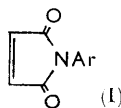


363. Action of Grignard Reagents on Heterocyclic Compounds. Part VI.¹ Action of Grignard Reagents on *N*-Arylmaleimides and Allied Compounds

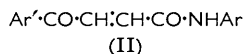
By W. I. AWAD, F. G. BADDAR, M. A. OMARA, and S. M. A. R. OMRAN

N-Arylmaleimides give, with Grignard reagents, β -aroyl-*N*-arylacrylamides (II). Azido-*N*-arylsuccinimides, however, most probably give β -arylamino- β -aroyl-*N*-arylpropionamides. The structure assigned to these compounds is inferred from the fact that the ultraviolet spectrum of compound (IVa) is identical with that of the product of interaction of aniline with β -benzoyl-*N*-phenylacrylamide (*inter alia*). Aziridine compounds (VII) react with Grignard reagents to give compounds to which structures (VIII) or (IX) are assigned. The structures of the above compounds are supported by ultraviolet and infrared spectra.

A STUDY of the stability of *N*-arylmaleimides towards Grignard reagents was needed in the investigation of the action of Grignard reagents on α -azido-*N*-arylsuccinimides and the corresponding aziridines.² As far as we are aware the only imides which have been subjected to the action of Grignard reagents are phthalimides.³ In the case of *N*-ethylphthalimide the reaction took place by addition to the carbonyl group and formation of substituted phthalimidines.⁴



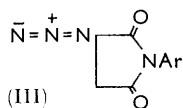
- a: Ar = Ph
 b: Ar = *p*-C₆H₄·Me
 c: Ar = *p*-C₆H₄·OMe
 d: Ar = *p*-C₆H₄Cl



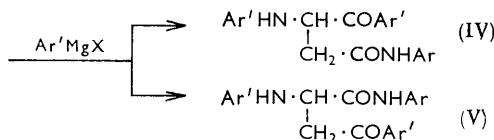
- a: Ar = Ph, Ar' = Ph
 b: Ar = Ph, Ar' = *p*-C₆H₄·Me
 c: Ar = *p*-C₆H₄·Me, Ar' = Ph
 d: Ar = *p*-C₆H₄·OMe, Ar' = Ph
 e: Ar = *p*-C₆H₄Cl, Ar' = Ph

When *N*-arylmaleimides (I), however, were treated with Grignard reagents, ring-opening took place in all cases, with the formation of β -aroyl-*N*-arylacrylamides (II), in good yield (cf. Table 2).

The structure of compounds (IIa, c, d, and e) was established by their identity with authentic specimens prepared by interaction of β -benzoylacryloyl chloride with the appropriate amine. Furthermore the infrared spectra of these compounds showed both C=O and N-H stretching frequencies (Table 2).



(III)



- a: Ar = Ph
 b: Ar = *p*-C₆H₄·Me
 c: Ar = *p*-C₆H₄Cl
 d: Ar = *p*-C₆H₄·OMe

- Ar' Ar'
 a: Ph Ph
 b: Ph *p*-C₆H₄·Me
 c: *p*-C₆H₄·Me Ph
 d: *p*-C₆H₄Cl Ph
 e: *p*-C₆H₄Cl CH₂Ph
 f: *p*-C₆H₄Cl *p*-C₆H₄·Me
 g: *p*-C₆H₄·OMe Ph
 h: *p*-C₆H₄·OMe CH₂Ph
 i: *p*-C₆H₄·OMe *p*-C₆H₄·Me

It is known⁵ that organic azides react with Grignard reagents to give triazines. When azido-*N*-arylsuccinimides (III), however, reacted with Grignard reagents, the reaction proceeded by another route, namely addition of two molecules of arylmagnesium halide

¹ Part V, Awad, Hafez, and Gadalleh, *J. Org. Chem.*, 1962, **26**, 1050.

² Awad, Omran, and Naguib, *Tetrahedron*, 1963, **19**, 1591.

³ Beis, *Compt. rend.*, 1904, **138**, 987.

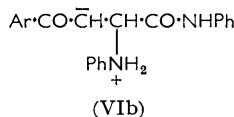
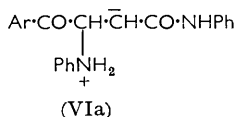
⁴ Sachs and Ludwig, *Ber.*, 1904, **37**, 385.

