salt (1.96 g). It was chromatographed on cellulose powder (320 g) using a solvent PrOH–NH_4OH–H_2O (6:3:1). Fractions of each 20 ml were collected every 15 min. Concentration of fraction Nos. 42—55, treatment with IR 120 (H^+), neutralization with $Ba(OH)_2$, evaporation of the solvent and addition of ether to the MeOH solution of the residue gave a barium salt (60 mg). Its *Rf* values of PPC and NMR spectrum showed that it was a mixture of VIII and XIII. *Anal.* Calcd. for $C_9H_{18}O_7NPBa \cdot 2H_2O$: C, 23.67; H, 4.86; N, 3.07. Found: C, 23.51; H, 4.97; N, 3.40. Fraction Nos. 95—180 were pooled and treated similarly to give the barium salt of XIV (110 mg) which was precipitated from aqueous solution with EtOH. PPC: *Rf* 0.25 (solvent A), 0.12 (solvent B). NMR δ: 0.94, 0.99 (each 3H, s, CH_3), 1.82 (2H, t, $J=6.9$ cps, H_g), 3.33 (2H, t, H_f), 3.78 (2H, m, H_a, H_b), 3.99 (2H, q, H_h), 4.00 (1H, s, H_e). *Anal.* Calcd. for $C_9H_{17}O_{10}NP_2Ba_2 \cdot 5H_2O$: N, 1.93; P, 8.54. Found: N, 2.33; P, 8,30.

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On the Double Bond Nature (endo or exo) in the Condensation Products of Cyclic Ketones with Cyanoacetate or Cyanoacetic Acid

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In 1948 in their brilliant synthesis of morphinan, Grewe, *et al.*[2] condensed ethyl 2-oxocyclohexanecarboxylate with ethyl cyanoacetate under the Cope's conditions[3] and obtained a condensation product in good yield. However, they made no mention about the nature of the double bond and the existence of isomers in their condensation product (Chart 1).

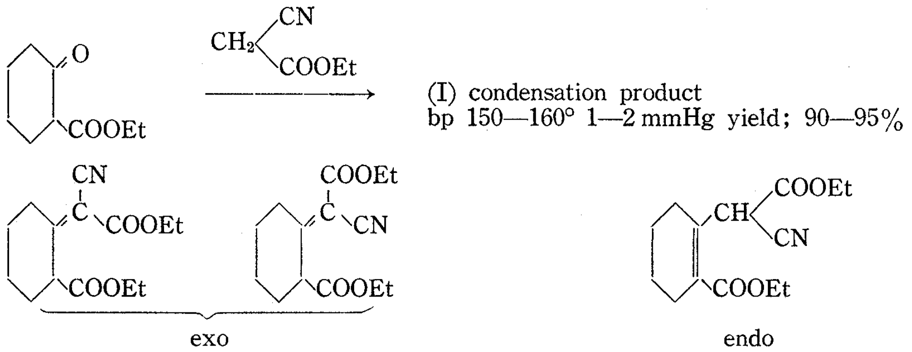

Chart 1

In simpler cases matters are rather straightforward. Thus, when cyclic ketones and cyanoacetic acid are Cope-condensed followed by decarboxylation, there are obtained in good yield unsaturated nitriles, in which the double bond is located "endo" as judged from their ultraviolet (UV) spectral data[4] (Chart 2).

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[1] Location: *a) 2-2-50 Kawagishi Toda, Saitama; b) 130 shiba shirokane-Sankocho, Minato-ku, Tokyo.*
[2] R. Grewe and A. Mondon, *Chem. Ber.*, **81**, 297 (1948).
[3] A. C. Cope, C. A. Hofmann, C. Wyckoff and E. Hordeubergh, *J. Am. Chem. Soc.*, **63**, 3452 (1941).
[4] S. Saito, *Chem. Pharm. Bull.* (Tokyo), 4, 237 (1956).

