ISOLATION OF PHOTO-DIELS-ALDER MONO-ADDUCTS OF 4,6-DIMETHYL-2-PYRONE AND FORMATION OF CROSS-ADDUCTS

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Abstract - The Diels-Alder mono-adducts between 4,6-dimethyl-2-pyrone and olefinic dienophiles could be isolated from the low temperature photochemical reactions. The adducts reacted with second olefins to afford cross-adducts with the concurrent decarboxylation. Irradiation of the cross-adducts to p-benzoquinone gave cage compounds.

The Diels-Alder (DA) reactions of 2-pyrones have been used as the key steps in syntheses of colchicine,[1] barrelene[2] and so on, by taking advantage of easy decarboxylation of the mono-adducts. The utilization is limited, however, because the DA reactions take place with difficulty owing to the aromaticity of 2-pyrones, and the resulting mono-adducts are thermally susceptible to decarboxylation and dehydrogenation to afford bis-adducts[3] and benzene derivatives.[4] We have previously reported that, in photochemical reactions with olefins at room temperature, 2-pyrones having electron-withdrawing substituents gave stable [4+2]cycloadducts,[5] whereas ones bearing electron-donating substituents afforded benzene derivatives with the concurrent decarboxylation.[6] Thus, the latter reactions at low temperature might be expected to give [4+2]cycloadducts.

Although the mono-adducts derived from 2-pyrones are diene-equivalents, the investigation of cross-bis[4+2]cycloadditions has been very limited.[7] It is

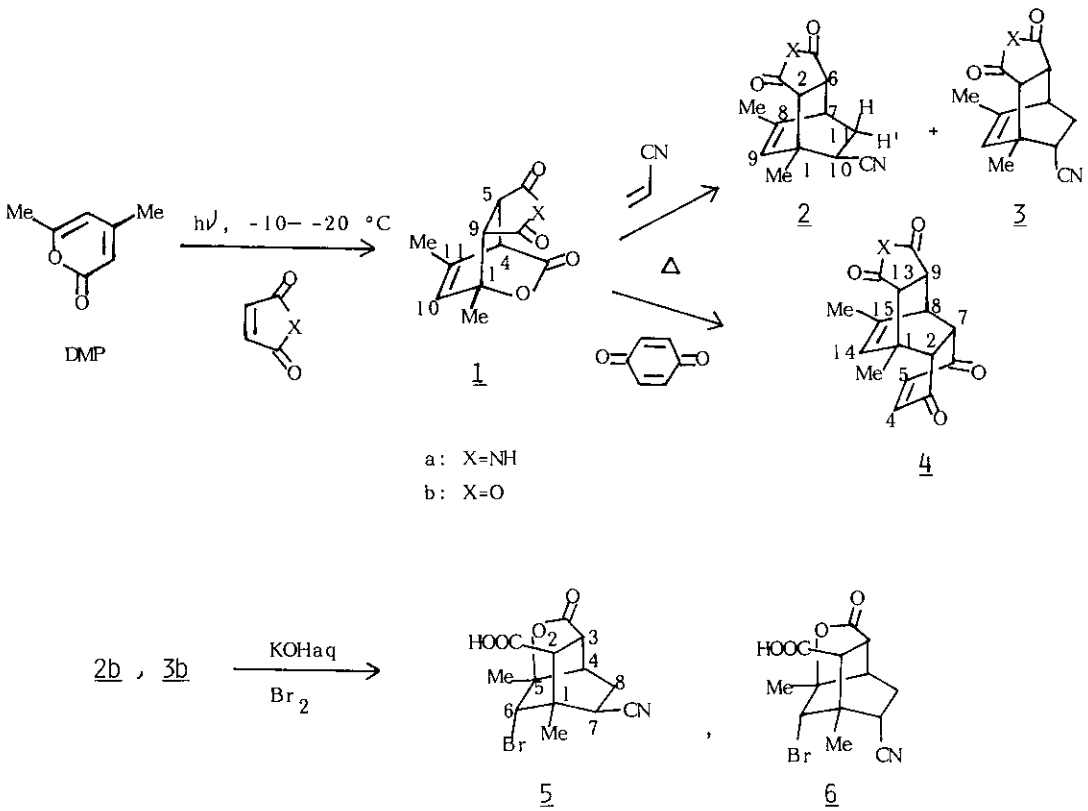
required that the mono-adducts have moderate lability in order to use them for the cross-[4+2]cycloadditions. The mono-adducts derived from 2-pyrones bearing electron-donating groups seemed to be suitable for this purpose.

