A Simultaneous Diels-Alder and Friedel-Crafts Reaction[1]

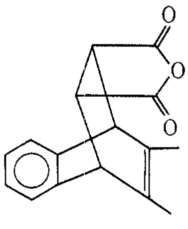
JOHN W. ZUZACK,* WILLIAM J. HUFKER, JR.,
AND HUGH B. DONAHUE

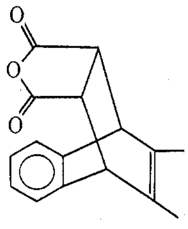
Department of Chemistry, St. Louis University,
St. Louis, Missouri 63103

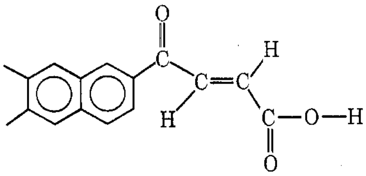
JOHN S. MEEK AND JOHN J. FLYNN[2]
Department of Chemistry, University of Colorado,
Boulder, Colorado 80302

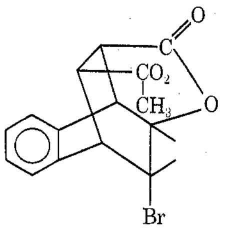
Received May 10, 1972

In the condensation of 2,3-dimethylnaphthalene with maleic anhydride in the presence of aluminum chloride four Diels-Alder adducts and three Friedel-Crafts condensation products are theoretically possible. In examining this reaction we have found that two adducts (**1** and **2**) and one condensation product (**3**) are formed.


1 (endo)


2 (exo)


3


4

So far this seems to be the first system found where maleic anhydride is involved in competing Diels-Alder and Friedel-Crafts reactions although these concurrent condensations have been noted between dicyanoacetylene and benzene.[3]

The thermal reaction of 2,3-dimethylnaphthalene and maleic anhydride was investigated by Kloetzel and Herzog who obtained a product melting at 177-178°.[4] They showed that addition had occurred at the 1,4 positions of the methyl-substituted, more electron-rich ring of the naphthalene but left unsettled whether their material was mainly **1** or **2**.

Yates and Eaton found that this Diels-Alder reaction was accelerated by aluminum chloride and obtained a 40% yield of product melting at 175-178° dec.[5] They converted their material into a bromolactone **4** and assigned structure **1** to the adduct.

Since a closely related keto acid on treatment with lead tetraacetate has been found to give a keto lactone *via* a carbonium ion rearrangement[6] the exo-endo assignment made by Yates and Eaton appeared in doubt if **2** gave a bromonium ion rearrangement. The work was reinvestigated, but no rearrangement was found. However, it was found that both the thermal reaction and the aluminum chloride catalyzed reaction gave two adducts, one melting at 193-195° and the other melting at 176-177°. Although the melting point of the latter corresponded to that reported for **1** by Yates and Eaton, pmr data indicated its structure was **2** and the higher melting isomer was **1**.

The pmr spectra showed that each compound had four aromatic protons corresponding to structures **1** and **2** and not the other two possible adducts. The higher melting adduct had the more shielded bridge protons which indicated they were in the shielding cone of the benzene moiety corresponding to **1**. Williams[7] has studied pmr spectra of rigid cyclic ketones in deuteriochloroform and noted how various peaks shift in going to a benzene solution. His work suggested that a similar effect might be found in the spectra of rigid cyclic anhydrides and would enable one to distinguish between adducts such as **1** and **2**. The complexing in benzene solution leads one to predict that the methyl groups in **1** would have greater shifts due to solvent shielding in going from chloroform to benzene, but bridgehead and bridge proton shifts would be almost identical. The data obtained are given in the table below and the solvent shifts were consistent with assigned structures.

TABLE I

Proton	Adduct[a]	Observed resonance, cps $CDCl_3$	 C_6H_6	 Shift
Bridge	a	197	145	52
	b	205	155	50
Bridgehead	a	253	230	23
	b	247	226	21
Methyl	a	108	88	20
	b	110	80	30

[a] a = higher melting adduct; b = lower melting adduct.

