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ON THE GEOMETRICAL ISOMERS OF ETHYL 2-CYANO-3-ETHOXYACRYLATE

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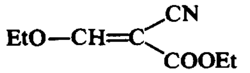
Abstract—The geometrical configuration of ethyl 2-cyano-3-ethoxyacrylate, 1, has been determined from NMR studies using the chemical-shift reagent Eu(fod)$_3$-d_{27}.

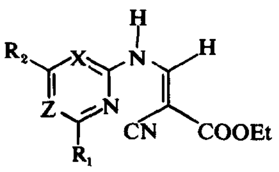
Ethyl 2-cyano-3-ethoxyacrylate, **1**, is an easily prepared[1-3] and commercially available compound, useful for the synthesis of mono-,[4,5] bi,[6,7] and tricyclic[8,9] heterocyclic systems.



$$\mathrm{EtO{-}CH{=}C}\begin{array}{l}\diagup\mathrm{CN}\\ \diagdown\mathrm{COOEt}\end{array}$$

1

In several cases it has been observed[6-8] that the condensation product of the title compound (or homologs of it) and aromatic amines contains a mixture of geometrical isomers of type **2**.



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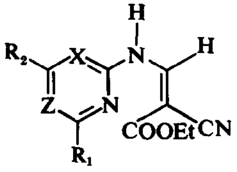
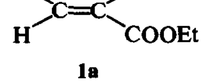
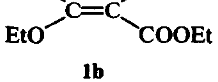


2′

It therefore seemed of interest to investigate if **1** contained a mixture of **1a** and **1b** and, if this was the case,[7] to estimate the isomer ratio and to determine which isomer had the thermodynamically more stable configuration.



1a



1b

A similar study has been reported[10] on 3-alkoxy-2-cyano-2-butenoic esters. The present communication describes the photochemical, partial conversion of one form of **1** into its thermodynamically less stable geometrical isomer and assignment of configuration for the more stable one with the help of lanthanide-shift NMR studies.

Synthetic or commercial **1**, purified by recrystallization and sublimation, seemed to contain only one geometrical isomer, since its NMR spectrum displayed one single olefinic proton signal at 8·00 ppm; the protons of the two different Et groups had almost identical chemical shifts (*cf* Fig 1).

Attempts to achieve isomer conversion of **1** by heating to *ca* 150° in dimethyl sulfoxide, in bromoform or in *o*-dichlorobenzene, or by treatment with base, or with acid were unsuccessful as judged from NMR spectra. Also exchange experiments with D$_2$O in the presence of base or acid showed none of the protons in **1** to be exchangeable in dimethyl sulfoxide or chloroform solutions.

Irradiation of a chloroform solution of **1** with a high-pressure mercury arc[11] led to a mixture of the starting material and a new compound (TLC). The NMR spectrum of the same mixture showed, in addition to the signals of the starting material, a new, identical set of signals, slightly displaced, with the olefinic proton resonance appearing at 7·40 ppm. We propose that the new product is the other geometrical isomer of **1**. The yield of rearranged material, 30%, as estimated from the integrals of the olefinic proton signals, did not change on further irradiation. Attempts to isolate the new isomer by preparative TLC proved unsuccessful, since it isomerized to the more stable form during the isolation process.

The NMR spectrum of the photoequilibrium mixture of the *E* and *Z*[12] isomers **1a** and **1b**, respectively, consisted of two sets of signals from the CH$_3$—CH$_2$—O—C=O groups and two sets of signals from the CH$_3$—CH$_2$—O— groups, in both cases almost entirely overlapping (*cf* Fig 2).

The correlation proposed by Simon *et al.*[13] for the assignment of geometrical configuration in ethylenic systems is based on a large number of model compounds. The difference in chemical shift values for the olefinic protons in **1a** and **1b** seems sufficiently large, 0·60 ppm, to obtain significant information by a comparison of the calculated and observed δ-values. The results predict (*cf* Table 1) that the more stable isomer should be represented by the *E* isomer **1a**).