⁵ Kharasch and Reinmuth, "Grignard Reactions of Nonmetallic Substances," Prentice-Hall, New York, 1954, p. 1226.

and elimination of a molecule of nitrogen to give β - (IV) or α -arylamino- β -aroyl-*N*-arylpropionamides (V). Both these structures are supported by the infrared spectra which revealed the presence of the N-H and C=O stretching frequencies (Table 3).

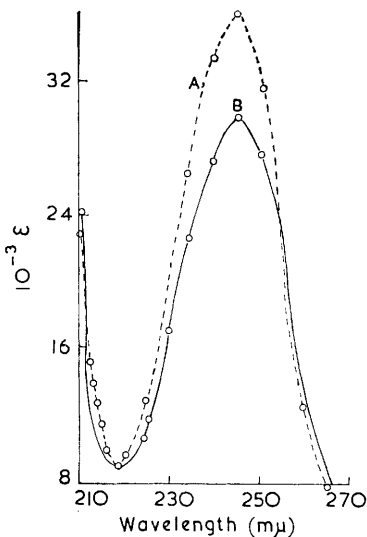
Attempts to prepare an authentic specimen of (IVa) by the addition of aniline to compound (IIa) gave rise to a product, m. p. 145°, which was different from the corresponding Grignard product, m. p. 218°.

However, the identity of their analytical data and ultraviolet spectra (see Figure) suggests that the two may be isomeric. Structure (Va) is assigned to the product, m. p. 145°, since it is formed by way of the carbanion (VIb), which is more stable than (VIa). This is due to the fact that the carbanionic portion in (VIb) is conjugated with a carbonyl group, whereas in (VIa) it is conjugated with an anilide group. Accordingly, the isomeric Grignard product is more probably represented by structure (IVa).

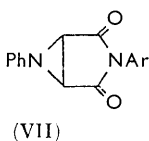


Another attempt to prepare an authentic sample of (IVa) by the interaction of anilino-*N*-phenylsuccinimide with phenylmagnesium bromide gave mainly anilino-*N*-phenylmaleimide, identified by m. p. and mixed ² m. p.

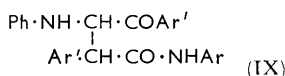
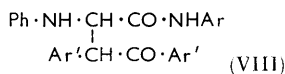
Ultraviolet spectra of A, compound (Va);
B, compound (IVa)



A study of the action of Grignard reagents on the aziridines ² (VII) gave products to which structures (VIII) or (IX) were assigned on the basis of analytical data and infrared spectra, which revealed the presence of N-H and C=O stretching frequencies (Table 4). The present data, however, does not enable us to differentiate between the two possible structures (VIII) or (IX).



- a: Ar = Ph
- b: Ar = *p*-C₆H₄Cl
- c: Ar = *p*-C₆H₄Me



- | Ar | Ar' |
|---|--|
| a: Ph | Ph |
| b: Ph | CH ₂ Ph |
| c: Ph | <i>o</i> -C ₆ H ₄ Me |
| d: <i>p</i> -C ₆ H ₄ Cl | Ph |
| e: <i>p</i> -C ₆ H ₄ Cl | <i>p</i> -C ₆ H ₄ Me |
| f: <i>p</i> -C ₆ H ₄ Cl | <i>o</i> -C ₆ H ₄ Me |
| g: <i>p</i> -C ₆ H ₄ Me | Ph |

The identity of compounds (IVa, c, d, and f) was established by the similarity of their ultraviolet spectra (Table 1). The absorption, λ_{max} 245 m μ (ϵ 29,950), of compound (IVa) may be the summation of the absorptions of the three isolated chromophores [aniline, λ_{max} 230 m μ (ϵ 7000);⁶ acetophenone, λ_{max} 241.5 m μ (ϵ 16,250); acetanilide, λ_{max} 238 m μ (ϵ 13,000)⁷ total ϵ 36,230]. The difference in the value of ϵ may be due to interaction of the three chromophores. The hypochromic effect observed for compound (VIIIa) or (IXa), as compared with (IVa), may be due to steric interference of the phenyl group with the anilino-group, as shown by Dreiding models.