The present paper describes the isolation of mono-adducts of 4,6-dimethyl-2-pyrone (DMP) with electrophilic olefins from the low temperature photoreaction, and the synthesis of the cross-adducts, some of which were converted into cage compounds, by using mono-adducts.

A mixture of DMP (24 mmol) and maleimide (24 mmol) in the presence of benzophenone (8.8 mmol) as a sensitizer in acetone (200 ml) was irradiated with a 400W high-pressure mercury lamp, under nitrogen, at -10 - -20 °C for 2 h to afford a DA adduct 1a, mp 101-104 °C (dec), in 60% yield. The reaction of DMP with maleic anhydride under the similar conditions gave also a DA adduct 1b, mp 90-93 °C (dec), in 52% yield. Adducts, 1a and 1b, were isolated and purified as follows: After irradiation, the solvent was removed *in vacuo* below 10 °C. To the residue was added chloroform (80 ml) and the solution was cooled in an ice-bath. The formed precipitate (1) was filtered and recrystallized from chloroform. The adduct 1b was heated at 40 °C for 2 h in acetonitrile to give a cyclohexadiene derivative quantitatively. The adduct 1a is rather stable, but it was also decarboxylated by heating at 70 °C to give a cyclohexadiene. The adducts 1a, 1b and the cyclohexadienes were not formed in the thermal reactions.

The *exo* configuration of both the adducts 1 was confirmed on the basis of spectral data.[8,9]

We next investigated reactions of 1 with second olefinic dienophiles leading to the formation of cross-adducts (Scheme 1). The adduct 1a (1.6 mmol) was allowed to react with acrylonitrile (16 mmol) in acetonitrile (30 ml) under reflux for 20 h to give cross-adducts 2a (mp 216-219 °C, 26% yield) and 3a (mp 212-213 °C, 20% yield).[10] The similar reaction of 1b with acrylonitrile for 30 h gave the corresponding cross-adducts 2b (mp 143-144 °C, 55% yield) and 3b (mp 158-161 °C, 38% yield),[11] which were bromolactonized to give cyclic compounds,[12] 5 (mp 256-259 °C, 69% yield) and 6 (mp 117-120 °C, 72% yield) respectively, indicating the *endo* configuration.[13] Thus, both 2a and 3a were assumed to be the *endo* configurations of the imido group. The positions of the cyano groups in 2 and 3 were confirmed by the ^{1}H-NMR spectra; the signals of 10-H showed doublet-doublet pattern (J=5-7 and 9-10 Hz) and their stereochemistry was confirmed by the chemical shift

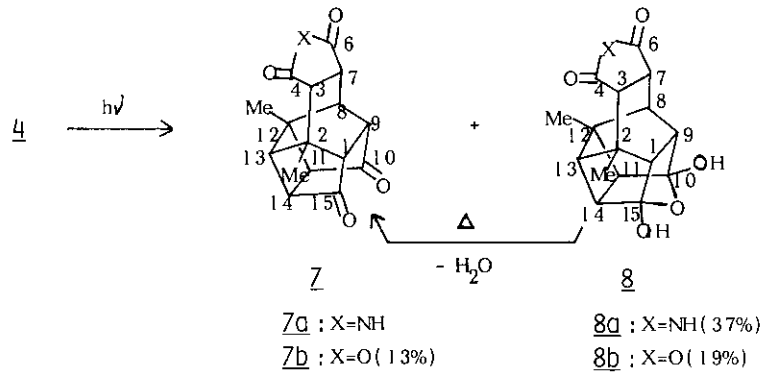


Scheme 1.

deviation between 2 and 3 at 2-H ($\Delta\delta$=0.13-0.45 ppm) owing to magnetic anisotropy of cyano groups.

Similarly, the adducts 1a (0.9 mmol) and 1b (0.9 mmol) reacted with p-benzoquinone (1.8 mmol) in acetonitrile (30 ml) under reflux for 18 h to give the cross-adducts 4a (mp>300°C, 96% yield) and 4b (mp 238-240 °C, 70% yield), respectively, whose structural elucidation was accomplished on the basis of spectral data.[14] The endo-endo configuration of 4 was confirmed by the result of photoreaction mentioned below as well as by the inspection of ^{1}H-NMR data.