The structures of the two adducts were also checked chemically by lactonization studies. The higher melting adduct was subjected to an iodolactonization reaction and gave two products, one melting at 167° and the other at 316°. The lower melting product gave a positive Beilstein test, slowly produced a violet color in acetic acid, and gave upon stirring with powdered zinc in acetic acid the starting anhydride. This substance was assigned the iodolactone structure **5**. The higher melting product gave a negative Beilstein test and a single ir carbonyl absorption at 1776 cm^{-1} which is characteristic of a γ-lactone. Therefore this compound was assigned structure **6**.

The lower melting adduct would not undergo lactone formation but yielded its dicarboxylic acid.

Both adducts were converted into monomethyl esters by warming with methanol. These esters were

---

[1] The first group of workers investigated the condensation of maleic anhydride and 2,3-dimethylnaphthalene to get suitable starting materials for the synthesis of compounds of pharmacological interest while the second investigated the reaction since they felt the structure proof of the reported product seemed ambiguous. In the course of this research it was discovered that the two independent investigations overlapped in part as well as supplemented each other and a joint publication seemed desirable.

[2] National Science Foundation Summer Research Participant, 1966 and 1968.

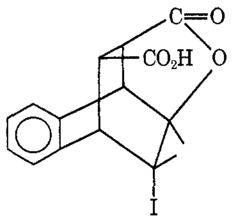
[3] E. Ciganek, *Tetrahedron Lett.*, **No. 34**, 3321 (1967).

[4] M. C. Kloetzel and H. L. Herzog, *J. Amer. Chem. Soc.*, **72**, 1991 (1950).

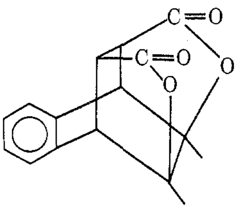
[5] P. Yates and P. Eaton, *ibid.*, **82**, 4436 (1960).

[6] C. M. Cimarusti and J. Wolinsky, *ibid.*, **90**, 113 (1968).

[7] D. H. Williams, *Excerpta Med. Found. Int. Congr. Ser.*, **No. 132**, 159 (1966).



5



6

then treated with iodine in a basic solution. The half-ester from the higher melting adduct quickly discharged the iodine color and gave an iodolactone whereas the half-ester of the lower melting adduct did not react with iodine in the presence of sodium carbonate.

The higher melting adduct was converted into a diacid and then to a bromolactonic acid which on treatment with diazomethane gave an ester whose melting point checked that reported by Yates and Eaton for **4**. It appears that material reported earlier[3,4] were mixtures of **1** and **2**.

Since the resonance of the methyl groups in **1** and **2** distinctly differed, the Diels–Alder reaction could be followed by pmr. In both the thermal and the aluminum chloride catalyzed reaction the ratio of the two adducts were found to be 2:1 in favor of the higher melting adduct. When either adduct alone was heated in boiling benzene for a week, the pmr spectra showed a slow formation of 2,3-dimethylnaphthalene in each case but the other adduct was not detectable. This indicated the adduct ratio was due to kinetic control and one isomer was not accumulating owing to a readily reversible reaction in boiling benzene.

The finding that the adduct ratio was approximately the same in both the thermal and the catalyzed reaction is not in agreement with the observation that the proportion of the endo adduct is enhanced by catalysis with aluminum chloride.[8]

It is of interest that in the competing Friedel–Crafts and Diels–Alder reaction different rings are attacked. In the first reaction a steric factor appears to override electronic considerations important in the latter reaction. The planes of the reactants need not be parallel in the transition state of the Friedel–Crafts reaction as they do in the Diels–Alder reaction, and it is doubtful the two reactions have similar transition states.