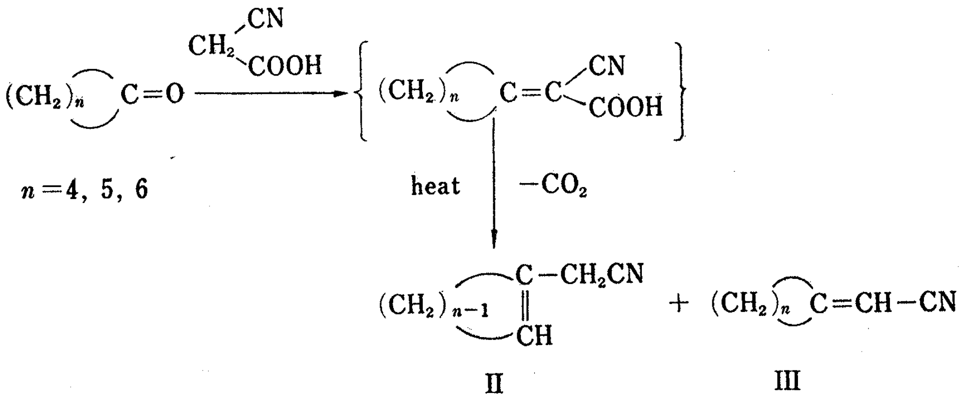

Chart 2

However, cyclic ketones and alkyl cyanoacetate after Cope's condensation yield unsaturated nitrile esters, whose double bond was proved to assume exo-position, as could be deduced by their UV spectral data (Chart 3).

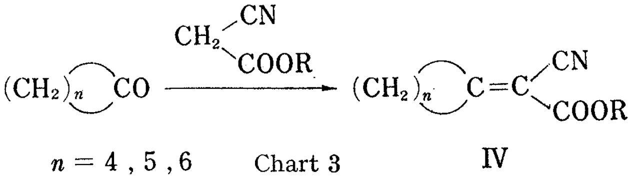

Chart 3

In the recent study of the synthesis of decahydroisoquinoline derivatives,[5] the present author made use of the comp. (I) as had been prepared by Grewe, *et al.*, and attempted to locate the double bond either by chemical or spectral means, but in vain.

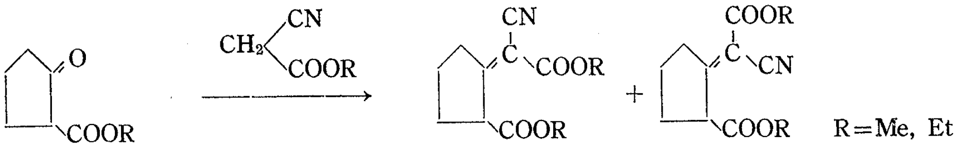

Chart 4

In the meanwhile, Kasture, *et al.*[6] condensed methyl 2-oxocyclopentanecarboxylate with methyl cyanoacetate under the Cope's conditions and they studied the nature of the duoble bond in the condensation product. From the position (wave numbers) of *ν* C≡N and

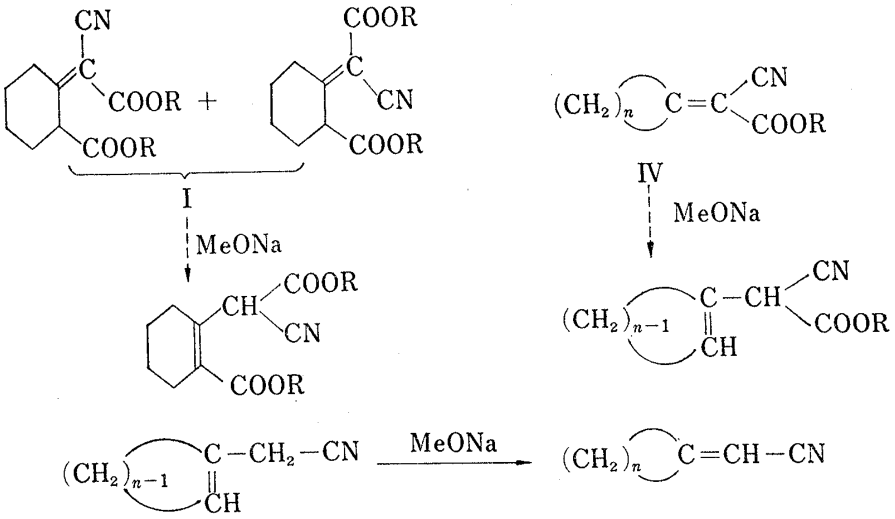

Chart 5

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5) N. Itoh, *Chem. Pharm. Bull.* (Tokyo), **16**, 455 (1968).