The photochemical intramolecular cyclization of the cross-adducts 4 might be expected to give the corresponding tricyclic cage γ-diketones. In fact, irradiation of a solution of 4a (2.1 mmol) in dichloromethane (100 ml) with a 400W high-pressure mercury lamp for 1 h afforded the cage γ-diketone hydrate 8a, mp>300 °C, which was converted to the diketone 7a, mp>300 °C, at 50 °C in vacuo. The similar photoreaction of 4b gave again the corresponding cage



Scheme 2.

γ-diketone 7b, mp 230 °C (sub), and its hydrate 8b, mp 210 °C (sub) (Scheme 2). Structural elucidation of the cage compounds, 7 and 8, was accomplished on the basis of the elemental analyses and spectral data[15]; ^{1}H- and ^{13}C-NMR spectra of 7 and 8 have no olefinic signals.

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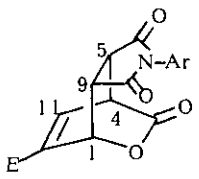
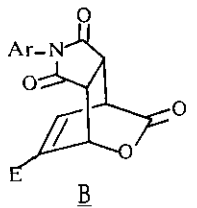
8. The formation of an exo-[4+2]adduct like 1 was also observed in the sensitized photoreaction of methyl 2-pyrone-5-carboxylate (MP). The sensitized photoreaction of MP with N-(p-nitrophenyl)maleimide under similar conditions gave the exo-adduct A, mp 220-222 °C, in 50% yield, whereas the endo-adduct B, mp 185-



A



B

Ar = p-$NO_2C_6H_4$
E = CO_2Me

188 °C, was obtained in 10% yield from the thermal reaction at 80 °C for 32 h. The exo and endo configurations were assigned on the basis of the chemical shifts of 5- and 9-H in A and B, respectively.

A: ^{1}H-NMR (DMSO-d_6) δ 8.37, 7.44 (each 2H, d, ArH), 7.52 (1H, dd, J=7.5, 2.0 Hz, 11-H), 5.84 (1H, t, J=2.0 Hz, 1-H), 4.16 (1H, dd, J=7.5, 3.0 Hz, 4-H), 3.82 (1H, dd, J=9.5, 2.0 Hz, 9-H), 3.80 (3H, s, CH_3), 3.64 (1H, dd, J=9.5, 3.0 Hz, 5-H).

B: ^{1}H-NMR (DMSO-d_6) δ 8.42, 7.42 (each 2H, d, ArH), 7.64 (1H, dd, J=7.0, 3.0 Hz, 11-H), 6.05 (1H, dd, J=4.0, 3.0 Hz, 1-H), 4.24 (1H, dd, J=7.0, 4.0 Hz, 4-H), 4.18 (1H, dd, J=8.0, 4.0 Hz, 9-H), 3.97 (1H, dd, J=8.0, 4.0 Hz, 5-H), 3.78 (3H, s, CH_3).

The exo configurations of 1 were determined on the basis of the comparison of NMR data of 1 with those of A and B, considering the shielding effect of methyl group.[16]

1a: IR (KBr) 1780, 1750, 1720 cm^{-1}; ^{1}H-NMR (DMSO-d_6) δ 11.28 (1H, bs, NH), 6.03 (1H, bs, 10-H), 3.52 (1H, bd, J=3.0 Hz, 4-H), 3.35 (1H, dd, J=3.0, 10.0 Hz, 5-H), 3.08 (1H, d, J=10.0 Hz, 9-H), 1.92, 1.74 (each 3H, s, CH_3); MS m/z 177 (M^+-CO_2).

1b: IR (KBr) 1870, 1790, 1750 cm^{-1}; ^{1}H-NMR (DMSO-d_6) δ 6.04 (1H, bs, 10-H), 3.92 (1H, dd, J=3.0, 10.0 Hz, 5-H), 3.64 (1H, dd, J=1.8, 3.0 Hz, 4-H), 3.52 (1H, d, J=10.0 Hz, 9-H), 1.92, 1.72 (each 3H, s, CH_3); MS m/z 178 (M^+-CO_2).

