H_{14}Cl_3NO_2S$ (378.71), calc. % (found %): C 47.57 (48.06), H 3.73 (3.83), N 3.70 (3.58). ^{13}C-NMR (100 MHz, $CDCl_3$): δ 27.4, 27.6, 30.2, 32.7 ($-CH_2-$); 45.8, 50.6, 52.9 (-CH<);56.4 (>C<); 123.4, 138.3, 141.4 (=CH-); 142.7(=C<); 162.1, 173.1 (>C=O). UV (ethanol): λ_{max} 240 nm (log ε 3.92).

9) Kanaoka and Hatanaka (Chem. Pharm. Bull. **22**, 2205 (1974)) irradiated **II** in the presence of cyclohexene, but isolated only the corresponding carbinol in poor yield by preparative TLC.

10) Compound **4**. IR (film): 3070, 2940, 2860, 1770, 1705, 1420, 1370, 1255, 995 cm^{-1}. MS (70 eV): m/z= 243 (M^+, 3 %), 175 (46 %),174 (37 %), 162(66 %), 161(34 %),115 (12 %), 82 (29 %), 81 (10 %), 67 (100 %), 54 (66 %),41(46 %). ^1H-NMR ($CDCl_3$): **4a** (main isomer): δ 6.92 (1H, d, J=6 Hz, H_a); 6.77 (1H, dd, J=7 Hz, J=6 Hz, H_b); 6.07 (1H, dt, J=7 Hz, J=1 Hz, H_c); 3.65 (1H,t, J=6 Hz, H_d). **4b**: δ 7.51 (1H, d, J=6 Hz, H_a); 6.80 (1H, dd, J=7 Hz, J=1.5 Hz, H_c); 6.08 (1H, dd, J=7 Hz, J=6 Hz, H_b); 3.67 (1H,t, J=6 Hz, H_d). **4c**: δ 7.16 (1H, dd, J=6 Hz, J=0.8 Hz, H_a); 6.38-6.45 (2H, AB-part of ABX, H_bH_c); 3.77 (1H, tt, X-part of ABX, H_d).

11) Compound **5**. IR (film): 3070, 3040, 2930, 2860, 1770, 1710, 1600, 1500, 1370, 1190 cm^{-1}. MS (70 eV): m/z= 305 (M^+, 9 %), 237 (62 %), 236 (69 %), 223 (100 %), 222 (52 %), 179 (52 %), 178 (31 %), 115 (14 %), 82 (7 %), 77 (31 %), 76 (38 %), 67 (48 %), 54 (38 %), 41 (66 %).
^1H-NMR ($CDCl_3$): **5a** (main-isomer): δ 7.06 (1H, d, J=6 Hz, H_a); 6.83 (1H, dd, J=7 Hz, J=6 Hz, H_b); 6.18 (1H, dt, J=7 Hz, J=1 Hz,H_c); 3.73 (1H, t, J=6 Hz, H_d). **5b**: δ 7.65 (1H, d, J=6 Hz, H_a); 6.91 (1H, dd, J=7 Hz, J=1.5 Hz, H_c); 6.13 (1H, dd, J=7 Hz, J=6 Hz, H_b); 3.74 (1H, t, J=6 Hz, H_d). **5c**: δ 6.41-6.52 (2H, AB-part of ABX, H_bH_c); 3.86 (1H, X-part of ABX, H_d); H_a-signal obscured by the N-phenyl aromatic protons.

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