6) T.R. Kasture and A. Srinivasan, *Tetrahedron*, **22**, 2575 (1966).

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nuclear magnetic resonance (NMR) spectral data they concluded that the product is a mixture of the *cis*–and *trans*–isomers due to the exo–situated double bond (Chart 4).

We now applied their technique to the compounds (I, II, IV), and were able to clarify their double bond character and also some additional properties intrinsic to them.

Thus in I and IV the double bond assumes exo–position and I is a mixture of *cis*– and *trans*–isomers. Sodium alkoxide treatment dose not bring about double bond shift in these

TABLE I

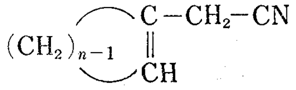
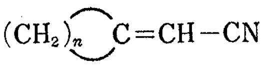
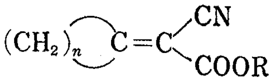
			
$n=4$	IR	ν_{CN} 2300 cm^{-1} (w)	ν_{CN} 2260 cm^{-1} (s)
		$\nu_{C=C}$ 1650 cm^{-1} (w)	$\nu_{C=C}$ 1640 cm^{-1} (s)
	NMR	(2H) 2.00 ppm (CH_2)	(4H) 1.78 ppm ($-CH_2-CH_2-$)
		(4H) 2.35 ppm $\left(\begin{matrix}-CH_2\\-CH_2\end{matrix}>C=\right)$	(4H) 2.50 ppm $\left(\begin{matrix}-CH_2\\-CH_2\end{matrix}>C=\right)$
		(2H) 3.11 ppm ($\equiv C-CH_2-CN$)	(H) 5.20 ppm $\left(\begin{matrix}=C-H\\ \vert \\ CN\end{matrix}\right)$
		(H) 5.73 ppm ($=C-H$)	
$n=5$	IR	ν_{CN} 2280 cm^{-1} (w)	ν_{CN} 2240 cm^{-1} (s)
		$\nu_{C=C}$ 1640 cm^{-1} (w)	$\nu_{C=C}$ 1633 cm^{-1} (s)
	NMR	(4H) 1.70 ppm ($-CH_2-CH_2-$)	(6H) 1.60 ppm $\{(CH_2)_3\}$
		(4H) 2.00 ppm $\left(\begin{matrix}-CH_2\\-CH_2\end{matrix}>C=\right)$	(4H) 2.37 ppm $\left(\begin{matrix}-CH_2\\-CH_2\end{matrix}>C=\right)$
		(2H) 2.91 ppm ($-CH_2-CN$)	(H) 4.95 ppm $\left(\begin{matrix}=C-H\\ \vert \\ CN\end{matrix}\right)$
		(H) 5.75 ppm ($=C-H$)	
$n=6$	IR	ν_{CN} 2280 cm^{-1} (w)	ν_{CN} 2240 cm^{-1} (s)
		$\nu_{C=C}$ 1620 cm^{-1} (w)	$\nu_{C=C}$ 1615 cm^{-1} (s)
	NMR	(6H) 1.65 ppm $\{(CH_2)_3\}$	(8H) 1.61 ppm $\{(CH_2)_4\}$
		(4H) 2.14 ppm $\left(\begin{matrix}-CH_2\\-CH_2\end{matrix}>C=\right)$	(4H) 2.55 ppm $\left(\begin{matrix}-CH_2\\-CH_2\end{matrix}>C=\right)$
		(2H) 3.04 ppm ($-CH_2-CH$)	(H) 5.15 ppm $\left(\begin{matrix}=C-H\\ \vert \\ CN\end{matrix}\right)$
		(H) 5.97 ppm ($=C-H$)	

TABLE II.