The keto acid **3** coming from the aluminum chloride catalyzed reaction was a yellow solid whose pmr spectrum indicated a trans double bond. Hydrogenation of the acid gave the known β-2(6,7-dimethylnaphthoyl)-propionic acid.[9]

Experimental Section

Nmr spectra were obtained with Varian A-60 and A-60A spectrometers. Spectra were obtained from 16% solutions in $CDCl_3$ with tetramethylsilane (TMS) as the internal standard. Melting points were measured in a copper block as well as with standardized thermometers. Analyses were performed in St. Louis or by Galbraith Laboratories, Knoxville, Tenn.

***endo*-1,4-(2′,5′-Diketo-3′,4′-tetrahydrofurano)-2,3-dimethyl-1,4-dihydronaphthalene (1).**—To a filtered solution of 39 g (0.25 mol) of 2,3-dimethylnaphthalene and 29 g (0.30 mol) of maleic anhydride in 1.6 l. of methylene chloride was added 33 g (0.25 mol) of anhydrous aluminum chloride over a 1–1.5-hr period. After stirring the mixture for an additional 3 hr, tetrahydrofuran was cautiously added to it until the deep red coloration of the solution was removed. The resulting solution was evaporated to about 500 ml and cooled overnight. The viscous mixture was diluted with an equal volume of cold acetone and filtered. The product was washed with acetone and air-dried. In four runs, yields ranged from 13 to 19%: mp 193–195°, nmr ($CDCl_3$) δ 1.80 (s, 6 H), 3.28 (m, 2 H), 4.20 (m, 2 H), 7.25 (m, 4, ArH); ir (mull) 1835 (C=O, asymmetric), 1754 cm^{-1} (C=O, symmetric).

Anal. Calcd for $C_{16}H_{14}O_3$: 75.57; H, 5.55. Found: C, 75.28; H, 5.61.

2,3-Dimethylnaphthalene (15.6 g) and maleic anhydride (19.6 g) were refluxed in 100 ml of benzene. Samples were removed, and the ratio of the adducts and percentage of reactions given in the discussion were calculated from integration of the methyl peaks. When samples of the purified adducts were heated in benzene for a week, more 2,3-dimethylnaphthalene was produced from **1** than from **2**.

***exo*-1,4-(2′,5′-Diketo-3′,4′-tetrahydrofurano)-2,3-dimethyl-1,4-dihydronaphthalene (2).**—A 1000-ml erlenmeyer flask covered by a watch glass containing 104 g (0.66 mol) of 2,3-dimethylnaphthalene and 600 g (6.12 mol) of maleic anhydride was heated on a steam bath for 2 days. To the hot reaction mixture enough water was added to form a mushy layer on top of the water. The crude product was collected by filtration, washed with hot water and air-dired, and then washed with hot benzene and dried: mp 178–180°; nmr ($CDCl_3$) δ 1.80 (s), 1.82 (s), 3.28 (m), 3.41 (m), 4.11 (m), 4.22 (m), 7.25 (m). The mixture was placed in 800 ml of benzene and heated 10 min; any insoluble matter was removed. The filtrate was cooled to 50–60° and filtered at that temperature to give 3.3 g (2%), mp 175–176°, of exo anhydride **2**. Yields of **2** were increased to a maximum of 19% by using the filtrate from previous runs as the recrystallization solvent: nmr ($CDCl_3$) δ 1.82 (s, 6 H), 3.41 (m, 2 H), 4.11 (m, 2 H), 7.20 (s, 4 ArH); ir (mull) 1835 (C=O, asymmetric), 1754 cm^{-1} (C=O, symmetric).

Anal. Calcd for $C_{16}H_{14}O_3$: C, 75.57; H, 5.55. Found: C, 75.36; H, 5.63.

