

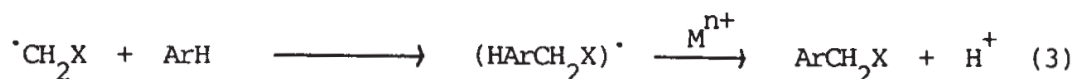
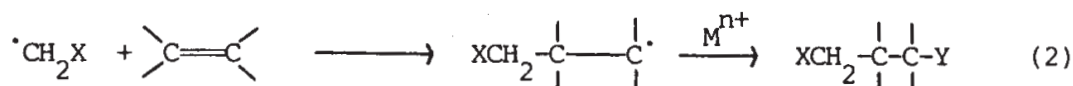
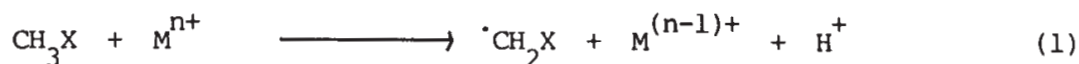
DIMETHYL ARYLMALONATES FROM CERIUM(IV) AMMONIUM NITRATE PROMOTED REACTIONS OF DIMETHYL
 MALONATE WITH AROMATIC COMPOUNDS IN METHANOL

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Summary: Aromatic compounds undergo homolytic malonylation by reaction with cerium(IV) ammonium nitrate and dimethyl malonate in methanol at room temperature.

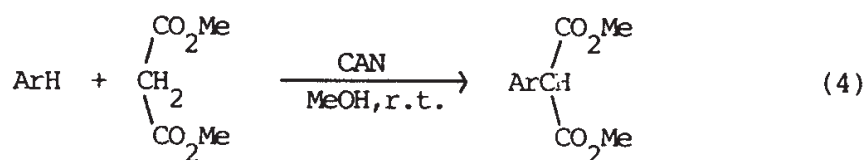
It is well known that electrophilic carbon radicals like $\cdot\text{CH}_2\text{X}$ and $\cdot\text{CHXY}$ (X and Y electron-withdrawing groups, i.e. COR, NO_2 , CO_2R , CN), generated by reactions of CH_3X and CH_2XY species with metal ions, like Mn^{+3} or Ce^{+4} , which are one electron oxidants (eq. 1), can react with alkenes or aromatic hydrocarbons to give addition and substitution products as shown in eqs. 2 and 3, respectively.¹ (Y is a ligand of the metal or the conjugate base of the solvent).



So far the reactions involving addition of $\cdot\text{CH}_2\text{X}$ and $\cdot\text{CHXY}$ to alkenes are those which have more intensively been investigated and results of great synthetic interest have recently been obtained.²

In contrast, less information is available concerning the reactions of electrophilic carbon radicals to aromatic compounds. The available data in this respect concern homolytic aromatic substitutions promoted by the radicals $\cdot\text{CH}_2\text{COCH}_3$ ³, $\cdot\text{CH}_2\text{NO}_2$ ⁴ and $\cdot\text{CH}_2\text{CO}_2\text{H}$ ^{1b,c} generated via oxidation of acetone, nitromethane and acetic acid, respectively, with Mn(III) or Ce(IV) salts.

In this note we now report on the first example of aromatic malonylation, which can be brought about with fair to good yields and under very mild conditions when cerium(IV) ammonium nitrate (CAN) is reacted with dimethyl malonate in the presence of aromatic compounds in MeOH. (eq. 4).



The aromatic compound (5-10 mmol), CAN (1 mmol), dimethyl malonate (5 mmol) are dissolved in 50 ml of MeOH and the mixture is allowed to stand at room temperature until disappearance of the CAN colour (about 30 min). The reaction mixture is worked up as usual and the arylmalonates are obtained after removal under vacuum of unreacted dimethyl malonate and aromatic compound. The results obtained (yields and, for toluene and anisole, isomeric distributions) are reported in the Table.

Table. Formation of Dimethyl Arylmalonates from the Reaction of Aromatic Compounds with Dimethyl Malonate Promoted by Cerium(IV) Ammonium Nitrate in MeOH.

