

Metal Catalysis in Organic Reactions. Part 4.† Stereospecificity in the Dimerization and Cyclotrimerization of Chiral Alk-1-yne

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The reaction of (*S*)-3-methylpent-1-yne with tri-isobutylaluminium in the presence of bis-*N*-methylsalicylideneaminenickel has been studied. Depending on the experimental conditions, the alkyne was converted mainly into (*E*)-(3*S*,7*S*)-3,7-dimethyl-4-methylenenon-5-ene or 1,3,5-tris-[(*S*)-1-methylpropyl]benzene. Both dimerization and cyclotrimerization occurred without racemization. In this context the stereospecificity of other catalysed cyclotrimerizations has been examined.

DESPITE the wide variety of catalysts reported to give rise to linear and/or cyclic oligomerization of terminal acetylenes,¹ to date no data on the oligomerization of simple chiral alk-1-yne have been published. Recently there has been reported the head-to-tail polymerization of optically active alk-1-yne to linear polyenes.²

We were interested in the oligomerization and cyclotrimerization of chiral acetylenes,^{3,4} in view of the importance of both chiral dienes and trisubstituted benzenes, respectively, as low molecular weight structural models of polyenes² and models with restricted conformational freedom for studying the chiroptical properties of the benzene chromophore.⁵

During recent studies on catalysis of organic reactions

† Part of this research was presented at the 12th Congresso Nazionale della Società Chimica Italiana, S. Margherita di Pula, 30th September—4th October, 1975 (Abstracts, p. 197).

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² F. Ciardelli, S. Lanzillo, and O. Pieroni, *Macromolecules*, 1974, **7**, 174.

by metals⁶ we have found that the presence of catalytic amounts of nickel complexes in the reaction between alk-1-yne, such as hex-1-yne, and tri-isobutylaluminium,^{6,7} gives rise to the formation of linear dimers [(*E*)-2,4-dialkylbuta-1,3-dienes] and of trialkylbenzenes (Scheme).⁶ Moreover a preference for formation of the diene or the benzene derivatives was found to be essentially dependent on the experimental conditions.⁶

In order to provide more information on the preparative aspects of this nickel-promoted reaction, the reaction of (*S*)-3-methylpent-1-yne with tri-isobutylaluminium in the presence of bis-*N*-methylsalicylideneaminenickel

³ L. Lardicci, C. Botteghi, and E. Benedetti, *J. Org. Chem.*, 1966, **31**, 1534.

⁴ A. M. Caporusso, G. P. Giacomelli, and L. Lardicci, *Atti Soc. Toscana Sci. Nat. (Pisa)*, 1973, **A80**, 40.

⁵ P. Salvadori, L. Lardicci, R. Menicagli, and C. Bertucci, *J. Amer. Chem. Soc.*, 1972, **94**, 8598.

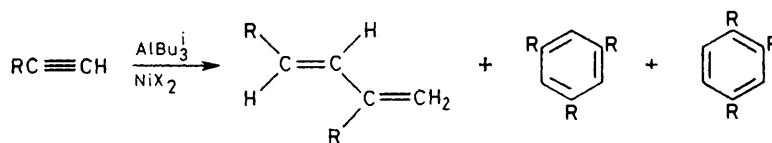
⁶ A. M. Caporusso, G. P. Giacomelli, and L. Lardicci, *J. Org. Chem.*, in the press.

⁷ L. Lardicci, A. M. Caporusso, and G. P. Giacomelli, *J. Organometallic Chem.*, 1974, **70**, 333.

[Ni(mesal)₂] was investigated. Thus, (*S*)-3-methylpent-1-yne, $[\alpha]_D^{20} +41.35^\circ$ (neat), optical purity 89%,³ was treated with an equimolecular amount of tri-isobutylaluminum in the presence of Ni(mesal)₂ (molar ratio Al : Ni 60 : 1) in the absence of solvents at 25 °C for 40 h.⁶ The reaction mixture, after hydrolysis, contained the diene (66%), 1,3,5-tris-(1-methylpropyl)benzene (14%), and 1,2,4-tris-(1-methylpropyl)benzene (3%), together with the alk-1-yne (2%) and the reduction product, 3-methylpent-1-ene (7%).⁷ Distillative work-up gave (*E*)-(3*S*,7*S*)-3,7-dimethyl-4-methylenon-5-ene, $[\alpha]_D^{25} +62.59^\circ$ (neat) (43% yield).