Iodolactonization of 1 in Aqueous Potassium Hydroxide.—The endo anhydride (15.70 g, 0.0616 mol) was placed in 1100 ml of 1% aqueous potassium hydroxide and the solution boiled until almost homogeneous. The few remaining undissolved crystals were removed by filtration. The solution was cooled to room temperature; the pH was adjusted with 6 *N* hydrochloric acid to 7.3 and 21 g (0.250 mol) of sodium bicarbonate added. To the resulting solution was added 120 ml of a solution of 18.0 g (0.0708 mol) of iodine and 37.0 g (0.222 mol) of potassium iodide This mixture was left to stand in the dark for 1 day. The resulting solid was filtered, washed with water, and air-dried to yield 3.5 g of the dilactone (**6**) (18.7%), mp 315–319°, which was recrystallized from acetonitrile to give 2.8 g of large colorless crystals, mp 315–316°, ir (mull) 1775 cm^{-1} (C=O, lactone).

Anal. Calcd for $C_{16}H_{14}O_4$: C, 71.10; H, 5.22. Found: C, 70.83; H, 5.35.

To the filtrate from the iodolactonization was added 6 *N* hydrochloric acid to pH 4. The resulting solid was heated with acetone, filtered, and dried, giving 4.6 g (22.4%) of iodolactone (**5**), mp 161–163°, which was recrystallized (methanol) to give 3.0 g of product, mp 166–167°. The analytical sample was prepared by washing with dilute hydrochloric acid, followed by warm water. It was then air-dried and recrystallized (methanol) giving a white solid, mp 171–173° (sealed tube), ir (mull) 1775 (C=O, lactone), 1680 cm^{-1} (C=O, carboxylic acid).

Anal. Calcd for $C_{16}H_{15}IO_4$: C, 48.26; H, 3.80. Found: C, 48.50; H, 4.03.

Attempted Iodolactonization of 2 in Aqueous Potassium Hydroxide.—The adduct **2**, mp 175–176°, was subjected to the same iodolactonization as above. The reaction mixture was adjusted to pH 4 with 6 *N* hydrochloric acid. The resulting solid was filtered, washed with water, and dried to yield 13.35 g (82.4% yield) of a white solid, mp 180–185°. It was recrystallized from methanol giving 10.0 g of the diacid of **2**, mp 241–243° (sealed tube). The analytical sample was prepared by washing with dilute hydrochloric acid, followed by warm water, air-dried, and recrystallized (methanol) to give a white solid, mp 241–243° (sealed tube).

Anal. Calcd for $C_{16}H_{16}O_4$: C, 70.57; H, 5.92. Found: C, 70.43; H, 6.38.

---

(8) T. Inukai and T. Kojima, *J. Org. Chem.*, **31**, 2032 (1966).

(9) R. H. Martin and J. Senders, *Bull. Soc. Chim. Belg.*, **64**, 221 (1955).

Preparation of the Diacid of 2.—The exo anhydride (**2**), 5.0 g (0.0196 mol), was dissolved in 500 ml of boiling 1% aqueous potassium hydroxide, filtered, and cooled to room temperature. The solution was adjusted to a pH of 4 with 6 *N* hydrochloric acid. The resulting mixture was filtered, washed with water, and air-dried, giving 4.5 g (84%) of a colorless solid, mp 242–244° (sealed tube). This substance was identical with the product of the attempted iodolactonization of **2**.

Zinc Reduction of the Iodolactone (5).—Exactly 1.0 g (0.0025 mol) of the iodolactone (**5**) was dissolved in 250 ml of glacial acetic acid. Excess zinc dust (0.64 g, 0.076 g-atom) was added, and the suspension was stirred for 10 hr. The unconsumed zinc was removed and the filtrate diluted with water to the cloud point. The solution was heated until homogeneous, cooled, and then filtered. The resulting white crystals were washed with cold glacial acetic acid and air-dried giving 0.25 g (39%) of the endo anhydride (**1**), mp 193–195°.

Half-Esters.—A 0.21-g sample of the exo anhydride, mp 175–177°, was heated in methanol until all of the solid dissolved. Evaporation of the 10 ml of solvent to dryness gave 0.25 g of the exo half-ester: mp 169–172°; pmr ($CDCl_3$) 1.77 (s, 6 CH_3), 3.10 (d, 2, $J = 1$ Hz), 3.38 (s, 3, OCH_3), 3.32 (d, 2, $J = 1$ Hz), and 7.20 (m, 4, ArH).

