

652. *Cyclohexane-1,3-diones. Part VII.*¹ *Reaction of 3-Methoxy-2,4-diphenylcyclohex-2-en-1-one with Acetone Cyanohydrin.*

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The study of the displacement of an alkoxy group by a cyano-group by use of acetone cyanohydrin has now been extended to the enol ethers of unsymmetrically substituted cyclohexane-1,3-diones. 3-Cyano-2,4- and 3-cyano-2,6-diphenylcyclohex-2-enone were both obtained from 2,4-diphenylcyclohexane-1,3-dione and their structures were elucidated. Dehydrogenation of these cyano-ketones and related compounds afforded several new *m*-terphenyls substituted in the central ring.

IN previous parts^{1,2} it has been shown that the enol ethers of 2-arylcycloalkane-1,3-diones react with acetone cyanohydrin to give the corresponding β -cyano-ketone. An unsymmetrically substituted compound such as 2,4-diphenylcyclohexane-1,3-dione (I), capable of giving rise to two enol ethers (IIa) and (IIb), should afford two corresponding cyano-ketones (IIIa) and (IIIb). It was hoped that the study of these compounds would afford more information about the exchange reaction.

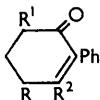
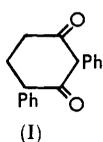
2,4-Diphenylcyclohexane-1,3-dione (I) was prepared³ by Robinson's modification of the Michael reaction. No crystalline enol ether was then isolated from treatment of this dione (I) with diazomethane, but reduction of the presumed mixture of isomers with lithium aluminium hydride gave, on dehydrogenation with sulphur, some 2'-hydroxy-*m*-terphenyl (Va). The action of diazomethane on the dione was re-investigated; the oil obtained gave a single enol ether, m. p. 137—138°, in 80% yield. The structure of this enol ether (IIa) or (IIb) was shown by reduction to the corresponding cyclohexenone, (IVa) or (IVb), which on dehydrogenation with sulphur gave 2'-hydroxy-*m*-terphenyl

¹ Part VI, preceding paper.

² Betts and Davey, Part V, *J.*, 1960, 1683.

³ Ames and Davey, *J.*, 1958, 1794.

(Va).⁴ This must have resulted from dehydrogenation of 2,6-diphenylcyclohex-2-en-1-one (IVa). In view of the accepted mechanism⁵ of the lithium aluminium hydride reduction of the enol ethers of cyclohexane-1,3-diones, the enol ether, m. p. 137—138°, must be 3-methoxy-2,4-diphenylcyclohex-2-en-1-one (IIa).



(IIa); R = Ph, R¹ = H, R² = OMe

(IIb); R = H, R¹ = Ph, R² = OMe

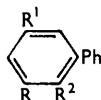
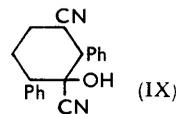
(IIIa); R = Ph, R¹ = H, R² = CN

(IIIb); R = H, R¹ = Ph, R² = CN

(IVa); R = R² = H, R¹ = Ph

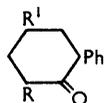
(IVb); R = Ph, R¹ = R² = H

(VI); R = H, R¹ = Ph, R² = Cl



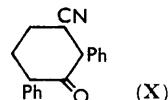
(Vb); R = H, R¹ = Ph, R² = OH

(VIII); R = Ph, R¹ = H, R² = CN



(VIIa); R = Ph, R¹ = H

(VIIb); R = H, R¹ = Ph



Treatment of the dione (I) with phosphorus trichloride afforded the chloro-compound (VI) which was hydrogenated to 2,6-diphenylcyclohexanone (VIIa), whose structure was proved by the non-identity of its oxime with that of the alternative isomer (VIIb).³ Selenium dehydrogenation of 2,6-diphenylcyclohexanone (VIIa) gave 2'-hydroxy-*m*-terphenyl (Va), whilst reaction with acetone cyanohydrin gave the corresponding cyanohydrin, which was acetylated and dehydrogenated to 2'-cyano-*m*-terphenyl (VIII).