For evaluating the stereospecificity of the dimerization process, a sample of the diene was ozonized to (*S*)-2-methylbutanoic acid, $[\alpha]_D^{25} +17.30^\circ$ (neat), optical purity 87%.⁸

To convert the alkyne mainly into the aromatic products, (*S*)-3-methylpent-1-yne, $[\alpha]_D^{20} +42.11^\circ$ (neat)



SCHEME

was treated with tri-isobutylaluminum in the presence of Ni(mesal)₂ (molar ratios alkyne : Ni 103 : 1, Al : Ni 16 : 1) in refluxing benzene for 5 h.⁶ 1,3,5-Tris-(1-methylpropyl)benzene was the main product (41%), formed together with 1,2,4-tris-(1-methylpropyl)benzene (9%) and the diene (13%); linear trimers and tetramers were also detected. Preparative g.l.c. yielded (*E*)-(3*S*,7*S*)-3,7-dimethyl-4-methylenon-5-ene, $[\alpha]_D^{25} +61.97^\circ$ (neat), and 1,3,5-tris-[(*S*)-1-methylpropyl]benzene, $[\alpha]_D^{25} +60.38^\circ$ (in n-heptane).

To evaluate the relationship between optical purity and rotatory power of the 1,3,5-tris-[(*S*)-1-methylpropyl]benzene, and hence the stereospecificity of the cyclotrimerization reaction, it appeared useful to convert the benzene derivative into (*S*)-2-methylbutan-1-ol *via* reductive ozonolysis. Unfortunately, to date only a few reports on the stereospecificity of the ozonolysis of optically active aromatic hydrocarbons have been published.⁹ Therefore (*R*)-2-phenylbutane, $[\alpha]_D^{25} -20.68^\circ$ (neat), optical purity 71%,¹⁰ was converted into (*R*)-2-methylbutan-1-ol, $[\alpha]_D^{25} +4.70^\circ$ (in n-heptane), optical purity 71%, through known procedures.^{9,11} On the basis of this result, which verified the stereospecificity of the reductive ozonolysis, 1,3,5-tris-[(*S*)-1-methylpropyl]benzene was converted into (*S*)-2-methylbutan-1-ol, $[\alpha]_D^{25} -5.80^\circ$ (in n-heptane), optical purity 88%.

These results show that both the dimerization and the

cyclotrimerization occur with high stereospecificity. Thus the synthesis of optically active (*E*)-2,4-dialkylbuta-1,3-dienes and 1,3,5-trialkylbenzenes can be conveniently achieved from chiral alk-1-yne^{3,4} through this nickel-promoted reaction.

In order to discover whether optically active benzene derivatives could be prepared by other catalytic methods, the cyclotrimerization of alk-1-yne by dicarbonyl-bis(triphenylphosphine)nickel¹² and by tri-isobutylaluminum-titanium tetrachloride¹³ was also studied. The former catalyst did not cause much aromatization: hex-1-yne was completely converted into a complex mixture which contained mostly linear enynes, in addition to 8% of 1,3,5-tri-n-butylbenzene and 11% of 1,2,4-tri-n-butylbenzene, and 3-methylpent-1-yne reacted very slowly, giving essentially linear enynes.

The cyclotrimerization of hex-1-yne by tri-isobutylaluminum-titanium tetrachloride was not so selective

as reported.¹³ In fact, by using this catalytic system under the reported conditions,¹³ hex-1-yne was completely converted into 1,3,5-tri-n-butylbenzene (50%) and 1,2,4-tri-n-butylbenzene (50%). On the other hand this cyclotrimerization occurs quite stereospecifically: (*S*)-3-methylpent-1-yne, $[\alpha]_D^{20} +41.18^\circ$ (neat), yielded 70% of 1,3,5-tris-[(*S*)-1-methylpropyl]benzene, $[\alpha]_D^{25} +59.32^\circ$ (in n-heptane) and 30% of 1,2,4-tris-[(*S*)-1-methylpropyl]benzene, $[\alpha]_D^{25} +63.90^\circ$ (in n-heptane). From a synthetic viewpoint, this last method, even if less selective, appears more suitable than the nickel-catalyzed reaction⁶ for preparing optically active trialkylbenzenes from chiral aliphatic alk-1-yne.

