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Reactions between Furfurylidenemalonic Esters and Grignard Reagents II. 1,4-, 1,6-, and 1,8-Additions of *t*-Butylmagnesium Chloride to Diethyl Furfurylidenemalonate

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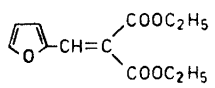
When the primary reaction products formed when *t*-butylmagnesium chloride reacts with diethyl furfurylidenemalonate are decomposed with dilute hydrochloric acid, a reduction product (diethyl furfurylmalonate) and 1,6- and 1,8-addition products (dihydrofuran derivatives) are formed besides the 1,4-addition product (diethyl 1-(2-furyl)-propylmalonate). However, the 1,8-addition product immediately rearranges prototropically to diethyl 5-*t*-butylfurfurylmalonate. The 1,6-addition products are more stable, but they also rearrange to diethyl 3-*t*-butylfurfurylmalonate on standing in an acid ether solution.

It has previously been demonstrated that 1,4-addition products and, in some cases, reduction products are formed when diethyl furfurylidenemalonate (I) reacts with simple aliphatic Grignard reagents.[1] When benzylmagnesium chloride is employed, both a 1,4-addition product and a 1,8-addition product are primarily formed. However, the latter, a 2,5-dihydrofuran derivative, immediately rearranges prototropically to diethyl 5-benzylfurfurylmalonate when the magnesium-containing reaction products are decomposed in dilute aqueous acid.

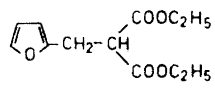
The present paper deals with the reactions between *t*-butylmagnesium chloride and diethyl furfurylidenemalonate (I). Gas chromatographic analysis of the products of the reactions on a column containing OV-17 as the stationary phase showed that five compounds had formed. Attempts to separate them by classical methods or by adsorption chromatography on bentonite and aluminium oxide were not successful. They were therefore identified by comparing their mass spectra obtained with a combined gas chromatograph/mass spectrometer with each other and with mass spectra of known or synthetized compounds.

The compound with the shortest retention time (compound A) proved to be diethyl furfurylmalonate (II) because the mass spectra and retention times of these compounds were identical.

The compound with the next shortest retention time (compound B) was identified as diethyl 2,2-dimethyl-1-(2-furyl)-propylmalonate (III) by comparison of its mass spectrum with the spectra of homologous compounds (see the interpretation in the experimental part). The conclusion is supported



I



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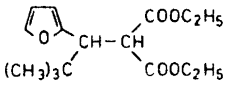
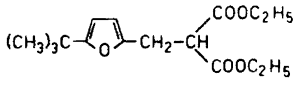


III



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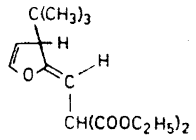
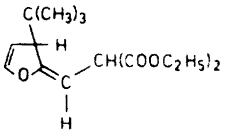


V



VI

by the fact that diethyl malonate and the chloride obtained from 2,2-dimethyl-1-(2-furyl)propanol-1 and thionyl chloride react to give a compound with a mass spectrum identical with that of compound B. This compound is accordingly a 1,4-addition product of *t*-butylmagnesium chloride to diethyl furfurylidenemalonate.

The third compound (C) had the same retention time as diethyl 5-*t*-butylfurfurylmalonate (IV). The identity of these compounds was further confirmed by their identical mass spectra. Compound C is accordingly formed by a 1,8-addition of the Grignard reagent to the unsaturated ester followed by a prototropical rearrangement of the primary reaction product. The reaction mechanisms are, of course, analogous to those which lead to the formation of diethyl 5-benzylfurfurylmalonate from benzylmagnesium chloride and diethyl furfurylidenemalonate.[1]

The mass spectra of the two remaining compounds (D and E) were practically identical. When an ether solution of the reaction products to which a small quantity of sulphuric acid had been added was stored for some time, the gas chromatogram showed that the two not yet identified compounds had disappeared and a new compound (F) had formed. The mass spectra of the three compounds showed that their molecular ions have equal masses. Further, the mass spectrum of compound F and that of diethyl 5-*t*-butylfurfurylmalonate (IV) were not identical, although clearly of the same type. Because a 1,6-addition is possible besides 1,4- and 1,8-additions, the best explanation of these facts is that compounds D and E are geometrical isomers with the structures V and VI. These compounds were transformed by the action of

hydrogen ions into diethyl 3-*t*-butylfurfurylmalonate (VII). The reaction mechanism of this prototropical rearrangement is analogous to that of the formation of the 5-butyl isomer above.

The molar ratios of the compounds A, B, C, D, and E in the reaction mixture calculated from the peak areas in the gas chromatograms and the structures of the compounds are 8 : 48 : 21 : 11 : 12. After the rearrangement of compounds D and E, the ratios of the compounds A, B, C, and F were 7 : 49 : 23 : 21. These data clearly show that compounds D and E are transformed into compound F. Further the ratios of the reduction product and the 1,4-, 1,6-, and 1,8-addition products are about 4 : 24 : 11 : 11.

