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Pyridoxal Model Compounds. II. The Diels-Alder Reaction of 9-Substituted 2-Methoxyanthracenes

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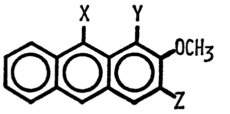
Synopsis. The Diels-Alder reactions of several 2-methoxyanthracenes with tetracyanoethylene (TCNE), dimethyl acetylenedicarboxylate (DMAD), and maleic anhydride (MA) were examined. TCNE gave charge-transfer complexes, but not an addition product in every case. MA gave one-to-one adducts with anthracenes, while DMAD afforded no adduct.

Following the regioselective formylation of 2-methoxyanthracenes,[1] the Diels-Alder reactions of maleic anhydride (MA), tetracyanoethylene (TCNE), and dimethyl acetylenedicarboxylate (DMAD) with 9-substituted 2-methoxyanthracenes were examined in an attempt to synthesize a possible precursor of asymmetric inversion catalysts. The anthracene derivatives used are shown in Fig. 1.

The qualitative results obtained are shown in Table 1. These results clearly show that only MA was effective in the Diels-Alder addition to 9-substituted 2-methoxyanthracenes; this is consistent with the fact that, in early reports concerning the Diels-Alder addition to 9-arylanthracenes, MA was frequently used as a dienophile.[2] Contrary to our expectation, however, TCNE resulted in only the formation of the corresponding charge-transfer complex, and DMAD gave no addition product. The lack of reactivity in these dienophiles may be explained by the steric interaction in the transition state between the aryl group at C_9 and the bulky functional group of the dienophiles.[3]



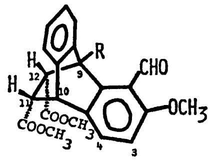
1 $X=CH_3$, $Y=Z=H$
2 X=4-isopropyl-*o*-tolyl, Y=Z=H
3 X=4-isopropyl-*o*-tolyl, Y=CHO, Z=H
4 X=3-tolyl, Y=Z=H
5 X=4-isopropyl-*o*-tolyl, Y=H, Z=CHO
6 X=phenyl, Y=Z=H
7 X=2,6-xylyl, Y=Z=H
8 X=2-methoxyphenyl, Y=Z=H

TABLE 1. THE QUALITATIVE RESULTS OF THE DIELS-ALDER REACTION OF DIENOPHILES WITH 9-SUBSTITUTED 2-METHOXYANTHRACENES

Compounds	TCNE[a]	DMAD[b]	MA[c]	(Yield %)
1	NR[e]	—	—	
2	C[d]	NR	A[f]	(14)
3	C	NR	A	(42)[g]
4	NR	NR	A	(20)[h]
5	—	NR	A	(40)[h]
6	—	—	A	(87)
7	—	—	A	(80)[h]
8	—	—	A	(75)

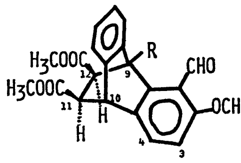
a) In THF at ambient temperature. b) With or without solvent such as xylene or ethanol at temperature lower than 100 °C. c) See Experimental. d) C stands for complex formation. e) NR represents that no reaction occured. f) A stands for the formation of one-to-one adduct. g) Yield after hydrolysis followed by esterification of the adduct. h) Apparent yield on TLC.

In relation to our interest in the construction of asymmetric inversion catalysts, the confirmation of the structure of adducts between MA and **3** was important. Thus, the reaction mixture was treated with aqueous 5% trimethylamine and then with diazomethane to convert the products to esters. Mainly, four products were detected on a thin-layer chromatogram; their R_f values were 0.5, 0.35, 0.25, and 0.18. The $R_f=0.35$ and 0.18 compounds were separated by elution chromatography with silica gel and shown to be one-to-one adducts of **3** with dimethyl maleate; the structures were unequivocally assigned to **9** and **10** respectively on the basis of their NMR spectra and lanthanide-induced NMR spectra. A comparison of the NMR spectra of **9** with that of **10** showed that two methoxycarbonyl groups, at C_{11} and C_{12}, were parallelly disposed to the nearer direction to the formyl-substituted benzeno-ring in **9** and to the more remote direction in **10**, because the two ester methyl groups in **10** showed the same chemical shifts at 3.58 ppm.



9

R=4-isopropyl-*o*-tolyl



10

R=4-isopropyl-*o*-tolyl

The ratio of the yield of **9** to that of **10** was 47 : 53; it was probably caused by the dipole interaction of the groups between the formyl group at C_1 of **3** and maleic anhydride.

Experimental

The IR spectra were obtained using a Shimadzu IR-27 apparatus. The ^1H-NMR spectra were recorded on a Varian HA-100D apparatus, with tetramethylsilane as the internal standard. The chemical shifts and the coupling constant were represented in δ and Hz units respectively. The UV spectra were measured by means of a Hitachi 124 spectrophotometer. Merck Art. 7734 and Wakogel B-5 FM were used for the preparative separation of the products on a silica gel column by elution chromatography and for thin-layer chromatography (TLC) respectively. The melting points are uncorrected.

Materials. All the dienophiles used, TCNE, DMAD, and MA, are commercially available. Compounds **1** through **8** were prepared by the previously reported method.[1b]

Reaction of Anthracenes with MA. In general, MA equivalent in weight to the anthracene derivative used was treated in a suitable amount of *m*-dichlorobenzene at 125—165 °C, and the reaction was monitored by TLC.