EXPERIMENTAL

Tri-isobutylaluminum, titanium tetrachloride, and hex-1-yne were commercial products (Fluka) which were purified by distillation before use. (*S*)-3-Methylpent-1-yne was prepared according to established procedures.³ Dicarbonyl-bis(triphenylphosphine)nickel was obtained from Strem Chemical Inc., Danvers, and bis-*N*-methylsalicylideneamine-nickel was prepared and purified as reported.¹⁴ All reactions were carried out under dry, purified nitrogen. G.l.c. analyses were performed with a Perkin-Elmer F 30 instrument (flame ionization detectors; 200 × 0.30 cm columns packed with 2.5% silicone gum rubber E 301 on 60–80 mesh Chromosorb W at 40–200 °C; nitrogen flow rate 10 ml min⁻¹). Preparative g.l.c. were carried out with a Perkin-Elmer F 21 instrument. All yields, unless otherwise indicated, are based on weights of products after distillation,

¹² L. S. Meriwether, E. C. Colthup, G. W. Kennerly, and R. N. Reusch, *J. Org. Chem.*, 1961, **26**, 5155.

¹³ V. O. Reikhsfel'd, K. L. Makovetskii, and L. L. Erokhina, *Zhur. obshchei Khim.*, 1962, **32**, 653; V. O. Reikhsfel'd and K. L. Makovetskii, *Russ. Chem. Rev.*, 1966, **35**, 510.

¹⁴ L. Sacconi, P. Paoletti, and G. Del Re, *J. Amer. Chem. Soc.*, 1957, **79**, 4062.

⁸ L. Lardicci, C. Botteghi, and E. Belgodere, *Gazzetta*, 1967, **97**, 610.

⁹ L. Verbit and H. C. Price, *J. Amer. Chem. Soc.*, 1972, **94**, 5151; L. Lardicci, R. Menicagli, A. M. Caporusso, and G. P. Giacomelli, *Chem. and Ind.*, 1973, 184.

¹⁰ L. Lardicci and R. Menicagli, *Atti Soc. Toscana Sci Nat. (Pisa)*, 1970, **A77**, 25.

¹¹ A. M. Caporusso, G. P. Giacomelli, and L. Lardicci, *Gazzetta*, 1976, **106**, 879.

or were determined by g.l.c. analysis of known weights of mixtures of products. Optical rotations were measured with a Schmidt-Haensch or a Perkin-Elmer 142 polarimeter. The following instruments were also used: Perkin-Elmer 225 spectrophotometer (i.r. spectra), Varian MAT CH-7 spectrometer (mass spectra), and JEOL JMN PS-100 spectrometer (^1H n.m.r. spectra).

Dimerization Procedure.—Tri-isobutylaluminum (35.7 g, 0.180 mol) was added to bis-*N*-methylsalicylideneamine-nickel (0.981 g, 0.003 mol) cooled at 0 °C. (*S*)-3-Methylpent-1-yne (14.8 g, 0.180 mol), $[\alpha]_{\text{D}}^{20} + 41.35^\circ$ (neat),³ was immediately added to the brownish homogeneous mixture, which was then heated at 25 ± 0.3 °C for 40 h. The mixture was cautiously hydrolysed with dilute sulphuric acid and extracted with ether. The crude product contained 3-methylpent-1-yne (2%), 3-methylpent-1-ene (7%), (*E*)-3,7-dimethyl-4-methylenon-5-ene (66%), 1,3,5-tris-(1-methylpropyl)benzene (14%), and 1,2,4-tris-(1-methylpropyl)benzene (3%). Fractional distillation gave (*E*)-(3*S*,7*S*)-3,7-dimethyl-4-methylenon-5-ene (6.5 g, 43%), which was further purified by preparative g.l.c. (20% butanediol succinate LAC 6R-860, 100 °C), b.p. 81° at 17 mmHg; n_{D}^{25} 1.4575; d_4^{25} 0.7755; $[\alpha]_{\text{D}}^{25} + 62.59^\circ$ (neat); *m/e* 166 (M^+ , 6%), 137(20), 109(28), 95(37), 81(62), 69(18), 67(37), 57(31), 55(54), 41(100), 29(89), and 27(40); ν_{max} (film) 3 090, 1 610, 965, and 880 cm^{-1} ; $\delta(\text{CDCl}_3)$ 0.95 (12 H, m, CH_3), 1.33 (4 H, m, CH_2), 2.20 (2 H, m, $\text{CH}=\text{C}$), 4.77 (1 H, m, $=\text{CH}_2$), 4.90 (1 H, d, *J* 1.5 Hz, $=\text{CH}_2$), 5.55 (1 H, m, *J* 15.7 and 7.5 Hz, $=\text{CH}$), and 6.0 (1 H, d, *J* 15.7 Hz, $=\text{CH}$).