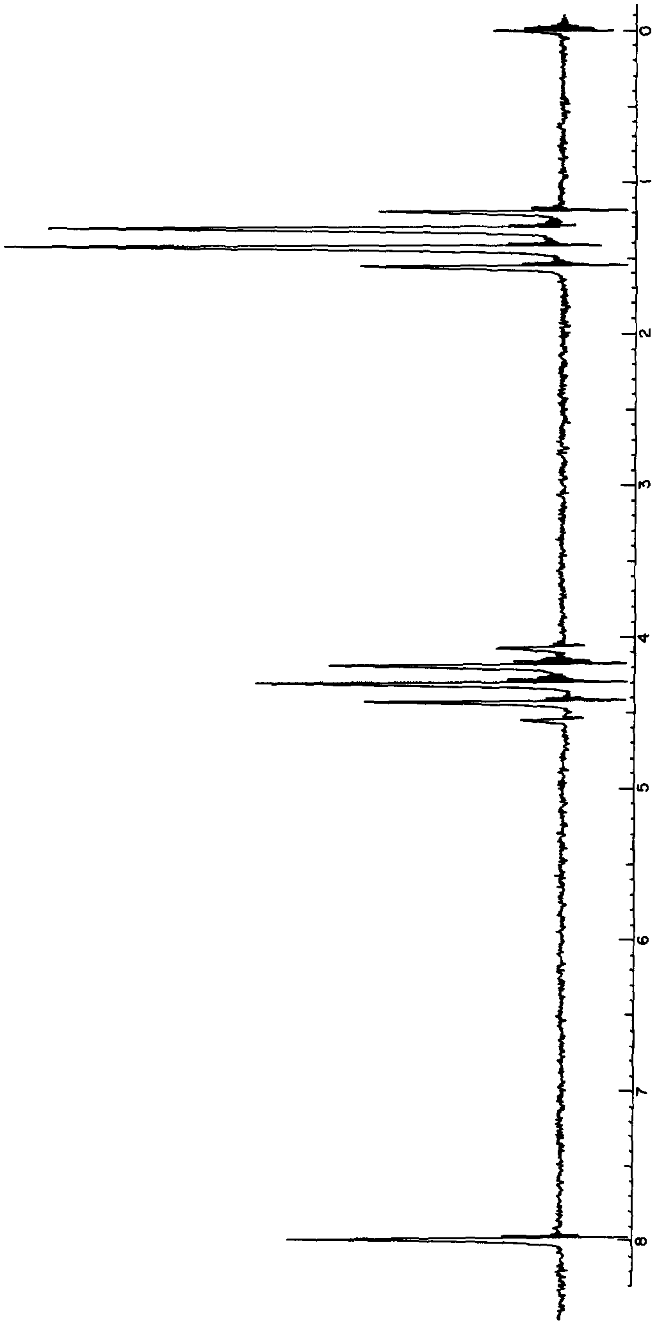


Fig 1. NMR spectrum ($CDCl_3$) of 1a.

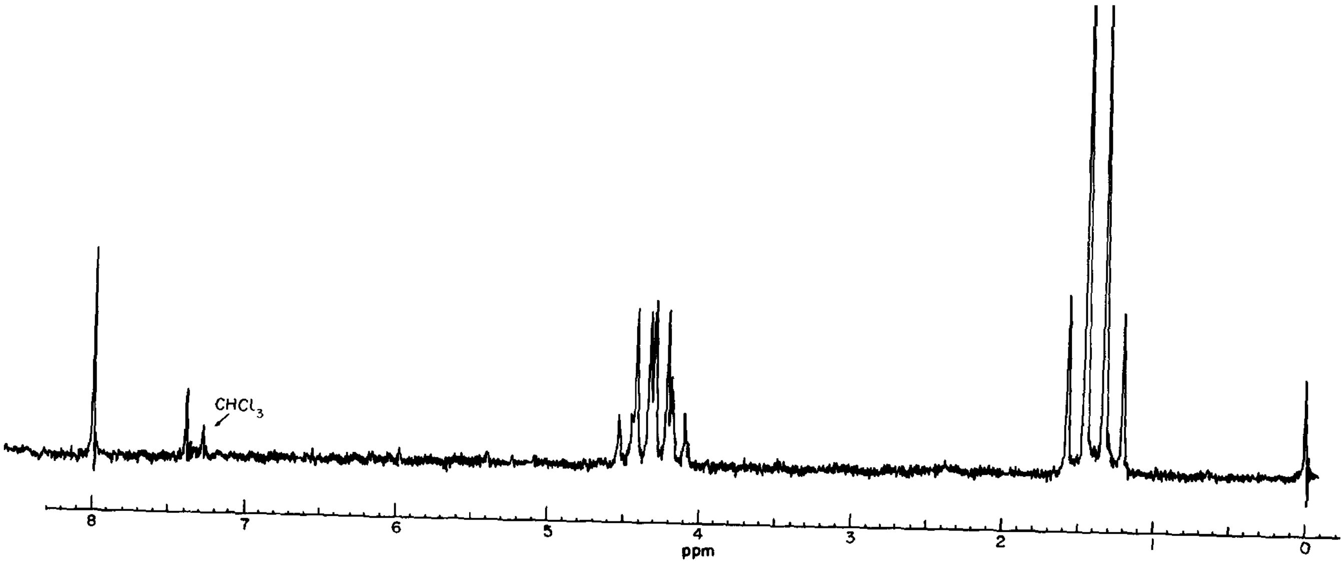


Fig 2. NMR spectrum ($CDCl_3$) of the photoequilibrium mixture of **1a** and **1b**.