9. The new compounds reported herein provided satisfactory elemental analyses.

10. 2a: IR (KBr) 2240, 1770, 1710 cm^{-1}; ^{1}H-NMR (DMSO-d_6) δ 11.11 (1H, s, NH), 5.48 (1H, bs, 9-H), 3.12 (1H, dd, J=8.0, 3.5 Hz, 6-H), 2.77 (1H, d, J=8.0 Hz, 2-H), 2.77 (1H, bs, 7-H), 2.56 (1H, dd, J=10.0, 6.0 Hz, 10-H), 1.80 (2H, m, 11-H, 11-H'), 1.68 (3H, d, J=2.0 Hz, 8-CH_3), 1.45 (3H, s, 1-CH_3); MS m/z 230 (M^+).

3a: IR (KBr) 2240, 1770, 1710 cm^{-1}; ^{1}H-NMR (DMSO-d_6) δ 11.12 (1H, s, NH), 5.52 (1H, bs, 9-H), 2.94 (1H, dd, J=8.0, 3.5 Hz, 6-H), 2.86 (1H, dd, J=10.0, 5.0

Hz, 10-H), 2.84 (1H, bs, 7-H), 2.64 (1H, d, J=8.0 Hz, 2-H), 2.10 (1H, ddd, J=12.5, 10.0, 2.0 Hz, 11-H), 1.72 (3H, d, J=2.0 Hz, 8-CH_3), 1.51 (1H, ddd, J=12.5, 5.0, 4.0 Hz, 11-H'), 1.51 (3H, s, 1-CH_3); MS m/z 230 (M^+).

11. 2b: IR (KBr) 2250, 1840, 1780 cm^{-1}; ^{1}H-NMR ($CDCl_3$) δ 5.58 (1H, bs, 9-H), 3.36 (1H, dd, J=8.0, 2.5 Hz, 6-H), 3.28 (1H, d, J=8.0 Hz, 2-H), 3.08 (1H, bs, 7-H) 2.33 (1H, dd, J=9.0, 7.5 Hz, 10-H), 1.94 (2H, m, 11-H, 11-H'), 1.78 (3H, d, J=2.0 Hz, 8-CH_3), 1.64 (3H, s, 1-CH_3); MS m/z 231 (M^+).
3b: IR (KBr) 2250, 1855, 1775 cm^{-1}; ^{1}H-NMR ($CDCl_3$) δ 5.67 (1H, bs, 9-H), 3.21 (1H, dd, J=8.0, 3.0 Hz, 6-H), 3.11 (1H, bs, 7-H), 2.81 (1H, d, J=8.0 Hz, 2-H), 2.57 (1H, dd, J=8.5, 5.5 Hz, 10-H), 2.11 (1H, ddd, J=12.0, 8.5, 2.0 Hz, 11-H), 1.85 (3H, d, J=2.0 Hz, 8-CH_3), 1.75 (1H, ddd, J=12.0, 5.5, 2.0 Hz, 11-H'), 1.69 (3H, s, 1-CH_3); MS m/z 231 (M^+).
12. 5: IR (KBr) 2250, 1780, 1730 cm^{-1}; ^{1}H-NMR (DMSO-d_6) δ 13.0 (1H, bs, COOH), 4.20 (1H, s, 6-H), 3.32 (1H, dd, J=8.0, 3.0 Hz, 7-H), 3.20 (1H, d, J=6.5 Hz, 2-H), 3.04 (1H, dd, J=6.5, 2.0 Hz, 3-H), 2.60 (1H, bs, 4-H), 2.28-2.12 (2H, m, 8-H, 8-H'), 1.45, 1.20 (each 3H, s, CH_3); MS m/z 327 (M^+).
6: IR (KBr) 2250, 1780, 1735 cm^{-1}; ^{1}H-NMR (DMSO-d_6) δ 12.8 (1H, bs, COOH), 4.07 (1H, s, 6-H), 3.55 (1H, t, J=8.0 Hz, 7-H), 3.13 (1H, d, J=6.0 Hz, 2-H), 2.97 (1H, dd, J=6.0, 2.0 Hz, 3-H), 2.54 (1H, bs, 4-H), 2.27 (2H, dd, J=8.0, 3.0 Hz, 8-H, 8-H'), 1.48, 1.26 (each 3H, s, CH_3); MS m/z 327 (M^+).
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14. 4a: IR (KBr) 1750, 1710, 1670 cm^{-1}; ^{1}H-NMR (DMSO-d_6) δ 11.09 (1H, bs, NH), 6.68 (2H, s, 4-, 5-H), 5.66 (1H, s, 14-H), 3.36-3.04 (3H, m, 7-, 8-, 9-H), 2.76 (2H, d, $J_{2,7}=J_{9,13}$=8.0 Hz, 2-, 13-H), 1.55, 1.36 (each 3H, s, CH_3); MS m/z 285 (M^+).
4b: IR (KBr) 1850, 1780, 1675 cm^{-1}; ^{1}H-NMR (DMSO-d_6) δ 6.72 (2H, s, 4-, 5-H), 5.59 (1H, s, 14-H), 3.62 (1H, dd, J=8.0, 3.5 Hz, 9-H), 3.36 (1H, dd, J=8.0, 3.5 Hz, 7-H), 3.22 (1H, m, 8-H), 3.22 (1H, d, J=8.0 Hz, 13-H), 2.88 (1H, d, J=8.0 Hz, 2-H), 1.57, 1.36 (each 3H, s, CH_3); MS m/z 286 (M^+).
15. 7a: IR (KBr) 1765, 1750, 1705 cm^{-1}; ^{1}H-NMR (DMSO-d_6) δ 11.1 (1H, s, NH), 3.16 (1H, dd, J=10.0, 3.5 Hz, 7-H), 2.96 (1H, d, J=10.0 Hz, 3-H), 2.6-2.2 (6H m, 1-, 8-, 9-, 11-, 13-, 14-H), 1.18, 1.08 (each 3H, s, CH_3); MS m/z 285 (M^+).
8a: IR (KBr) 3400, 1765, 1700 cm^{-1}; ^{1}H-NMR (DMSO-d_6) δ 11.1 (1H, s, NH), 6.94, 6.76 (each 1H, s, OH), 2.92 (1H, dd, J=10.0, 3.5 Hz, 7-H), 2.66 (1H, d,