EXPERIMENTAL

The reactions between t-*butylmagnesium chloride and diethyl furfurylidenemalonate.* The experiments were performed on a semimicro scale exactly according to the previously described method.[1-3] The reaction products were analysed by gas chromatography (column 1/8″ × 1.8 m, stationary phase 1 % OV-17, nitrogen flow rate 28 ml/min, initial temperature 100°, linear programming 10°/min). Five peaks with the relative retention times 1.00 (compound A), 1.21 (compound B), 1.26 (compound C), 1.42 (compound D), and 1.46 (compound E) were obtained. The compounds in the reaction mixture were stable. A gas chromatogram of a reaction mixture that had been stored for one month was identical with that first obtained. The mass spectra of the compounds were taken on a combined gas chromatograph/mass spectrometer (LKB 9000). The most important ions in these spectra are collected in Table 1.

The reaction products from one experiment were dissolved in about 30 ml of ether and a small quantity of sulphuric acid was added. After one week, the ether solution was shaken first with water and then with an aqueous solution of sodium hydrogen carbonate. The gas chromatogram showed now four peaks with the retention times (relative to that of compound A) 1.00 (compound A′), 1.21 (compound B′), 1.26 (compound C′), and 1.33 (compound F). The mass spectra of the compounds and the retention times revealed that the compounds A, B, and C were identical with the compounds A′, B′, and C′, respectively. The most important ions in the mass spectrum of compound F are listed in Table 1.

*Diethyl 5-*t*-butylfurfurylmalonate* (IV). Methyl 5-*t*-butylfuroate was reduced to 5-*t*-butylfurfuryl alcohol, which was transformed into the corresponding chloride. This chloride was used to introduce the 5-*t*-butylfurfuryl group into diethyl malonate.

Methyl 5-*t*-butylfuroate, b.p. 105 – 106°/12 mmHg, was prepared from methyl furoate and *t*-butyl chloride according to Gilman and Calloway.[4] The ester was reduced with lithium aluminium hydride in the usual way.[5] However, in all experiments, before all the ester had been added, a semi-solid doughy substance, probably an aluminium or lithium alcoholate, precipitated. This apparently prevented the reaction from proceeding to completion and the product was consequently heavily contaminated by unreduced ester. This ester was removed by alkaline hydrolysis and the butylfurfuryl alcohol extracted with ether. From 39.8 g of methyl 5-*t*-butylfuroate and 12.9 g of lithium aluminium hydride, 11.6 g (34 %) of 5-*t*-butylfurfuryl alcohol, b.p. 89 – 90°/8 mmHg, was obtained after a reduction time of 10 h. NMR spectrum: two furan protons gave an AB system at τ 3.98 and 4.20, $J = 3.3$ Hz; two methylene protons a doublet at τ 5.62 coupled to the hydroxy proton, $J = 4$ Hz; one hydroxy proton a very ill-defined triplet at τ 6.80; nine methyl protons a singlet at τ 8.77. On irradiation at the frequency of the hydroxy proton, the methylene signal was transferred into a singlet.

5-*t*-Butylfurfuryl alcohol was transformed into 5-*t*-butylfurfuryl chloride by the method which Kirner [6] used for the preparation of furfuryl chloride from furfuryl alcohol. The yield of pure substance, b.p. 75°10 mmHg, was 37 %.

This chloride (6.61 g), diethyl malonate (5.85 g), sodium (0.88 h), and dry ethanol (30 ml) were used in a malonic ester synthesis performed in the usual way.[7] The gas chromatographic analysis of the reaction products showed that three compounds were present.

Table 1. Abundances of important ions in the mass spectra of the compounds B, C, D, E, and F.

m/e	Abundance in the spectrum of compound					Type of ion
	B	C	D	E	F	
297	1	4	–	–	5	$(M+1)^+$
296	4	24	1	1	27	$M^{+\cdot}$
282	–	15	–	–	–	
281	1	87	1	1	14	$(M-CH_3)^+$
251	4	6	–	–	–	$(M-OC_2H_5)^+$
241	6	–	3	3	–	
240	41	2	21	20	1	$(M-C_4H_8)^{+\cdot}$
239	2	–	2	1	–	$(M-C_4H_9)^+$
223	–	5	–	–	16	$(M-73)^+$ X[a]
222	1	20	1	1	85	$(M-74)^+$ XI
208	–	12	–	–	6	
207	–	81	1	2	42	
187	2	–	2	2	3	
188	–	–	–	–	24	
180	–	3	–	–	1	
179	1	12	1	–	6	
167	27	3	41	37	12	
166	100	7	100	100	4	$(M-130)^{+\cdot}$, *e.g.* XII
139	11	5	15	13	6	
138	19	12	20	19	12	
137	31	100	3	4	100	$(M-159)^+$, *e.g.* VIII, IX
122	7	13	5	5	17	
121	48	54	51	47	78	$(Furyl\text{-}CH=CH-CO)^+$
95	6	9	2	3	11	
94	10	3	13	14	3	
82	2	2	2	2	2	
81	11	5	8	8	6	$(Furyl\text{-}CH_2)^+$
58	2	1	3	6	1	
57	37	19	51	51	28	$t\text{-}C_4H_9^+$