Before examining the reaction of acetone cyanohydrin with the enol ether (IIa), we studied its reaction with the cyclohexenone (IVa); a di-adduct (IX), was the main product, and some mono-adduct (X) was also produced. The structures given were assigned on the basis of absorption spectra. There was no evidence to suggest that the di-adduct was a lactam (cf. Part V²).

The exchange of acetone cyanohydrin with 3-methoxy-2,4-diphenylcyclohex-2-en-1-one (IIa) was studied at room temperature with triethylamine as catalyst; two isomers (IIIa and IIIb) (analysis and infrared spectra), m. p.s 121° and 158°, were obtained in 33% and 27% yield, respectively. With methanolic potassium hydroxide as catalyst the yields were 27% and 24%. Differentiation between these two isomers was achieved by consideration of the methylene absorptions in the spectra of chloroform solutions. The bands at 1451 cm.⁻¹ (IIIa) and 1450 cm.⁻¹ (IIIb) are ascribed to the methylene group adjacent to the phenyl group and the additional bands at 1417 cm.⁻¹ (isomer, m. p. 158°) and 1429 cm.⁻¹ (isomer, m. p. 121°) to the systems CH₂•CO and CH₂•C=C respectively.^{6a} The isomer of m. p. 121° is therefore 3-cyano-2,4-diphenyl- (IIIa) and that of m. p. 158°, 3-cyano-2,6-diphenyl-cyclohex-2-en-1-one (IIIb). Proof was afforded by the observation that 3-cyano-2,5-diphenylcyclohex-2-en-1-one was converted by sodium hydroxide into 2'-hydroxy-*p*-terphenyl.² 3-Cyano-2,6-diphenylcyclohex-2-en-1-one (IIIb) reacted with sodium hydroxide to give 2'-hydroxy-*m*-terphenyl (Va); similarly, the isomer (IIIa) gave the isomeric 4'-hydroxy-*m*-terphenyl (Vb), m. p. 89°.⁴ Since both these isomeric cyanoketones were obtained from a single enol ether (IIa) it appears that there is no single mechanism for the exchange and that cyanide attack can occur not only at the carbon atom to which the alkoxy group is attached, but also at the carbonyl group.

Reaction of the cyano-compound (IIIb) with more acetone cyanohydrin at 90° furnished

⁴ Lüttringhaus and Saaf, *Annalen*, 1939, **542**, 241; 1945, **557**, 25.

⁵ Frank and Hall, *J. Amer. Chem. Soc.*, 1950, **72**, 1645; Blanchard and Goering, *ibid.*, 1951, **73**, 5863; Born, Pappo, and Szmuskovicz, *J.*, 1953, 1779.

⁶ Bellamy, "Infrared Spectra of Complex Molecules," Methuen, London, 1958, (a) p. 23, (b) p. 139.

H, 5.8. Calc. for $C_{18}H_{14}O$: C, 87.8; H, 5.7%). Lüttringhaus and Saaf⁴ record m. p. 101° for this isomer and m. p. 89° for the 4'-hydroxy-isomer.

1-Cyano-2,6-diphenylcyclohexan-1-ol.—13% Methanolic potassium hydroxide (0.1 c.c.) was added to 2,6-diphenylcyclohexanone (1.0 g.) in acetone cyanohydrin (10 c.c.), and the mixture was set aside overnight and then poured into water. The solid was filtered off, dried, and crystallised from ethyl acetate–light petroleum to yield the *cyano-derivative* (0.8 g.), needles, m. p. 183° (Found: C, 82.4; H, 6.8; N, 5.3. $C_{19}H_{19}NO$ requires C, 82.3; H, 6.9; N, 5.7%).

2'-Cyano-*m*-terphenyl (VIII).—1-Cyano-2,6-diphenylcyclohexan-1-ol (1.0 g.) was refluxed for 1 hr. with acetic anhydride (10 c.c.) containing one drop of concentrated sulphuric acid. The solution was poured into water (300 c.c.) and left overnight. The crude acetyl derivative thus obtained was heated at 350° for 3 hr. with selenium (1.0 g.). 2'-Cyano-*m*-terphenyl (0.4 g.) crystallised from ethanol as needles, m. p. 135° (Found: C, 88.9; H, 5.0; N, 5.4. $C_{19}H_{13}N$ requires C, 89.4; H, 5.1; N, 5.5%).