J=10.0 Hz, 3-H), 2.2-1.8 (6H, m, 1-, 8-, 9-, 11-, 13-, 14-H), 1.28, 0.99 (each 3H, $C\underline{H}_3$); ^{13}C-NMR (DMSO-$\underline{d}_6$) δ 180.2, 179.5 (each s, C=O), 109.7, 106.1 (each s, 10-, 15-C), 59.2, 44.6 (each s, 2-, 12-C), 54.5, 51.1, 46.1, 42.8, 40.3, 39.5, 37.9 (each d, 1-, 3-, 7-, 8-, 11-, 13-, 14-C), 22.2, 19.7 (each q, $\underline{C}H_3$); MS m/z 285 (M^+-H_2O).

7b: IR (KBr) 1860, 1780, 1755 cm^{-1}; ^{1}H-NMR (DMSO-$\underline{d}_6$) δ 3.60 (1H, dd, J=11.0, 3.5 Hz, 7-H), 3.38 (1H, d, J=11.0 Hz, 3-H), 2.98 (1H, ddd, J=9.0, 6.5, 3.0 Hz, 14-H), 2.8-2.28 (5H, m, 1-, 8-, 9-, 11-, 13-H), 1.20, 1.06 (each 3H, s, CH_3); MS m/z 286 (M^+).

8b: IR (KBr) 3400, 1860, 1775 cm^{-1}; ^{1}H-NMR (DMSO-$\underline{d}_6$) δ 7.01, 6.85 (each 1H, s, OH), 3.34 (1H, dd, J=10.5, 3.5 Hz, 7-H), 3.09 (1H, d, J=10.5 Hz, 3-H), 2.28 (1H, ddd, J=10.0, 4.0, 2.0 Hz, 14-H), 2.56-1.80 (5H, m, 1-, 8-, 9-, 11-, 13-H), 1.22, 0.97 (each 3H, s, $C\underline{H}_3$); ^{13}C-NMR (DMSO-$\underline{d}_6$) δ 174.4, 173.0 (each s, C=O), 110.0, 106.3 (each s, 10-, 15-C), 52.4, 44.9 (each s, 2-, 12-C), 54.7, 51.1, 46.3, 43.1, 40.3, 40.2, 39.6, 38.3 (each d, 1-, 3-, 7-, 8-, 11-, 13-, 14-C), 21.7, 19.5 (each q, $\underline{C}H_3$); MS m/z 286 (M^+-H_2O).

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