The similarity in the structure of the compounds (VIII) or (IX), obtained by the action of Grignard reagents on aziridines, was inferred from the fact that these compounds have identical ultraviolet spectra (Table 1).

TABLE 1

| Ultraviolet spectral data | | | | |
|---------------------------|-----------------------------------|----------------|-----------------------------------|------------|
| Compound | λ_{max} (m μ) | ϵ | λ_{min} (m μ) | ϵ |
| (IVa) | 245 | 29,950 | 218 | 9189 |
| (IVc) | 246 | 29,420 | 220 | 10,650 |
| (IVd) | 247 | 29,520 | 221 | 9082 |
| (IVf) | 248 | 32,510 | 222 | 12,830 |
| (VIIIa) or (IXa) | 250, ~225—230 | 15,590, 16,410 | 240 | 4850 |
| (VIIIg) or (IXg) | 252, ~227—230 | 17,860, 17,360 | 240 | 15,730 |
| (VIIId) or (IXd) | 256 | 19,110 | 238 | 13,940 |
| (VIIIe) or (IXe) | 256, ~220—225 | 20,250, 25,310 | 240 | 15,200 |
| (Va) | 245 | 35,730 | 218 | 9072 |

~ = inflexion.

EXPERIMENTAL

Ultraviolet (in ethanol) and infrared (KBr disc) spectra were measured on Perkin-Elmer Spectracord model 4000A and Infracord model 137 spectrophotometers, respectively. M. p.s are not corrected. Analyses were carried out by Alfred Bernhardt, Max-Planck Institute, Mulheim, Germany.

Action of Grignard Reagents on N-Arylmaleimides (I).—A solution of the Grignard reagent (0.02 mole) in ether (30 ml.) was added slowly with continuous shaking to a solution of the *N*-arylmaleimide (0.01 mole) in benzene (50 ml.). The mixture was heated on a water-bath for 3 hr., left overnight at 25—30°, and decomposed by a cold saturated solution of ammonium chloride. The ether-benzene was separated, dried (Na₂SO₄), and evaporated. The residual oil was solidified by repeated trituration with light petroleum (b. p. 50—70°) and the *product* (Table 2) crystallised from a suitable solvent.

TABLE 2

| β -Aroyl- <i>N</i> -arylacrylamides | | | | | | | | | | | |
|---|--------------|----------|-----------|------|------|---|--------------|------|------|----------------------------|------------------|
| Com- pound | Yield (%) | M. p. | Found (%) | | | Formula | Required (%) | | | ν (cm. ⁻¹) | |
| | | | C | H | N | | C | H | N | N-H | C=O |
| (IIa) | 80 | 143° | 77.1 | 5.2 | 5.6 | C ₁₆ H ₁₃ NO ₂ | 76.45 | 5.2 | 5.55 | 3333 | 1680 |
| (IIb) | 87 | 190—191* | 77.45 | 5.6 | 5.45 | C ₁₇ H ₁₅ NO ₂ | 76.95 | 5.7 | 5.3 | 3333 | 1681, 1645 |
| (IIc) | 87 | 168* | 77.25 | 5.65 | 5.5 | C ₁₇ H ₁₅ NO ₂ | 76.95 | 5.7 | 5.3 | 3400 | 1680(m), 1660 |
| (IId) | 50 | 164† | 72.8 | 5.55 | 5.6 | C ₁₇ H ₁₅ NO ₃ | 72.6 | 5.35 | 5.0 | 3400 | 1650 |
| (IIe) | 80 | 202† | 67.45 | 4.15 | 4.95 | C ₁₆ H ₁₂ ClNO ₂ ‡ | 67.25 | 4.2 | 4.9 | 3400 | 1650 |

* From benzene. † From toluene. ‡ Found: Cl, 12.65; required: Cl, 12.4%.

*Preparation of β -Benzoyl-*N*-phenylacrylamide (IIa).*—A solution of aniline (2 g.) in ether (20 ml.) was added dropwise with continuous shaking to a solution of β -benzoylacryloyl chloride [from β -benzoylacrylic acid (1.7 g.) and phosphorus pentachloride (2 g.)]⁸ in ether (20 ml.).

⁶ Gillam and Stern, "An Introduction to Electronic Absorption Spectroscopy in Organic Chemistry," Methuen, London, 1954, pp. 126, 229.