Table 1. Observed (in $CDCl_3$) and calculated[13] values for the chemical shifts of the olefinic protons in the different isomers of 1 and 3

Observed		Calculated		Difference
Isomer	δ, ppm	Isomer	δ, ppm	δ, ppm
"stable"	8·00	*E*, (**1a**)	8·20	0·20
"unstable"	7·40	*Z*, (**1b**)	7·77	0·37
"stable"	7·95	*E*, (**3a**)	8·20	0·25
"unstable"	7·35	*Z*, (**3b**)	7·77	0·42

To strengthen the above conclusion we have studied the effect of $Eu(fod)_3$-d_{27}[14] on the NMR spectrum of pure **1a**. In Fig 3a the induced chemical shift for the protons are plotted against $[Eu(fod)_3]/[substrate]$, and the Δ_{Eu}-values[15] calculated from the first straight part of each curve. The original δ-values for the corresponding protons in the ethoxy and carbethoxy groups are very close (*cf* Fig 3a) and consequently the assignment of Δ_{Eu}-values was uncertain. Therefore a lower homolog of **1**, ethyl 2-cyano-3-methoxyacrylate, **3**, containing only one type of Et group, was prepared.[1] The NMR spectrum of **3**, which is in complete agreement with the assumed structure, contained only one olefinic proton signal. Its position, 7·95 ppm, is close to the one observed for the more stable isomer of the ethoxy compound, **1a**. We therefore believe that **3a** is the predominating form (*cf* Table 1).

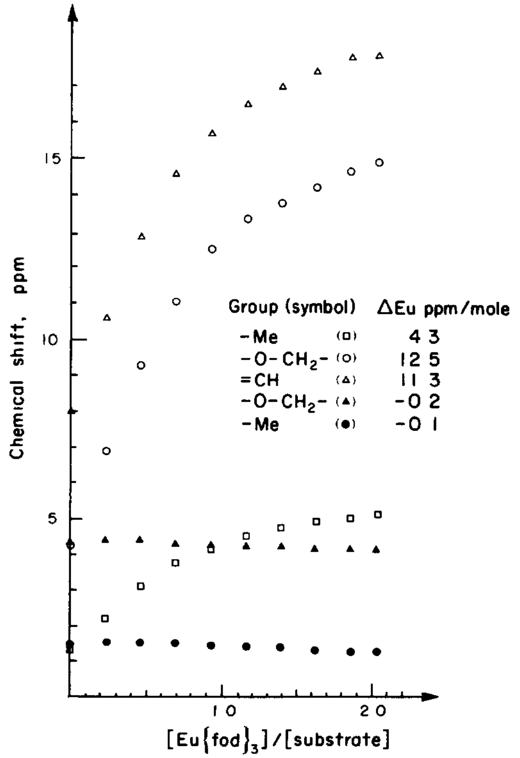


Fig 3a. Plots of the chemical shift values ($CDCl_3$) for **1a** as a function of the molar ratio [Eu(fod)]/[substrate].

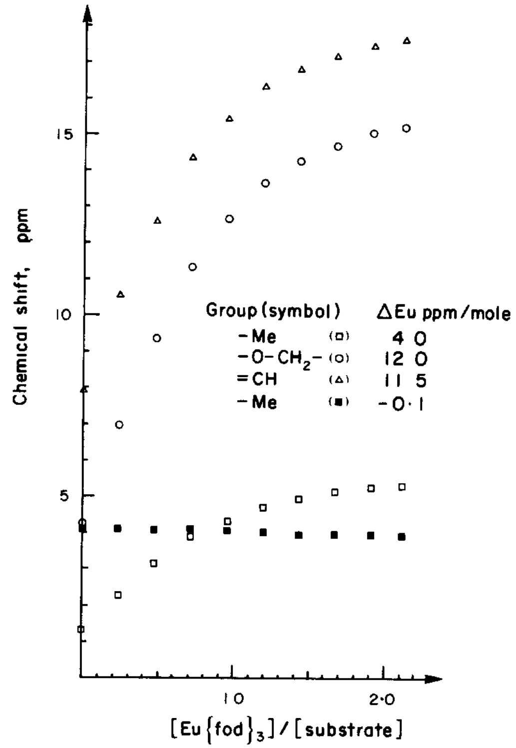
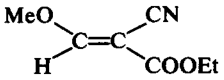
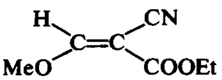


Fig 3b. Plots of the chemical shift values ($CDCl_3$) for **3a** as a function of the molar ratio $[Eu(fod)_3]/[substrate]$.