Cyclotrimerization Procedure.—(a) *With tri-isobutylaluminum-bis-N-methylsalicylideneamine-nickel.* Tri-isobutylaluminum (11.5 g, 0.058 mol) was added slowly to a stirred, ice-cooled solution of the nickel complex (1.16 g, 3.55 mmol) in anhydrous benzene (90 ml). (*S*)-3-Methylpent-1-yne (30 g, 0.365 mol), $[\alpha]_{\text{D}}^{20} + 42.11^\circ$ (neat), was then added and the flask was heated with an oil-bath at 80 °C. After 6 h, the mixture was hydrolysed with dilute sulphuric acid and extracted with ether. G.l.c. analysis of the ether layer showed the presence of (*E*)-3,7-dimethyl-4-methylenon-5-ene (13%), 1,3,5-tris-(1-methylpropyl)benzene (41%), and 1,2,4-tris-(1-methylpropyl)benzene (9%) as major products with minor amounts of linear trimers, *m/e* 246 (M^+), and tetramers, *m/e* 328 (M^+). Fractional distillation gave a sample (2.2 g) of (*E*)-(3*S*,7*S*)-3,7-dimethyl-4-methylenon-5-ene which, purified by preparative g.l.c. showed $[\alpha]_{\text{D}}^{25} + 61.97^\circ$ (neat) and a C_{18} fraction (13.7 g) containing 1,3,5-tris-[(*S*)-1-methylpropyl]benzene (60%) and 1,2,4-tris-(1-methylpropyl)benzene (11%). The mixture was separated by preparative g.l.c. (20% butanediol succinate LAC 6R-860; 170 °C) to yield pure 1,3,5-tris-[(*S*)-1-methylpropyl]benzene, b.p. 93° at 0.6 mmHg; n_{D}^{25} 1.4808; $[\alpha]_{\text{D}}^{25} + 60.38^\circ$ (*c* 3.70 in *n*-heptane); *m/e* 246 (M^+ , 17%), 231(3), 217(100), 105(8), 91(9), 57(34), 41(24), and 29(21); ν_{max} (film) 1 760, 1 600, 870, and 720 cm^{-1} ; $\delta(\text{CCl}_4)$ 0.80 (9 H, t, CH_3), 1.21 (9 H, d, CH_2), 1.57 (6 H, m, CH_2), 2.53 (3 H, m, $\text{CH}=\text{Ar}$), and 6.72 (3 H, s, ArH).

(b) *With tri-isobutylaluminum-titanium tetrachloride.* A stirred, ice-cooled solution of tri-isobutylaluminum (0.298 g, 1.50 mmol) in benzene was treated with titanium tetrachloride (0.0952 g, 0.50 mmol), and hex-1-yne (4.12 g, 50.2 mmol) in anhydrous benzene (10 ml) was then added during 15 min while the temperature of the mixture rose from 20 to 40 °C. After 2 h, the reaction was quenched by adding a mixture of

methanol (50 ml) and 2*N*-hydrochloric acid (50 ml). Distillation of the organic layer yielded a fraction (4 g, 95%), b.p. 118° at 0.6 mmHg, containing 1,3,5-tri-*n*-butylbenzene (50%) and 1,2,4-tri-*n*-butylbenzene (50%).

By the same general procedure, (*S*)-3-methylpent-1-yne (6 g, 73.0 mmol), $[\alpha]_{\text{D}}^{20} + 41.18^\circ$ (neat) gave a mixture (5.9 g, 98%) containing 1,3,5-tris-(1-methylpropyl)benzene (70%) and 1,2,4-tris-(1-methylpropyl)benzene (30%). Preparative g.l.c. (8% Carbowax 20M + 2% KOH; 175 °C) afforded pure 1,3,5-tris-[(*S*)-1-methylpropyl]benzene (49%), $[\alpha]_{\text{D}}^{25} + 59.32^\circ$ (*c* 4.16 in *n*-heptane), and 1,2,4-tris-[(*S*)-1-methylpropyl]benzene (23%), b.p. 108° at 1 mmHg; n_{D}^{25} 1.4872; $[\alpha]_{\text{D}}^{25} + 63.90^\circ$ (*c* 4.27 in *n*-heptane); *m/e* 246 (M^+ , 21%), 231(5), 217(100), 175(13), 161(15), 119(17), 105(8), 91(12), 57(29), 41(21), and 29(23); ν_{max} (film) 1 890, 1 775, 1 612, 1 500, 890, and 825 cm^{-1} ; $\delta(\text{CCl}_4)$ 0.82 (9 H, t, CH_3), 1.18 (3 H, d, CH_3), 1.19 (3 H, d, CH_3), 1.21 (3 H, d, CH_3), 1.56 (2 H, m, CH_2), 1.58 (2 H, m, CH_2), 1.60 (2 H, m, CH_2), 2.49 (1 H, m, $\text{CH}=\text{Ar}$), 2.92 (1 H, m, $\text{CH}=\text{Ar}$), 2.96 (1 H, m, $\text{CH}=\text{Ar}$), and 6.76–7.02 (3 H, m, ArH).