⁷ Suzuki, *J. Chem. Phys.*, 1960, **32**, 1706.

⁸ Lutz, *J. Amer. Chem. Soc.*, 1930, **52**, 3405.

The yellow precipitate was filtered off, washed with sodium carbonate solution and warm water, and crystallised from benzene–light petroleum (b. p. 60–80°). The product so obtained gave no depression on admixture with that obtained by Grignard reaction.

Under similar conditions, *p*-toluidine (2.1 g.), *p*-anisidine (2.4 g.), and *p*-chloroaniline (2.5 g.), gave, respectively, compounds (IIc–e), identified by mixed m. p.

Action of Grignard Reagents on Azido-N-arylsuccinimides (III).—The Grignard reagent (0.028 mole) in ether (30 ml.) was added slowly with continuous shaking to a solution of the azido-*N*-arylsuccinimide (0.007 mole) in benzene (50 ml.). The mixture was heated on a water-bath for 3 hr., left overnight at room temperature, and worked up as usual. The ether–benzene layer was separated, dried (Na₂SO₄), and evaporated. The residual oil was solidified by trituration with light petroleum (b. p. 50–70) and the product (Table 3) crystallised from a suitable solvent.

Addition of Aniline to β-Benzoyl-N-phenylacrylamide.⁹—A mixture of (IIa) (0.8 g.) and freshly distilled aniline (3 g.) was heated gently on a water-bath for 3 hr. until solution was complete. The violet solution was cooled in ice and the precipitated was filtered off, washed with a little ether, and crystallised from ethanol to give *α*-anilino-β-benzoyl-*N*-phenylpropionamide (0.8 g.), m. p. 145° (Found: C, 76.75; H, 5.95; N, 8.25. C₂₂H₂₀O₂N₂ requires C, 76.7; H, 5.85; N, 8.15%).

Action of Phenylmagnesium Bromide on Anilino-N-phenylsuccinimide.¹⁰—A solution of phenylmagnesium bromide [from bromobenzene (2.4 g.) in ether (20 ml.) and magnesium (0.4 g., 0.08 mole)] was added to a hot solution of anilino-*N*-phenylsuccinimide (1.3 g., 0.02 mole) in benzene (100 ml.). The mixture was heated for 3 hr. on a boiling-water bath, left

TABLE 3
β-Arylamino-β-aroyle-*N*-arylpropionamides

| Compound | Yield (%) | M. p. | Found (%) | | | Formula | Required (%) | | | ν (cm. ⁻¹) | |
|----------|-----------|------------|-----------|------|------|---|--------------|------|------|------------------------|------|
| | | | C | H | N | | C | H | N | N·H | C=O |
| (IVa) | 65 | 218° * | 76.7 | 5.95 | 8.4 | C ₂₂ H ₂₀ N ₂ O ₂ | 76.7 | 5.85 | 8.15 | 3410 | 1667 |
| (IVb) | 65 | 239 * | | | 7.4 | C ₂₄ H ₂₄ N ₂ O ₂ | | | 7.5 | 3333 | 1640 |
| (IVc) | 65 | 212 * | 76.45 | 6.15 | 8.05 | C ₂₃ H ₂₂ N ₂ O ₂ | 77.05 | 6.2 | 7.8 | 3333 | 1640 |
| (IVd) | 70 | 220–221 * | 69.55 | 5.1 | 7.2 | C ₂₂ H ₁₉ ClN ₂ O ₂ † | 69.7 | 5.05 | 7.4 | 3333 | 1660 |
| (IVe) | 70 | 200 * | 71.15 | 5.8 | 6.55 | C ₂₄ H ₂₃ ClN ₂ O ₂ ‡ | 70.85 | 5.7 | 6.9 | 3333 | 1650 |
| (IVf) | 75 | 212 * | 70.75 | 5.65 | 6.75 | C ₂₄ H ₂₃ ClN ₂ O ₂ § | 70.85 | 5.7 | 6.9 | 3333 | 1650 |
| (IVg) | 65 | 217 ¶ | 73.1 | 5.85 | 7.65 | C ₂₃ H ₂₂ N ₂ O ₂ ¶ | 73.8 | 5.9 | 7.5 | 3333 | 1657 |
| (IVh) | 60 | 195–196 ¶¶ | 73.95 | 6.35 | 7.2 | C ₂₅ H ₂₆ N ₂ O ₃ ¶¶ | 74.6 | 6.5 | 6.95 | 3380 | 1660 |
| (IVi) | 60 | 210–211 ¶¶ | 74.5 | 6.35 | 6.45 | C ₂₅ H ₂₆ N ₂ O ₃ ** | 74.6 | 6.5 | 6.95 | 3333 | 1650 |