[a] The abundances of these ions decrease to 2 % for compound C and 4 % for compound F, if the abundances of the ^{13}C isomers of the ions at *m/e* 222 are observed.

The product with the shortest retention time was 5-*t*-butylfurtyryl ethyl ether. Mass spectrum: $M^{+\cdot}$ at *m/e* 182, calc. 182, rel. abund. 30.5 %; $(M+1)^+$ at *m/e* 183, rel. abund. 3.8 %, calc. 3.7 %; $(M-CH_3)^+$ at *m/e* 167, base peak; $(M-OC_2H_5)^+$ at *m/e* 137, rel. abund. 38 %; readily identified ions with high abundances at *m/e* 57, 45, 43, and 29.

The compound with the longest retention time was apparently diethyl di(5-*t*-butylfurfuryl)malonate. Mass spectrum: $M^{+\cdot}$ at *m/e* 432, calc. 432, rel. abund. 14.8 %; $(M+1)^+$ at *m/e* 433, rel. abund. 4.3 %, calc. 4.0 %; $(M-CH_3)^+$ at *m/e* 417, rel. abund. 3.0 %; $(M-COOC_2H_5)^+$ at *m/e* 359, rel. abund. 5.8 %; $(M-5\text{-}t\text{-butylfurfuryl})^+$ at *m/e* 295, rel. abund. 7.9 %; unknown ion at *m/e* 245, rel. abund. 94 %; $(5\text{-}t\text{-butylfurfuryl})^+$ at *m/e* 137, base peak; readily identified ions with high abundances at *m/e* 45, 29, 28, and 15.

The main product, which had a retention time between those of the above products, was isolated by repeated distillation under reduced pressure, finally in a Todd distillation assembly. The pure substance, diethyl 5-*t*-butylfurfurylmalonate (IV), came over a 107°/1 mmHg. (Found: C 64.93; H 8.20. Calc. for $C_{16}H_{24}O_5$: C 64.84; H 8.16.) The NMR spectrum (*cf.* Table 2) confirms the structure.

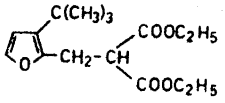
Table 2. Chemical shifts (τ) and coupling constants (J) in the NMR spectrum of diethyl 5-*t*-butylfurfurylmalonate.

Proton(s)	τ	Spin system	J in Hz
a	6.44	AB_2	7.9
b	6.87		
c and d	4.20, 4.28	AB	3.3
e	8.77	–	–
f	5.88	AX	7.1
g	8.77		

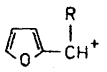
Diethyl 2,2-dimethyl-1-(2-furyl)propylmalonate (III). An attempt was made to prepare this ester by the method used to prepare diethyl 5-*t*-butylfurfurylmalonate by substituting 2,2-dimethyl-1-(2-furyl)propanol-1[8] for 5-*t*-butylfurfuryl alcohol. Gas chromatography revealed that the reaction products consisted of three compounds. The mass spectrum of the third compound ($M^{+\cdot}$ at m/e 296) is discussed below. Attempts to isolate this compound in the pure state were not successful.

Identification of the products of the reaction between t-butylmagnesium chloride and diethyl furfurylidenemalonate. Compound A and diethyl furfurylmalonate (II) had the same retention time and identical mass spectra. Compound A was thus a reduction product.

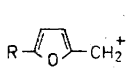
Compound C was identified as diethyl 5-*t*-butylfurfurylmalonate (IV) because both compounds had the same retention times and identical mass spectra. Substance C was thus a prototropically rearranged 1,8-addition product.



VII



VIII



IX

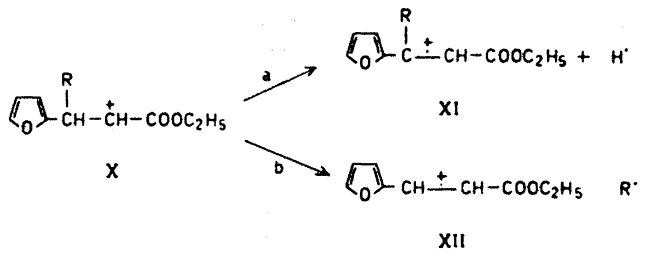
It is necessary to discuss the mass spectra of diethyl 5-*t*-butylfurfurylmalonate and the substituted malonates presented in Part I[1] before the compounds B and F can be identified.