Attempted Cyclotrimerization of Alk-1-yne by Dicarbonyl-bis(triphenylphosphine)nickel.—A solution of the nickel complex (0.0196 g, 0.0307 mmol) and hex-1-yne (0.82 g, 10 mmol) in anhydrous benzene (5 ml) was heated to reflux (oil-bath). After 6 h, g.l.c. analysis revealed the presence of 1,3,5-tri-*n*-butylbenzene (8%) and 1,2,4-tri-*n*-butylbenzene (11%), together with linear dimers (12%), *m/e* 164 (M^+), and linear trimers (67%), *m/e* 246 (M^+). 3-Methylpent-1-yne, treated with the nickel complex as above, gave 1,3,5-tris-(1-methylpropyl)benzene (5%), 1,2,4-tris-(1-methylpropyl)benzene (1%), linear dimers (5%), *m/e* 164 (M^+), and linear trimers (28%), *m/e* 246 (M^+).

Ozonolysis of (*E*)-(3*S*,7*S*)-3,7-Dimethyl-4-methylenon-5-ene.—Ozonized oxygen (*ca.* 3%) was passed through a solution of the diene (1.1 g, 6.6 mmol), $[\alpha]_{\text{D}}^{25} + 62.59^\circ$ (neat), in *n*-pentane (20 ml) at -70 °C for 1 h. The solvent was removed at reduced pressure and the mixture, diluted with ethanol (30 ml), was stirred at 80 °C with 10% sodium hydroxide (40 ml) and 30% hydrogen peroxide (22 ml) for 5 h. After work-up, distillation of the acid fraction provided (*S*)-2-methylbutanoic acid (47%), n_{D}^{25} 1.4045, $[\alpha]_{\text{D}}^{25} + 17.30^\circ$ (neat).⁸ The chemical purity of the product was checked by g.l.c. analysis of the corresponding methyl ester.

Ozonolysis of (*R*)-2-Phenylbutane.—(*R*)-2-Phenylbutane † (2.1 g, 15.7 mmol), $[\alpha]_{\text{D}}^{25} - 20.68^\circ$ (neat)¹⁰ was ozonized in acetic acid solution (30 ml) according to the Verbit procedure.⁹ Most of the acetic acid was removed under vacuum at 40 °C, and the crude ozonide was decomposed in ethereal solution (100 ml) with lithium aluminium hydride (6 g). After hydrolysis, preparative g.l.c. (8% Carbowax 20M + 2% KOH; 100 °C) gave (*R*)-2-methylbutan-1-ol, $[\alpha]_{\text{D}}^{25} + 4.70^\circ$ (*c* 3.80 in *n*-heptane). A sample of (*S*)-2-methylbutan-1-ol, $[\alpha]_{\text{D}}^{25} - 5.75^\circ$ (neat),¹⁶ showed $[\alpha]_{\text{D}}^{25} - 6.53^\circ$ (*c* 3.41 in *n*-heptane).

Ozonolysis of 1,3,5-Tris-[(*S*)-1-methylpropyl]benzene.—As described above, 1,3,5-tris-[(*S*)-1-methylpropyl]benzene (1 g, 4.06 mmol), $[\alpha]_{\text{D}}^{25} + 60.38^\circ$ (*c* 3.70 in *n*-heptane), was converted into (*S*)-2-methylbutan-1-ol, $[\alpha]_{\text{D}}^{25} - 5.80^\circ$ (*c* 3.55 in *n*-heptane), by reductive ozonolysis.

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¹⁵ D. A. McCaulay, A. P. Lien, and P. J. Launer, *J. Amer. Chem. Soc.*, 1954, **76**, 2354.

¹⁶ R. Rossi, P. Diversi, and G. Ingrosso, *Gazzetta*, 1968, **98**, 1391.

† A sample of (*R*)-2-phenylbutane was kindly supplied by Dr. Rita Menicagli.