* From benzene. † Found: Cl, 9.3; requires Cl, 9.35%. ‡ Found: Cl, 8.35; requires Cl, 8.7%. § Found: Cl, 9.0; requires Cl, 8.7%. ¶ From xylene. ¶¶ From toluene. ** Found: OMe, 7.65; requires OMe, 7.7%.

TABLE 4

| Compound | Yield (%) | M. p. | Found (%) | | | Formula | Calc. (%) | | | ν (cm. ⁻¹) | |
|------------------|-----------|-----------|-----------|------|------|---|-----------|------|------|------------------------|--------|
| | | | C | H | N | | C | H | N | N·H | ** C=O |
| (VIIIa) or (IXa) | 94 | 207° * | 79.8 | 5.9 | 6.85 | C ₂₈ H ₂₄ N ₂ O ₂ | 79.95 | 5.75 | 6.65 | 3333 | 1667 |
| (VIIIb) or (IXb) | 93 | 108 * | 80.3 | 6.1 | 6.45 | C ₃₀ H ₂₆ N ₂ O ₂ | 80.35 | 6.3 | 6.25 | 3380 | 1650 |
| (VIIIc) or (IXc) | 90 | 190 * | 80.3 | 6.25 | 6.3 | C ₃₀ H ₂₈ N ₂ O ₂ | 80.35 | 6.3 | 6.25 | 3450, | 1650 |
| | | | | | | | | | | 3333 | |
| (VIIId) or (IXd) | 83 | 203 * | 74.45 | 5.1 | 5.9 | C ₂₈ H ₂₃ ClN ₂ O ₂ † | 73.95 | 5.1 | 6.15 | 3333 | 1650 |
| (VIIIe) or (IXe) | 92 | 129 ‡ | 74.0 | 5.8 | 5.9 | C ₃₀ H ₂₇ ClN ₂ O ₂ § | 74.6 | 5.65 | 5.8 | 3333 | 1667 |
| (VIIIf) or (IXf) | 83 | 203–204 ‡ | 74.15 | 5.8 | 5.8 | C ₃₀ H ₂₇ ClN ₂ O ₂ ¶ | 74.6 | 5.65 | 5.8 | 3400 | 1640 |
| (VIIIg) or (IXg) | 90 | 209–210 ‡ | 79.65 | 6.05 | 6.7 | C ₂₈ H ₂₆ N ₂ O ₂ | 80.15 | 6.05 | 6.45 | 3333 | 1660 |

* From benzene. † Found: Cl, 7.75. Calc. Cl, 7.8%. ‡ From ethanol. § Found: Cl, 7.5. Calc. Cl, 7.35%. ¶ Found: Cl, 7.7%. ** Another weak band at about 3600 cm.⁻¹ appeared in CHCl₃ probably due to enolic OH.

overnight, and worked up as usual. The product (1 g.) was crystallised from toluene to give anilino-*N*-phenylmaleimide, m. p. 230, undepressed on admixture with an authentic specimen.¹

Action of Grignard Reagents on Aziridine-N-arylmalimide (VIII).²—The solution of the

⁹ Bougault, *Ann. Chim. Phys.*, 1908, [8], 15, 509.

¹⁰ Tingle and Bates, *J. Amer. Chem. Soc.*, 1909, 31, 1239.

Grignard reagent (0.08 mole) in ether (20 ml.) was added slowly with continuous shaking to a solution of aziridine-*N*-arylmaleimide (0.02 mole) in benzene (50 ml.), heated on a water-bath for 4 hr., left overnight, and the mixture worked up as usual. The ether-benzene layer was separated, dried (Na_2SO_4), evaporated to dryness, and the product (Table 4) crystallised from a suitable solvent.

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