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Reactions of Organometallic Compounds with Conjugated Enol Ethers: Synthesis of β-Arylacrylates, Diarylmethylmalonates and Analogous Compounds

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It has been reported earlier that the addition of enol ether such as ethoxymethylenemalonic ester (EMME) to aryl Grignard reagents at the ether reflux temperature leads to the formation of symmetrical diarylmethylmalonates in good yields. In order to get the mono-conjugate addition products, *i. e.*, the corresponding acrylates, the Grignard reaction was studied at lower temperatures, and the desired acrylates were obtained, as expected.

The temperature effect was studied by using 1-naphthylmagnesium bromide as the organometallic compound. At −50 to −60°C as well as at −10 to −14°C, diethyl 1-naphthylmethylenemalonate was obtained in 31.5% and 26.6% yield respectively. However, at 8 to 10°C both the acrylate as well as the second conjugate addition product were isolated indicating that higher temperatures promote the second conjugate addition. Phenyllithium when reacted with EMME at −50 to −60°C also gave the acrylate in 22.2% yield. The analogous compounds *i. e.* ethoxymethyleneacetoacetate and ethoxymethyleneacetylacetone, when reacted with Grignard reagents gave even at ether reflux temperature only the respective acrylates and not the double conjugate addition products.

In contrast to aryl Grignard reagents, benzylmagnesium chloride gave both the addition compounds at ether reflux temperature. The acrylate when further reacted with phenylmagnesium bromide at 0°C gave 1,2-diphenylethylmalonate, a product of second conjugate addition which was hydrolysed to a known acid.[1] The reaction of benzylmagnesium chloride with ethoxymethylenecyanoacetate and ethoxymethylenemalononitrile gave only the second conjugate addition products in over 50% yield and not the acrylates as in the above case.

Thus the conjugate addition reaction seems to depend on the structure of both organometallic compound as well as the conjugated enol ether.

Experimental

The reactions of Grignard reagents with these enol ethers were carried out by the normal procedure[2]

1) S. D. Gupte and S. V. Sunthankar, *J. Org. Chem.*, **24**, 1334 (1959).
2) E. Knoevenagel, *Ber.*, **31**, 31 (1898).