3a



3b

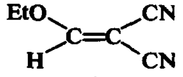
Irradiation of **3** under conditions identical with those used for **1** produced an 80 : 20 (NMR) photoequilibrium mixture of starting material and a new isomer. This compound, which easily isomerizes back to the starting material (NMR and TLC), showed an olefinic proton resonance signal at 7·35 ppm. The calculated[13] values (*cf* Table 1) predict, as was the case for **1**, that the *E* isomer **3a** represents the more stable configuration.

The effect of the shift-reagent on the NMR spectrum of **3** was studied and the results were plotted as before. The methylene protons in the carbethoxy group had a Δ_{Eu}-value of 12·0 (*cf* Fig 3b). By analogy therefore we assign the Δ_{Eu}-value of 12·5 (*cf* Fig 3a) to the carbethoxy methylene protons in **1a**.

To make configurational assignments we now need information about the site of complexation.

There are three possibilities: the cyano nitrogen, the ether oxygen, and the ester carbonyl O atom. Studies on mono-functional model compounds[16] indicate that the above order represents the progression of complexation ability. We therefore assume that, at the low concentrations of shift-reagent used here, where mononuclear complexes are predominant, co-ordination takes place only at the carbonyl oxygen atom. A *O—Eu*-distance of 2·8 Å was chosen, the distances r_i and the angles Θ_i for the protons (*cf* Fig 4) in **1a**, **1b**, **3a**, and **3b** were estimated from Dreiding models, and the observed Δ_{Eu}-values were plotted against $(3\cos^2\Theta_i - 1)\cdot r_i^{-3}$.[17] A straight line is obtained for the *E*-forms **1a** and **3a** (*cf* Fig 5a), while no correlation can be observed for the corresponding *Z*-configurations (*cf* Fig 5b). We therefore conclude that **1a** and **3a** are the thermodynamically more stable isomers.

The correctness of the assumption that co-ordination takes place exclusively at the carbonyl oxygen atom is indirectly supported by an identical study on 2-cyano-3-ethoxyacrylonitrile, **4**. Here the very low Δ_{Eu}-values (*cf* Fig 6) indicate that no appreciable complexation occurs at the ethoxy oxygen or at the cyano groups.



4

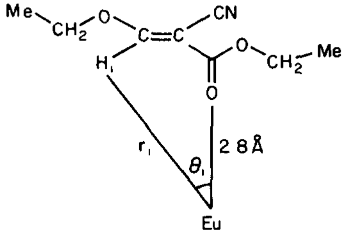


Fig 4. Model of the *E* configuration of **1** (and **3**).

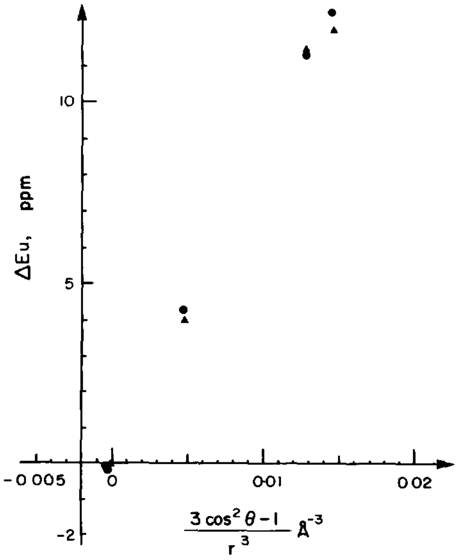


Fig 5a. Plots of the Δ_{eu}-values for the *E* configurations of **1** (●) and **3** (▲) as a function of $(3\cos^2\Theta - 1)\cdot r^{-3}$.