Acetone Cyanohydrin Exchange Reactions.—(i) With 2,6-diphenylcyclohex-2-en-1-one. To 2,6-diphenylcyclohex-2-en-1-one (4.4 g.) in acetone cyanohydrin (10 c.c.) was added triethylamine (0.05 c.c.) and the mixture was set aside overnight. The solution was poured into water, and the product (1.8 g.) filtered off. Fractional crystallisation from methanol gave 1,3-dicyano-2,6-diphenylcyclohexan-1-ol (1.1 g.), prisms, m. p. 228–229° (Found: C, 79.6; H, 6.2; N, 8.9. $C_{20}H_{18}N_2O$ requires C, 79.4; H, 6.0; N, 9.3%), ν_{max} . (KBr disc), 3411 (OH), 2247, and 2237 cm^{-1} (C≡N); followed by 3-cyano-2,6-diphenylcyclohexan-1-ol (0.2 g.), needles, m. p. 208–209°, from ethyl acetate–light petroleum (Found: C, 82.5; H, 6.1; N, 5.1. $C_{19}H_{17}NO$ requires C, 82.9; H, 6.2; N, 5.1%), ν_{max} . (KBr disc) at 2237 (C≡N) and 1718 cm^{-1} (C=O).

Treatment of 1,3-dicyano-2,6-diphenylcyclohexan-1-ol (0.3 g.) with acetic anhydride (5 c.c.) containing one drop of concentrated sulphuric acid gave the corresponding *acetate*, as plates, m. p. 211–212°, from ethyl acetate (Found: C, 77.0; H, 5.6; N, 8.1. $C_{22}H_{20}N_2O_2$ requires C, 76.7; H, 5.8; N, 8.1%).

(ii) With 3-methoxy-2,4-diphenylcyclohex-2-en-1-one. To the enol ether (1.0 g.) in acetone cyanohydrin (10 c.c.) was added triethylamine (0.05 c.c.). The mixture was set aside overnight and then poured into water and acidified (Congo Red). The aqueous solution was decanted, and the residual gum dissolved in hot methanol and left overnight. The solid was crystallised from ethyl acetate–light petroleum, furnishing 3-cyano-2,6-diphenylcyclohex-2-en-1-one (0.26 g., 27%), prisms, m. p. 158–159° (Found: C, 83.1; H, 5.8; N, 5.1. $C_{19}H_{15}NO$ requires C, 83.5; H, 5.5; N, 5.1%). The infrared spectrum (Nujol mull) showed bands at 2215 (conjugated C≡N), 1677 ($\alpha\beta$ -unsaturated ketone), and 1581 cm^{-1} (phenyl system). Unchanged material was recovered from attempts to prepare an oxime. After the methanolic mother-liquor had been set aside for several days a second crop of crystals was collected and recrystallised from ethyl acetate–light petroleum, yielding 3-cyano-2,4-diphenylcyclohex-2-en-1-one (0.32 g., 33%), needles, m. p. 121° (Found: C, 83.3; H, 5.8; N, 5.1%). The infrared spectrum (Nujol mull) showed bands at 2215 (conjugated C≡N), 1677 ($\alpha\beta$ -unsaturated ketone), 1599, and 1487 cm^{-1} (phenyl system). Treatment of this cyano-ketone with hydroxylamine afforded an *oxime*, needles, m. p. 237–238°, from ethanol (Found: C, 78.8; H, 5.7; N, 9.5. $C_{19}H_{16}N_2O$ requires C, 79.1; H, 5.6; N, 9.7%). When the exchange reaction was repeated with use of 13% methanolic potassium hydroxide (0.1 c.c.) as catalyst, a mixture of the two foregoing cyano-ketones (24% and 27%, respectively) was again isolated.