Aromatic Compound	Yields of Arylmalonates, % ^a	Isomeric Distribution		
		<u>ortho</u>	<u>meta</u>	<u>para</u>
Benzene	53			
Toluene ^b	59	50.8	21.4	27.8
Anisole ^b	87	82.3	1.7	16.0
Chlorobenzene ^c	33	50	50 (<u>meta</u> + <u>para</u>)	
Mesitylene	66			
Naphthalene	50	α-isomer		

(a) Yield of isolated product calculated with respect to reacted CAN by assuming a 2:1 CAN:ArH stoichiometry.

(b) Isomeric distribution determined by v.p.c. analysis of the mixture of isomeric methyl arylacetates (comparison with authentic specimens) obtained by decarboxymethylation of the crude reaction product.

(c) Isomeric distribution estimated by the PMR spectrum of the crude reaction product. Since the signals of benzylic CH of meta- and para-chlorophenylmalonate coincide, only the overall percent of meta and para isomer is given.

The highest yield is obtained with anisole, the lowest with chlorobenzene and this is in line with $\cdot\text{CH}(\text{CO}_2\text{Me})_2$ being an electrophilic radical. The electrophilic character of $\cdot\text{CH}(\text{CO}_2\text{Me})_2$ has also been demonstrated by relative rate measurements (competitive experiments⁵) which have shown that the overall reactivity of anisole is 7.3 times larger than that of toluene. This value is significantly larger than that (2.3) determined for the reaction with $\cdot\text{CH}_2\text{COCH}_3$ ^{3b},

thus indicating that two carbomethoxy groups are more effective than a single CH_3CO group in determining the electrophilic character of an alkyl radical.

The greater sensitivity of $\cdot\text{CH}(\text{CO}_2\text{Me})$ than of $\cdot\text{CH}_2\text{COCH}_3$ to the effects of electron donating substituents is also shown by the isomeric distributions observed in the reactions of toluene and anisole. With toluene the para/meta isomeric ratio is 1.3 with the former radical and 0.7 with the second. The corresponding values with anisole are 9.4 and 5. Thus, with both the methyl and the methoxy group (+R substituents) the more electrophilic radical affords the higher percent of para isomer.

In spite of the larger steric requirements of $\cdot\text{CH}(\text{CO}_2\text{Me})_2$ with respect to $\cdot\text{CH}_2\text{COCH}_3$, the two radicals do not exhibit very important differences in the sensitivity to steric effects. With anisole the percents of ortho isomer are very similar: 84.3 with $\cdot\text{CH}_2\text{COCH}_3$ and 82.3 with $\cdot\text{CH}(\text{CO}_2\text{Me})_2$. With toluene a somewhat more marked decrease is observed: from 66.0 with the former radical to 50.8 with the second.

The not great significance of steric effects in the reactions of $\cdot\text{CH}(\text{CO}_2\text{Me})_2$ is also shown by the easy malonylation of mesitylene.

The synthetic scope of the reaction (4) is greatly widened by the facile conversion of arylmalonates to arylacetic acids. Accordingly, as reported in note b of the Table, it was convenient to determine the isomeric distribution in the reactions of anisole and toluene by analysis of the mixture of arylacetates obtained by decarboxymethylation of dimethyl arylmalonates in NaCl-wet DMSO.⁶ Moreover, electrochemical regeneration of Ce(IV) is possible⁷ and this might open the way to a Cerium(IV)-mediated electrochemical synthesis of arylmalonates.⁸ Work in this direction is in progress in our laboratory.

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References and notes

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5. A mixture of anisole (10 mmol) and toluene (20 mmol) has been reacted with diethyl malonate (5 mmol) and CAN (1 mmol). The relative yield of anisyl- and tolyl-malonates has been determined in the reaction product (after removing the excess of aromatics) by NMR (integration of signals at δ 3.80 and δ 2.33, aromatic OCH_3 and CH_3 groups, respectively). In this experiment dimethyl malonate has been replaced by diethyl malonate since with the former there is overlapping of the NMR signals of the aromatic OCH_3 group of anisyl-malonates with those of CO_2CH_3 groups of both anisyl- and tolyl-malonates.
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