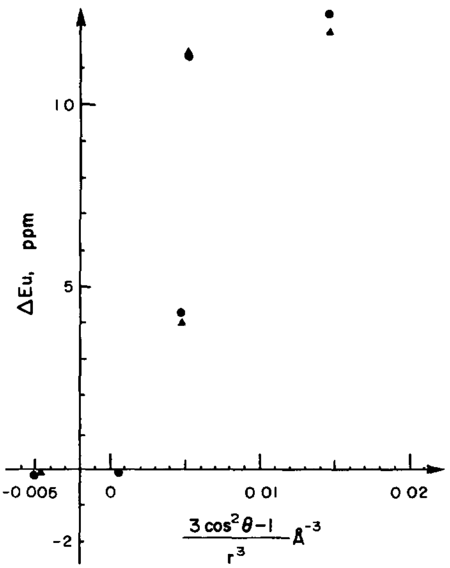


Fig 5b. Plots of the Δ_{Eu}-values for the *Z* configurations of **1** (●) and **3** (▲) as a function of $(3\cos^2\Theta - 1)\cdot r^{-3}$.

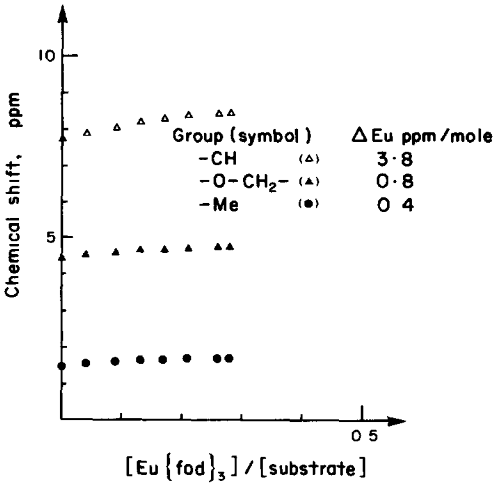


Fig 6. Plots of the chemical shift values ($CDCl_3$) for **4** as a function of the molar ratio $[Eu(fod)_3]/[substrate]$.

EXPERIMENTAL

General. NMR spectra were recorded in $CDCl_3$, dried over molecular sieve (Linde 5A), with a Varian A-60 spectrometer. The chemical shifts are reported in δ-values, using TMS as internal standard. The mass spectrum was determined with a GEC-AEI MS-20 mass spectrometer. Analytical and preparative TLC was performed on Silica Gel GF_{254} (Merck) plates, with CH_2Cl_2–EtOAc, 4:1, as the moving phase, and the spots were visualized with short-wave UV light.

The different Δ_{Eu}-values were determined as follows: a weighed amount of the actual substance was dissolved in 0·3 ml of dry $CDCl_3$ and known amounts of $Eu(fod)_3$-d_{27} dissolved in the same solvent were added. After each addition, the NMR tube was left spinning in the probe for about 15 min before the NMR spectrum was determined.

Ethyl 2-cyano-3-ethoxyacrylate, **1**. Commercially obtained (Kay-Fries Chemicals Inc.) **1** was recrystallized several times from EtOH and then sublimed at 25°/0·02 torr. The white crystals (m.p. 53°, lit.[1] 52–53°) showed only one spot on TLC (R_f = 0·62).

2-Cyano-3-ethoxyacrylonitrile, **4**. Commercially obtained (Fluka AG, Chemische Fabrik) **4** was recrystallized from EtOH and sublimed at 25°/0·02 torr, giving white crystals, m.p. 67–68°, lit.[18] 67°.

Ethyl 2-cyano-3-methoxyacrylate, **3**, was prepared according to Gregoire de Bellemont.[1] The crude product was recrystallized from EtOH and sublimed at 25°/0·02 torr, giving white crystals (m.p. 98–99°, lit.[1] 99°), which showed only one spot on TLC (R_f = 0·58). NMR: triplet (J = 7·0 Hz) at 1·32 (3H, Me), singlet at 4·16 (3H, OMe), quartet (J = 7·0 Hz) at 4·29 (2H, OCH_2), and singlet at 7·95 ppm (1H, =CH). MS: $M^+ = 155$.

Photochemical isomerization of **1a**. A soln of 50 mg of **1a** in 5 ml chloroform in a quartz cell was irradiated in an optical bench using a high-pressure mercury arc (Philips HPK 125W). After 1 hr the irradiation was interrupted and the soln evaporated *in vacuo* at 30°. TLC of the residue showed the presence of two compounds, one with the same R_f-value as **1a** and another with a lower R_f-value (0·50). Two bands, R_f = 0·62 and 0·50, respectively, were isolated by preparative TLC. These were extracted with methylene chloride. After evaporation *in vacuo* at 30°, both fractions showed the same R_f-value, 0·62. Therefore, **1b** had been rearranged into **1a**.

Photochemical isomerization of **3a**. This experiment was performed exactly as described for **1a**. The results were analogous and the R_f-values for the two isomers were 0·58 and 0·44 for the starting material and the new isomer, respectively.

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