Action of Alkali on the Cyano-ketones.—3-Cyano-2,6-diphenylcyclohex-2-en-1-one (1.5 g.) in ethanol (70 c.c.) was refluxed with 20% aqueous sodium hydroxide (2 c.c.) for 2.5 hr. The solvent was evaporated under reduced pressure, the residue diluted with water, and the solid filtered off, dried, and extracted with light petroleum. 2'-Hydroxy-*m*-terphenyl (0.3 g.) crystallised from light petroleum as needles, m. p. and mixed m. p. 101°. This experiment was repeated with 3-cyano-2,4-diphenylcyclohex-2-en-1-one (1.5 g.), and the product was recrystallised from light petroleum, giving 4'-hydroxy-*m*-terphenyl (0.4 g.) as needles, m. p. 88.5° (Found: C, 88.2; H, 5.5. Calc. for $C_{18}H_{14}O$: C, 87.8; H, 5.7%). Lüttringhaus and Saaf⁴ give m. p. 89°.

1,5-Dicyano-2,8-diphenyl-7-azabicyclo[3,2,1]octan-6-one (XI).—3-Cyano-2,6-diphenylcyclohex-2-en-1-one (1.0 g.) in acetone cyanohydrin (10 c.c.) containing triethylamine (0.05 c.c.) was refluxed for 45 min. The solution was poured into water, and the solid collected and dried. Recrystallisation from ethyl acetate furnished the *azabicyclo-ketone* (0.2 g., 19%), prisms, 220–222° (Found: C, 76.9; H, 5.3; N, 13.2. $C_{21}H_{19}N_3O$ requires C, 76.9; H, 5.2; N, 12.8%).

The infrared spectrum (KBr disc) showed bands at 3289 (NH, fused-ring γ -lactam), 2247 (C \equiv N), 1715 (C=O; fused-ring γ -lactam), and 742 and 704 cm^{-1} (phenyl system). After several days the mother-liquor deposited unchanged cyano-ketone (0.4 g., 40%), m. p. and mixed m. p. 158°.

4-Bromo-3-cyano-2,4-diphenylcyclohex-2-en-1-one (XII).—3-Cyano-2,4-diphenylcyclohex-2-en-1-one (6.0 g.) in methanol (200 c.c.) was added to potassium borohydride (3.6 g.) in water (30 c.c.), and the mixture set aside for 5 hr. The solution was poured into water, and the semi-solid collected. All attempts to crystallise this material were unsuccessful. To this oil in dry carbon tetrachloride (100 c.c.) was added *N*-bromosuccinimide (4.2 g.) and benzoyl peroxide (0.05 g.), and the mixture was refluxed for 2 hr. The succinimide was filtered off, and the carbon tetrachloride evaporated under reduced pressure. The residual gum was triturated with benzene to yield **4-bromo-3-cyano-2,4-diphenylcyclohex-2-en-1-one** (1.2 g.), prisms, m. p. 149°, from ethyl acetate (Found: C, 64.9; H, 4.3; N, 4.0; Br, 22.6. $\text{C}_{19}\text{H}_{14}\text{BrNO}$ requires C, 64.7; H, 4.0; N, 4.0; Br, 22.7%). The infrared spectrum (KBr disc) showed bands at 2208 (conjugated C \equiv N), 1686 ($\alpha\beta$ -unsaturated ketone), and 544 cm^{-1} (C–Br).

2'-Cyano-4'-hydroxy-*m*-terphenyl (XIIIa).—The foregoing bromo-compound (1.0 g.) in dry pyridine (10 c.c.) was refluxed for 1 hr., the solution poured into dilute hydrochloric acid, and the product filtered off. **2'-Cyano-4'-hydroxy-*m*-terphenyl** crystallised from ethyl acetate–light petroleum as needles, m. p. 183° (Found: C, 83.9; H, 4.7; N, 5.2. $\text{C}_{19}\text{H}_{13}\text{NO}$ requires C, 84.1; H, 4.7; N, 5.2%).

3-Cyano-2,6-diphenylcyclohex-2-en-1-ol.—3-Cyano-2,6-diphenylcyclohex-2-en-1-one (1.6 g.) in methanol (60 c.c.) was added to potassium borohydride (1.0 g.) in water (10 c.c.). After 5 hr. the solution was poured into water, and the precipitate (1.6 g.) collected and dried. **3-Cyano-2,6-diphenylcyclohex-2-en-1-ol** (0.8 g.) crystallised from benzene–light petroleum as prisms, m. p. 113–114° (Found: C, 83.2; H, 6.3; N, 5.2. $\text{C}_{19}\text{H}_{17}\text{NO}$ requires C, 82.9; H, 6.2; N, 5.1%).