R=Et or Me

$n=4$	R=Me	IR	ν_{CN} 2250 cm^{-1}, ν_{CO} 1730 cm^{-1}, $\nu_{C=C}$ 1620 cm^{-1}
		NMR	(4H) 1.85 ppm ($-CH_2-CH_2-$)
			(4H) 2.90 ppm ($-CH_2-\overset{\Vert}{C}-CH_2-$)
			(3H) 3.80 ppm (OCH_3)
$n=5$	R=Et	IR	ν_{CN} 2250 cm^{-1}, ν_{CO} 1725 cm^{-1}, $\nu_{C=C}$ 1600 cm^{-1}
		NMR	(3H) 1.31 ppm ($-OCH_2-\underline{CH_3}$)
			(6H) 1.66 ppm $\{(CH_2)_3)\}$
			(4H) 2.78 ppm ($-CH_2-\overset{\Vert}{C}-CH_2-$)
			(2H) 4.20 ppm ($-OCH_2-$)
$n=6$	R=Et	IR	ν_{CN} 2250 cm^{-1}, ν_{CO} 1730 cm^{-1}, $\nu_{C=C}$ 1600 cm^{-1}
		NMR	(3H) 1.31 ppm ($OCH_2-\underline{CH_3}$)
			(8H) 1.60 ppm $\{(CH_2)_4\}$
			(4H) 2.85 cm^{-1} ($CH_2-\overset{\Vert}{C}-CH_2-$)
			(2H) 4.25 cm^{-1} ($-OCH_2-$)

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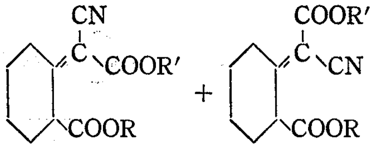
TABLE III.



R=R′=Me	IR		ν_{CN} 2250 cm^{-1}, ν_{CO} 1720 cm^{-1}, $\nu_{C=C}$ 1600 cm^{-1}
	NMR	(6H)	1.60 ppm $\{(CH_2)_3\}$
		(2H)	2.40 ppm (allyl)
		(3H)	3.65 and 3.68 ppm $(O\cdot CH_3)$
		(3H)	3.75 and 3.78 ppm $(O\cdot CH_3)$
		(H)	4.05 ppm (C–H triplet)
R=Me R′=Et	NMR	(3H)	1.27 ppm $(OCH_2\text{–}\underline{CH_3})$
		(3H)	3.75 and 3.80 ppm (OCH_3)
		(3H)	4.30 ppm $\{(H)C\text{–}H + (2H)OCH_2\}$
		(6H)	2.00 ppm $\{CH_2)_3\}$
		(2H)	3.12 ppm (allyl)

compounds. On the contrary, the comp. (II) exists mainly as cycloalkenylacetonitrile (endo double bond) contaminated with a minute amount of exo–isomer. However, on being treated with sodium alkoxide in ether the double bond shifts readily from endo– to exo–position even at room temp. (Chart 5).

Some pertinent infrared (IR) and NMR data are tabulated herein (Table I, II, III, and Fig. 1).

Experimental[7]

Ethyl Cycloalkylidenecyanoacetate (IV)——A mixture of cycloketone (0.1M), ethyl cyanoacetate (0.1M), ammonium acetate (1.0 g), glacial acetic acid (2 ml) and dry benzene (10 ml) was heated under reflux till no more water separated (6 hr). The cooled reaction mixture was washed several times with water and the benzene removed *in vacuo*. The residue was distilled *in vacuo* (Table IV).