In Part I it was established that the ions $(M-159)^+$ are important fission products of the molecular ions of furyl substituted malonates. These ions consist of the substituent attached to the central carbon atom of the malonate. It was also pointed out that the relative abundances of these ions decrease with increasing size of the group R if the ions are of the type VIII ($R \neq H$).

Diethyl furfurylmalonate, diethyl 5-benzylfurfurylmalonate, and diethyl 5-*t*-butylfurfurylmalonate give ions of type IX ($R = H$, $C_6H_5CH_2$, and $(CH_3)_3C$, respectively) in the corresponding fission reactions. The abundances of these ions are 100 %.

In Part I it was also showed that another series of fragmentation reactions of the molecular ions leads to the formation of ions of type X, which are not stable, but decompose either by reaction *a* to ions of type XI, *i.e.* $(M-74)^{+\cdot}$, and hydrogen atoms or by reaction *b* to the ion XII (m/e 166) and alkyl radicals. In both cases the fragmentation does not come to a stop but proceeds with loss of ethoxy radicals. If R is methyl or ethyl, reaction *a* predominates, but with increasing size of the substituent R, reaction *a* is suppressed and reaction *b* gains in importance.

Diethyl furfurylmalonate and its 5-benzyl and 5-*t*-butyl substituted derivatives undergo the fragmentation reaction *a*. Reaction *b* cannot occur when the substituent is attached to the furan nucleus.



Against this background, the abundances of some ions in the mass spectrum of diethyl 2,2-dimethyl-1-(2-furyl)propylmalonate (III) can easily be predicted. Thus, the ion $(M-159)^+$ should have a relatively low, but not extremely low abundance. Further, the ions formed in the fragmentation reaction *b* should be very abundant, whereas those formed in reaction *a* should have low abundances.

When the question which of the compounds B, D, E, and F is diethyl 2,2-dimethyl-1-(2-furyl)propylmalonate (III) is to be answered, the compounds D and E must first be excluded because they undergo a prototropic rearrangement which diethyl 2,2-dimethyl-1-(2-furyl)propylmalonate cannot be expected to do. The remaining compounds, B and F, have very different mass spectra and it is easily established that only the mass spectrum of compound B complies with the above predictions. This implies that compound B is diethyl 2,2-dimethyl-1-(2-furyl)-propylmalonate (III). This conclusion is strongly supported by the fact that compound B and the unisolated compound from the attempt to prepare diethyl 2,2-dimethyl-1-(2-furyl)propylmalonate have the same retention times and identical mass spectra.

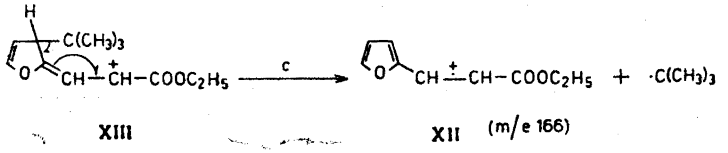
The only fact that might contradict this result is the presence of the abundant ion at *m/e* 240 because this was not detected in the spectra of the malonic esters in Part I. The ion in question had apparently been formed by loss of the *t*-butyl group of the molecular ion as an isobutylene molecule. It is quite understandable that such a reaction occurs more easily than, for example, the formation of a propylene molecule from a compound with an isopropyl substituent.

The spectrum of compound F resembles, but is not identical with the spectrum of diethyl 5-*t*-butylfurfurylmalonate. This fact implies that the *t*-butyl group of compound F is bound to the furan nucleus. Because the only possible isomer is that with the substituent in position 3, compound F seems to be diethyl 3-*t*-butylfurfurylmalonate (VII).

The two remaining compounds, D and E, rearrange to diethyl 3-*t*-butylfurfurylmalonate. Their mass spectra are almost identical. These facts and their formation in the reaction between *t*-butylmagnesium chloride and furfurylidenemalonic ester suggest that they have the structures V and VI.

The mass spectra of the compounds D and E are very similar to the spectrum of diethyl 2,2-dimethyl-1-(2-furyl)propylmalonate (compound B). The most important differences are found in the abundances of the ions at *m/e* 137. The very low abundances of these ions in the spectra of the compounds D and E show that the *t*-butyl group must be bound otherwise than in compound B.

The formation of the ions at *m/e* 166 in the spectra of the compounds D and E is easily explained by the fragmentation of the ion XIII according to reaction c. The ion XIII originates in the molecular ion which first loses an ethoxy radical and then a carbon



monoxide molecule. The formation of the ions at *m/e* 240 from the molecular ion of the compounds D and E by loss of an isobutylene molecule is understandable.

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