9-(4-Isopropyl-*o*-tolyl)-2-methoxyanthracene (**2**) gave a one-to-one adduct in a 14% yield after a reaction for 6 days; mp 210—211 °C. Found: C, 79.15; H, 6.04%. Calcd for $C_{29}H_{26}O_4$: C, 79.43; H, 5.98%.

A mixture of 9-(4-isopropyl-*o*-tolyl)-2-methoxy-1-anthracenecarbaldehyde (**3**) (1.5 g) and 1.5 g of MA in 10 ml of *m*-dichlorobenzene was heated without stirring at 135—145 °C for 40 h. In order to obtain the products as esters, the reaction was then treated with 20 ml of aqueous 5% trimethylamine at room temperature for 2 h, followed by treatment with an ether solution of diazomethane after a usual work-up. Mainly four products were detected on TLC (benzene–ethyl acetate=9 : 1 v/v); their R_f values were 0.5, 0.35, 0.25, and 0.18. On the basis of the color reaction of the products when sprayed with a $FeCl_3$(2 g)–concd HCl (5 ml)–H_2O(95 ml) solution,[4] the products, $R_f=0.35$ and 0.18, were the compounds bridged between the C_9 and C_{10} of the anthracene ring.

The compound showing $R_f=0.35$ was obtained in a 19.6% yield and found to be a racemic mixture of dimethyl (9R,10R,11R,12R)-1-formyl-9-(4-isopropyl-*o*-tolyl)-2-methoxy-9,10-dihydro-9,10-ethano-11,12-anthracenedicarboxylate (**9**) and its enantiomer on the basis of the following properties: colorless fine needles from ethanol, mp 189—190 °C. Found: C, 75.04; H, 6.19%. Calcd for $C_{32}H_{32}O_6$: C, 74.98; H, 6.29%. IR (KBr disk): 1740 ($-COOCH_3$), 1705($-CHO$), and 1215(=C–O–C) cm^{-1}. UV(ethanol): λ_{max} (log ε) 212 (4.60), 272(3.49), 280(3.53), and 290(3.53)nm. NMR(CCl_4): 1.32(6H, d, $J=7.0$, $-CH(\underline{CH}_3)_2$), 1.65(3H, s, $Ar-\underline{CH}_3$), 2.94(1H, quin, $J=7.0$, $-\underline{CH}(CH_3)_2$), 3.66(3H, s, $-OCH_3$), 3.33 (3H, s, C_{11}– or $C_{12}-COO\underline{CH}_3$), 3.48(3H, s, C_{12}– or $C_{11}-COO\underline{CH}_3$), 3.08 (1H, quar, $J=1.75$ and 10.75, $C_{11}-\underline{H}$), 3.94 (1H, d, $J=10.75$, $C_{12}-\underline{H}$), 4.61(1H, d, $J=1.75$, $C_{10}-\underline{H}$), 6.66 (1H, d, $J=8.5$, $C_3-\underline{H}$), 7.23(1H, d, $J=8.5$, $C_4-\underline{H}$), and 9.06 (1H, s, $-CHO$). MS: (M^+)*m*/*e* 512.

The compound showing $R_f=0.18$ was obtained in a 22.5% yield and found to be a racemic mixture of dimethyl (9*R*,10R,11S,12S)-1-formyl-9-(4-isopropyl-*o*-tolyl)-2-methoxy-9,10-dihydro-9,10-ethano-11,12-anthracenedicarboxylate (**10**) and its enantiomer on the basis of the following data: colorless crystals from ethanol, mp 195—196 °C. Found: C, 75.08; H, 6.00%. Calcd for $C_{32}H_{32}O_6$: C, 74.98; H, 6.29%. IR (KBr disk): 1760($-COOCH_3$), 1690($-CHO$), and 1260 (=C–O–C) cm^{-1}. UV(ethanol): 212(4.60), 261(3.79), 270 (sh)(3.68), 281(sh)(3.51), and 318(3.56) nm. NMR($CDCl_3$–CCl_4 1 : 1 v/v): 1.31(6H, d, $J=7.0$, $-CH(\underline{CH}_3)_2$), 3.75(3H, s, $-OCH_3$), 3.58(6H, s, C_{11}– and $C_{12}-COO\underline{CH}_3$), 3.17(1H, quar, $J=1.75$ and 11.0, $C_{11}-\underline{H}$), 3.80(1H, d, $J=11.0$, $C_{12}-\underline{H}$), 4.69(1H, d, $J=1.75$, $C_{10}-H$), 6.86(1H, d, $J=8.25$, $C_3-\underline{H}$), 7.47(1H, d, $J=8.25$, $C_4-\underline{H}$), and 9.30(1H, s, $-CHO$). MS: (M^+) *m*/*e* 512.

9-Phenyl-2-methoxyanthracene (**6**) gave a one-to-one adduct in a 87% yield after a reaction for 14.5 h; colorless crystals, mp 224—226 °C. Found: C, 78.25; H, 4.66%. Calcd for $C_{25}H_{18}O_4$: C, 78.52; H, 4.74%.

9-(*m*-Tolyl)-2-methoxyanthracene (**4**), 9-(4-isopropyl-*o*-tolyl)-2-methoxy-3-anthracenecarbaldehyde (**5**), 9-(2,6-xylyl)-2-methoxyanthracene (**7**), and 9-(2-methoxyphenyl)-2-methoxyanthracene (**8**) were found to react with MA to give yields of 20% (after 18 h) for **4**, 40% (6 days) for **5**, (2 days) for **7**, and 75% (14 h) for **8** on the basis of the TLC spots.

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References

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4) The compounds, $R_f=0.5$ and 0.25, were detected as brown spots and, on the other hand, the compounds, $R_f=0.35$ and 0.18, as green spots.