Anal. Calcd for $C_{17}H_{18}O_4$: C, 71.31; H, 6.34. Found: C, 71.19; H, 6.27.

The higher melting endo adduct was similarly converted into a half-ester, mp 187–189° (lit.[5] mp 184–185°). The pmr of this half-ester was similar to that of the exo isomer, but no coupling between the bridge and bridgehead protons was observed and the integration suggested the acidic proton might lie in the aromatic region: pmr ($CDCl_3$) 1.83 (s, 6) 3.00 (s, 2), 3.64 (s, 3), 3.92 (s, 2), 7.18 (m, 4.6).

The half-esters were dissolved in 5 ml of 5% sodium carbonate and treated with an iodine stock solution.[10] The exo half-ester (0.18 g) did not decolorize the first four drops of iodine, and 0.12 g was recovered unchanged. When 0.37 g of the endo half-ester, mp 187–189°, was similarly treated, the iodine was immediately decolorized and a precipitate formed: yield 0.13 g; mp 105–110° dec; pmr ($CDCl_3$) 1.83 (s, 3), 2.35 (s, 3), 2.95 (m, 2), 3.7 (m, 1), 3.80 (s, 3), 4.17 (d, 1, $J = 1$ Hz), 7.34 (m, 4, ArH).

Anal. Calcd for $C_{17}H_{17}IO_4$: C, 49.53; H, 4.16. Found: C, 49.31; H, 3.99.

A 2-g sample of the endo anhydride was heated in 40 ml of 5% sodium carbonate until solution was effected. Cooling, acidification, and drying gave 2.10 g of a solid; 1 g of this acid was added to 75 ml of 0.1 *N* sodium bicarbonate. This solution was diluted with 75 ml of water and filtered. Bromine was added dropwise to the filtrate until the bromine color persisted. After 30 min the solution was acidified, decolorized with a trace of sodium bisulfite, and filtered, yield 0.90 g, mp 215–218°. Recrystallization from ethanol did not improve the product: pmr (acetone-d_6) 1.61 (s, 3), 2.05 (s, 4), 2.93 (m, 2), 4.01 (m, 2), 7.36 (m, 4); ir 1770 cm^{-1} (C=O, lactone).

Anal. Calcd for $C_{16}H_{15}BrO_4$: C, 54.70; H, 4.27. Found: C, 54.49; H, 4.19.

A solution of 0.35 g of this bromolactone acid was treated with an ethereal solution of diazomethane. The product was recrystallized from ethanol and gave 0.20 g of solid, mp 191–193°. A mixture of this solid and a sample of the methyl bromolactone (lit.[5] mp 191.5–192°) prepared by the method of Yates and Eaton[5] melted without depression.

Preparation of 3.—A mixture of 3.9 g of a 2,3-dimethylnaphthalene, 2.5 g of maleic anhydride, and 3.4 g of aluminum chloride in 400 ml of methylene chloride was allowed to react at room temperature. After decomposition of the complex with acid, 10% sodium carbonate was used to make the solution basic and extract a yellow acid. Acidification, filtration, and recrystallization from acetic acid gave 0.70 g of **3**: mp 188–189°; pmr (dimethyl sulfoxide-d_6) 2.40 (s, 6), 6.68 (d, 1, $J = 16$ Hz), 7.61 and 7.83 (4), 8.00 (d, 1, $J = 16$ Hz), 8.50 (s, 1); ir (KBr) 1760, 1690 (C=O, acid), 1670 cm^{-1} (C=O, ketone). The analytical sample melted at 190–191° to give a red liquid.

Anal. Calcd for $C_{16}H_{14}O_3$: C, 75.59; H, 5.51. Found: C, 75.35; H, 5.47.