4'-Cyano-2'-hydroxy-*m*-terphenyl (XIIIb).—*N*-Bromosuccinimide (3.5 g.) and benzoyl peroxide (0.05 g.) were refluxed with 3-cyano-2,6-diphenylcyclohex-2-en-1-ol (5.0 g.) in dry carbon tetrachloride (150 c.c.) for 2 hr. The succinimide was filtered off, and the filtrate concentrated. The resulting uncrystallisable oil was refluxed for 1 hr. in dry pyridine (10 c.c.), and the solution poured into dilute hydrochloric acid. The solid was collected and crystallised from ethyl acetate to yield **4'-cyano-2'-hydroxy-*m*-terphenyl** (0.7 g.), prisms, m. p. 146° (Found: C, 84.5; H, 4.8; N, 5.6. $\text{C}_{19}\text{H}_{13}\text{NO}$ requires C, 84.1; H, 4.7; N, 5.2%).

2,4,5-Triphenylcyclohexane-1,3-dione.—To sodium (1.6 g.) in dry ethanol (100 c.c.) was added ethyl phenylacetate (8.2 g.) followed by 1,4-diphenylbut-3-en-2-one (11.1 g.), and the mixture was refluxed for 3 hr. and then set aside overnight. The solvent was evaporated, the residue diluted with water, and the remaining solid was filtered off. Acidification of the filtrate afforded **2,4,5-triphenylcyclohexane-1,3-dione** (2.7 g.), needles, m. p. 204°, from methanol (Found: C, 85.2; H, 5.7. $\text{C}_{24}\text{H}_{20}\text{O}_2$ requires C, 84.7; H, 5.9%). Use of ethyl phenylmalonate (11.8 g.) in place of ethyl phenylacetate likewise furnished the dione (0.6 g.), m. p. and mixed m. p. 204°.

3-Methoxy-2,4,5(or 2,5,6)-triphenylcyclohex-2-en-1-one.—Treatment of the dione (1.3 g.) in methanol with a slight excess of ethereal diazomethane gave a single *enol ether* (0.5 g.), prisms,

Com- pound	λ_{max} ($\text{m}\mu$)	ϵ	Com- pound	λ_{max} ($\text{m}\mu$)	ϵ	Com- pound	λ_{max} ($\text{m}\mu$)	ϵ	Com- pound	λ_{max} ($\text{m}\mu$)	ϵ
(a) <i>Products from reactions with acetone cyanohydrin</i>											
IIIa	236	11,400	XI	335	3650	IX	241	572	X	241	471
	297	5400		257	2000		246.5	587		247	514
IIIb	234	11,050		263.5	1800		251.5	687		251.5	613
	292	4200		268	1700		257	716		257.5	707
				291	1800		263	629		263.5	589
							267	429		267	405
(b) <i>Terphenyls</i>											
Va *	238	25,100	VIII	224	23,500	XIIIa	225	33,950	XIIIb	220	27,950
	295	5100		242	22,700		239	24,500		266	13,850
Vb	247	27,300		300	4900		320	8350		312	8400
	263	16,800									
	302	4200									
(c) <i>Other compounds</i>											
I	232	8600	IIa	231	9450	VI	215	14,500	XII	229	15,700
	270	12,700		271	12,850		230	11,300		306	5600
						IVa	240	8900			

* Ames and Davey³ report λ_{max} 238 (ϵ 22,200) and 295 $\text{m}\mu$ (ϵ 4820) in ethanol.

m. p. 137—138°, from methanol (Found: C, 84.5; H, 6.5; OMe, 8.2. $C_{25}H_{22}O_2$ requires C, 84.7; H, 6.3; OMe, 8.8%).

Ultraviolet Spectra.—The absorption spectra, recorded in the Table were determined for 96% ethanolic solutions with a Unicam S.P. 500 spectrophotometer. Italicised values denote inflexions.

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