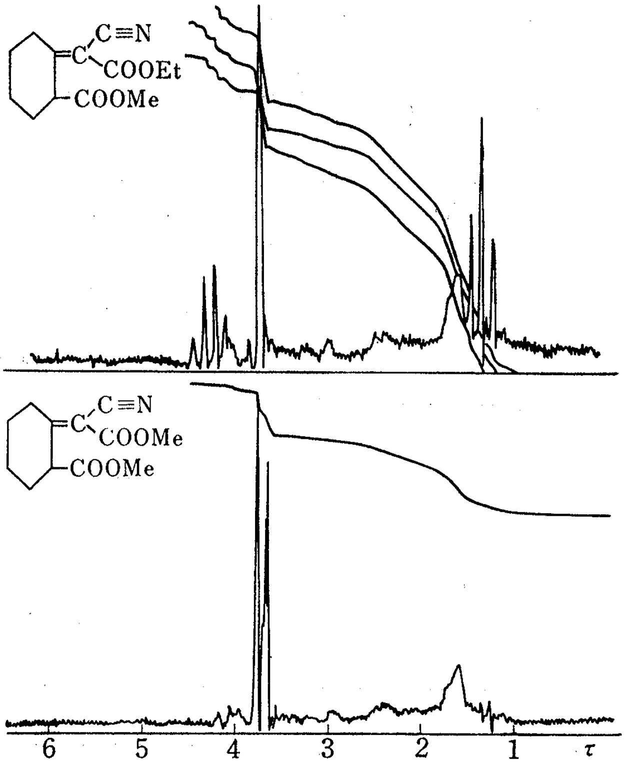


Fig. 1. Nuclear Magnetic Resonance Spectrum of I in $CDCl_3$ Solution

Alkyl 2-Methoxycarbonylcyclohexylidenecyanoacetate (I)——A mixture of alkyl cyanoacetate(0.016M), methyl 2-oxocyclohexanecarboxylate (0.016M), glacial acetic acid (0.8 ml), ammonium acetate (0.3 g), and dry benzene (3 ml) was heated under reflux till no more water separated (14 hr). The cooled reaction mixture was washed several times with 5% NaOH and H_2O, and the benzene was removed *in vacuo*. The residue was purified by distillation *in vacuo* (Table V).

Cycloalkylideneacetonitrile (III)——A mixture of cycloalkenylacetonitrile (0.01M), sodium methylate (0.02M) and dry ether (20 ml) was set aside for 24 hr at room temp.

After diluting ether, the mixture was washed with 5% HCl then with water and dried (Na_2SO_4). The solvent was removed *in vacuo* and residue distilled to give III (Table VI).

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7) All boiling points are uncorrected. IR spectra were recorded with a J.A.S.C.O. Model I.R-S. NMR spectra were taken on a Hitachi Perkin–Elmer H 60.

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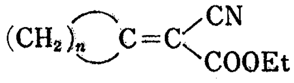
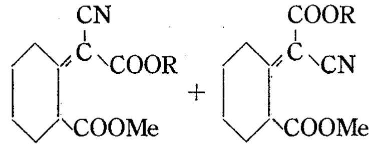
TABLE IV.



$(CH_2)_n C=C(CN)COOEt$

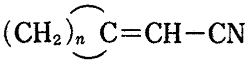
	Yield (%)	mmHg/bp (°C)	Formula	Analysis (%) Calcd. C	Calcd. H	Calcd. N	Found C	Found H	Found N
$n=4$	84	7/137—8	$C_{10}H_{13}O_2N$	67.02	7.31	7.82	66.94	7.14	7.59
$n=5$	88	7/140—141	$C_{11}H_{15}O_2N$	68.37	7.82	7.25	68.10	7.69	7.12
$n=6$	51	5/143—144	$C_{12}H_{17}O_2N$	69.54	8.27	6.76	69.33	8.33	6.70

TABLE V.



	Yield (%)	mmHg/bp (°C)	Formula	Analysis (%) Calcd. C	Calcd. H	Calcd. N	Found C	Found H	Found N
R=Me	65	2/149—154	$C_{12}H_{15}O_4N$	60.75	6.37	5.90	60.48	6.21	5.75
R=Et	71	2/150—157	$C_{13}H_{17}O_4N$	62.14	6.82	5.57	61.97	6.54	5.39

TABLE VI.



$(CH_2)_n C=CH-CN$

	Yield (%)	mmHg/bp (°C)	Formula	Analysis (%) Calcd. C	Calcd. H	Calcd. N	Found C	Found H	Found N
$n=4$	84	20/90—95	C_7H_9N	78.46	8.47	13.01	78.28	8.46	12.94
$n=5$	75	20/100—105	$C_8H_{11}N$	79.29	9.15	11.56	79.14	9.05	11.43
$n=6$	64	20/110—115	$C_9H_{13}N$	79.95	9.69	10.36	79.75	9.53	10.24

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