Hydrogenation of 0.25 g of the acid over 10% palladium on charcoal gave 0.16 g of white crystals, mp 182–183 dec (lit.[9] mp 179–180°). Authentic material was prepared by the method or Morten and Senders, but the use of methylene chloride in place of nitrobenzene as solvent for the aluminum chloride, 2,3-dimethylnaphthalene, and succinic anhydride gave much less tar and the product melted at 183–184° dec. A mixture of this material and that from the hydrogenation melted at 183–184° dec, and the products had identical spectra.

Analysis of the material left from the extraction of **3** showed a 33% yield of **1** and **2** in which the ratio of **1** to **2** was 2:1.

Registry No.—**1**, 36736-37-5; **1** half-ester iodide, 36808-03-4; **1** bromolactone, 36808-04-5; **2**, 36736-38-6; **2** diacid, 36808-06-7; **2** half-ester, 36807-55-3; **3**, 36807-56-4; **5**, 36807-57-5; **6**, 36803-78-8.

Acknowledgment.—This investigation was supported in Missouri through Contract No. DA 18-108-CML-6601 and DA 18-035-AMC-382A from the U. S. Army Research and Development Laboratories, Edgewood Arsenal, Maryland.

The Utilization of Magnesium Enolates in the Michael Reaction

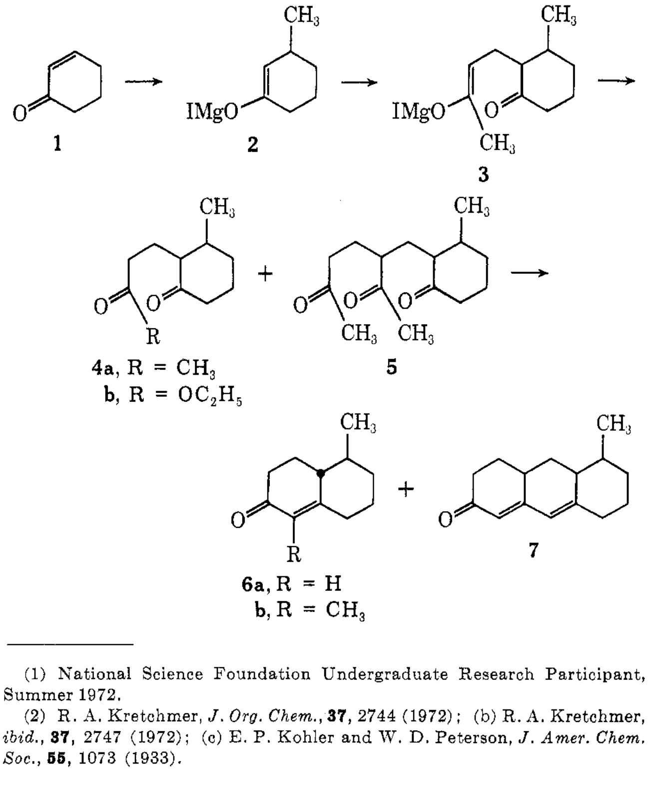
RICHARD A. KRETCHMER,* EDWARD D. MIHELICH,[1] AND JOHN J. WALDRON

Department of Chemistry, Illinois Institute of Technology, Chicago, Illinois 60616

Received July 11, 1972

The Michael reaction of magnesium enolates has recently been demonstrated to be a potential side reaction in the conjugate addition of Grignard reagents to α,β-unsaturated ketones.[2] We wish to report the application of this observation to the stereospecific synthesis of 2,3-disubstituted cyclohexanones and 1,5-substituted $\Delta^{1,9}$-octal-2-one derivatives.

SCHEME I



---

(10) C. S. Rondestvedt, Jr., and C. D. Ver Nooy, *J. Amer. Chem. Soc.*, **77**, 4878 (1955).

(1) National Science Foundation Undergraduate Research Participant, Summer 1972.

(2) R. A. Kretchmer, *J. Org. Chem.*, **37**, 2744 (1972); (b) R. A. Kretchmer, *ibid.*, **37**, 2747 (1972); (c) E. P. Kohler and W. D. Peterson, *J. Amer. Chem. Soc.*, **55**, 1073 (1933).