TABLE 1. PRODUCTS OF THE REACTION OF GRIGNARD REAGENTS WITH CONJUGATED ENOL ETHERS

Grignard reagent (Reaction temp.)	Enol ether $EtOCH{=}CR^1R^2$	Product $R^3CH{=}CR^1R^2$ ($R^3R^4CH\text{-}CHR^1R^2$)	Molecular formula	Yield %	Bp °C/mmHg (Mp °C) (Crystn. Solv.)	Anal. C% Found (Calcd)	H% Found (Calcd)	N% Found (Calcd)	Cl% Found (Calcd)
PhMgBr (−50 to −60°C)	$R^1{=}R^2{=}COOEt$	$R^1{=}R^2{=}COOEt$ $R^3{=}Ph$	$C_{14}H_{16}O_4$	50.5	105—110/0.0125 lit.*1 163—170/5	67.90 (67.73)	7.00 (6.50)		
α-Naph.MgBr (−50 to −60°C)	$R^1{=}R^2{=}COOEt$	$R^3{=}\alpha$-Naph.	$C_{18}H_{18}O_4$	31.5	140—145/0.004 lit.*2 203—205/2	71.90 (72.46)	7.42 (6.08)		
(−10−14°C)		$R^3{=}\alpha$-Naph.		26.6					
(8 to 10°C)		$R^3{=}\alpha$-Naph.		21.9					
		($R^3{=}R^4{=}\alpha$-Naph)	$C_{28}H_{26}O_4$	28.2	(112—113) (lit.*2 113—114)	78.30 (78.85)	5.90 (6.14)		
At ether reflux temp									
$PhCH_2MgCl$	$R^1{=}R^2{=}COOEt$	$R^3{=}PhCH_2$	$C_{15}H_{18}O_4$	19.4	110—115/0.003	68.20 (68.68)	6.70 (6.92)		
		($R^3{=}R^4{=}PhCH_2$)	$C_{22}H_{26}O_4$	57.7	150—155/0.006	74.30 (74.55)	7.10 (7.40)		
o-$ClC_6H_4CH_2$-Mg Br	$R^1{=}R^2{=}COOEt$	$R^3{=}o$-$ClC_6H_4CH_2$	$C_{15}H_{17}O_4Cl$	31	120—125/0.01	60.50 (60.71)	6.10 (5.73)		12.60 (11.98)
		($R^3{=}R^4{=}o$-Cl $C_6H_4CH_2$)	$C_{22}H_{24}O_4Cl_2$	57	160—165/0.02	62.20 (62.41)	6.00 (5.67)		17.00 (16.78)
p-ClC_6H_4-CH_2MgBr	$R^1{=}R^2{=}COOEt$	$R^3{=}p$-$ClC_6H_4CH_2$	$C_{15}H_{17}O_4Cl$	22	125—130/0.009	61.20 (60.71)	5.90 (5.73)		12.80 (11.98)
		($R^3{=}R^4{=}p$-Cl $C_6H_4CH_2$)	$C_{22}H_{24}O_4Cl_2$	62	(52—53) (methanol)	62.30 (62.41)	5.50 (5.67)		17.10 (16.78)
PhMgBr	$R^1{=}COCH_3$ $R^2{=}COOEt$	$R^1{=}COCH_3$ $R^2{=}COOEt$ $R^3{=}Ph$	$C_{13}H_{14}O_3$	39.4	90— 95/0.025 lit.*3 189—191/15	71.00 (71.54)	6.92 (6.47)		
$PhCH_2MgCl$	$R^1{=}COCH_3$ $R^2{=}COOEt$	$R^3{=}PhCH_2$	$C_{14}H_{16}O_3$	47.2	95—100/0.02	72.70 (72.39)	7.20 (6.94)		
α-Naph.MgBr	$R^1{=}COCH_3$ $R^2{=}COOEt$	$R^3{=}\alpha$-Naph.	$C_{17}H_{16}O_3$	38.7	135—140/0.007	76.70 (76.10)	5.80 (6.01)		
C_6H_5MgBr	$R^1{=}R^2{=}COCH_3$	$R_3{=}Ph$	$C_{12}H_{12}O_2$	10.1	90— 95/0.002 lit.*4 180—185/15	76.10 (76.57)	6.60 (6.43)		
$PhCH_2MgCl$	$R^1{=}COOEt$ $R^2{=}CN$	($R^1{=}COOEt$ $R^2{=}CN$) $R^3{=}R^4{=}PhCH_2$	$C_{20}OH_{21}NO_2$	58.8	155—160/0.002	78.50 (78.14)	6.82 (6.89)		
$PhCH_2MgCl$	$R^1{=}R^2{=}CN$	($R^1{=}R^2{=}CN$ $R^3{=}R^4{=}PhCH_2$)	$C_{18}H_{16}N_2$	53.8	(111) (ethanol)	83.10 (83.04)	6.13 (6.20)		
o-$ClC_6H_4CH_2$-MgBr	$R^1{=}R^2{=}CN$	($R^1{=}R^2{=}CN$ $R^3{=}R^4{=}oClC_6H_4CH_2$)-	$C_{18}H_{14}N_2Cl_2$	52	(122—3) (ethanol)	65.20 (65.65)	4.10 (4.25)	8.10 (8.51)	

*1 El. Ahmadi, I. Heiba and C. Anderson, *J. Am. Chem. Soc.*, **81**. 1119 (1959).
*2 M. S. Newman and D. Lednicer, *ibid.*, **78**, 4765 (1956).
*3 G. Casimir, *Ann. Chim.* (*Paris*), **7**, 807, (1962).
*4 E. Knoevenagel and R. Werner, *Liebig's Ann.*, **281**, (1894).

at suitable temperatures. The experiment given below will serve as an example.

Diethyl (1,2-Diphenylethyl)-malonate. To a filtered solution of phenylmagnesium bromide (from magnesium 0.7 g and bromobenzene 3.925 g) cooled in ice bath was added a solution of diethyl benzylmethylenemalonate (5.24 g) in ether (25 m*l*). The reaction mixture was stirred for 3 hr. After the usual work up the product was purified by fractional distillation at temperature 140—150°C/0.004 mmHg.

Found: C, 74.50; H, 7.50%. Calcd for $C_{21}H_{24}O_4$: C, 74.09; H, 7.11%.

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