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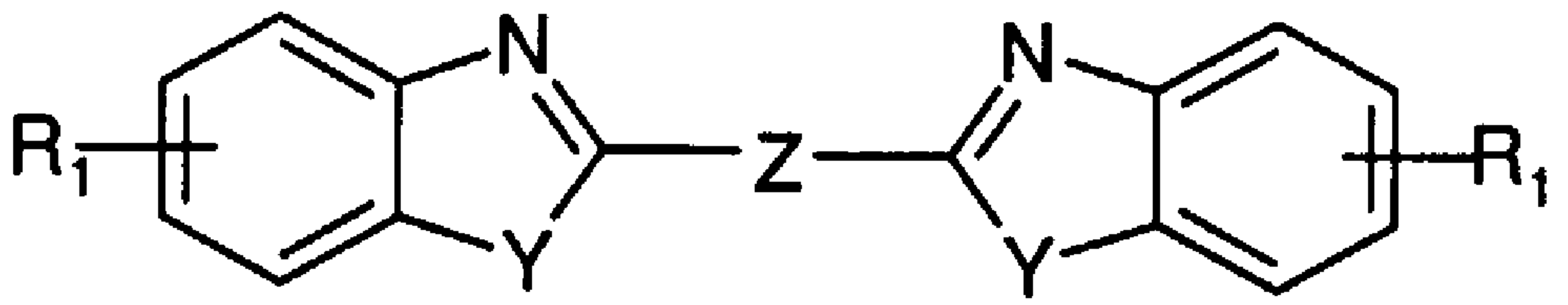
(72) Inventeurs/Inventors:
ELIU, VICTOR PAUL, DE;
HAUSER, JULIA, DE

(73) Propriétaire/Owner:
CIBA SPECIALTY CHEMICALS HOLDING INC., CH

(74) Agent: FETHERSTONHAUGH & CO.

(54) Titre : PROCEDE DE PREPARATION DE COMPOSES BIS-BENZAZOLYLE
(54) Title: A PROCESS FOR THE PREPARATION OF BIS-BENZAZOLYL COMPOUNDS



(1)

(57) Abrégé/Abstract:
The present invention provides a process for the preparation of a compound of formula (I) wherein Y represents -O-, -S- or -N(R_2)-, R_2 being hydrogen, C_1-C_{10}alkyl or aralkyl; Z represents a 2,5-furanyl, 2,5-thiophenyl, 4,4'-stilbenyl or a 1,2-ethylenyl residue and R_1 represents hydrogen, halogen, C_1-C_{10}alkoxyl, cyano, COOM or SO_3M, M being hydrogen or an alkaline or alkaline earth metal, characterized by reacting a compound of formula (II) with a dicarboxylic acid of formula (III): HOOC-Z-COOH, or an ester thererof, Y, Z and R_1 being as previously defined, in N-methylpyrrolidone or N,N-dimethylacetamide, in the presence of an acidic catalyst and, optionally, in the presence of a secondary solvent capable of removing water from the reaction mixture, which are useful as optical whitening agents for natural and synthetic materials.

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(71) **Applicant** *(for all designated States except US)*: **CIBA SPECIALTY CHEMICALS HOLDING INC.** [CH/CH]; Klybeckstrasse 141, CH-4057 Basel (CH).

(72) **Inventors; and**
(75) **Inventors/Applicants** *(for US only)*: **ELIU, Victor, Paul** [DE/DE]; Im Lögelhardt 2, 79539 Lörrach (DE). **HAUSER, Julia** [DE/DE]; Walter-Wetzel-Weg 10, 79639 Grenzach-Wyhlen (DE).

(74) **Common Representative: CIBA SPECIALTY CHEMICALS HOLDING INC.**; Patentabteilung, Klybeckstrasse 141, CH-4057 Basel (CH).

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(54) **Title:** A PROCESS FOR THE PREPARATION OF BIS-BENZAZOLYL COMPOUNDS

(57) **Abstract:** The present invention provides a process for the preparation of a compound of formula (I) wherein Y represents -O-, -S- or -N(R_2)-, R_2 being hydrogen, C_1-C_{10}alkyl or aralkyl; Z represents a 2,5-furanyl, 2,5-thiophenyl, 4,4'-stilbenyl or a 1,2-ethylenyl residue and R_1 represents hydrogen, halogen, C_1-C_{10}alkoxyl, cyano, COOM or SO_3M, M being hydrogen or an alkaline or alkaline earth metal, characterized by reacting a compound of formula (II) with a dicarboxylic acid of formula (III): HOOC-Z-COOH, or an ester therof, Y, Z and R_1 being as previously defined, in N-methylpyrrolidone or N,N-dimethylacetamide, in the presence of an acidic catalyst and, optionally, in the presence of a secondary solvent capable of removing water from the reaction mixture, which are useful as optical whitening agents for natural and synthetic materials.

A Process for the Preparation of Bis-Benzazolyl Compounds

The present invention relates to a process for the preparation of bis-benzazolyl compounds which are useful as optical whitening agents for natural and synthetic materials.

Various methods for the preparation of such compounds are known.

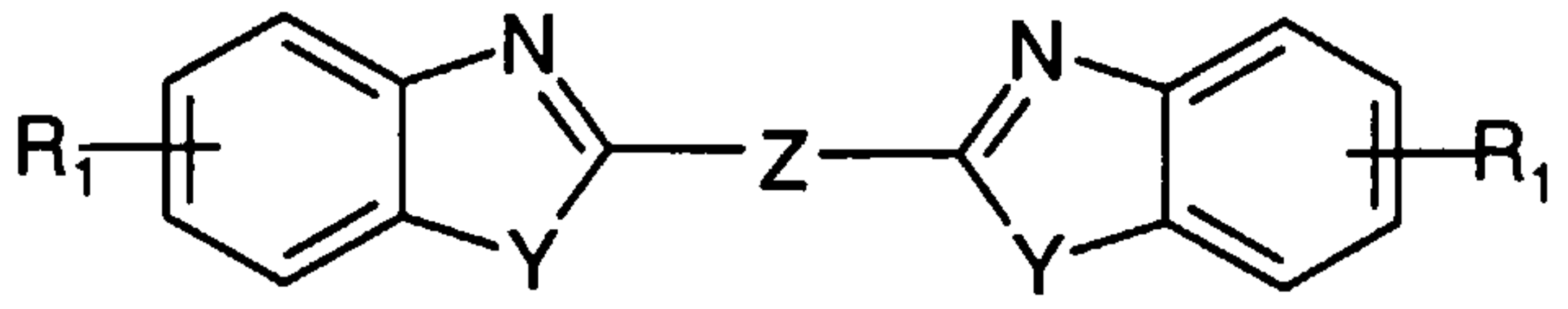
Thus, for example, US Patent 4,508,903 describes the preparation of 4,4'-bis.benzoxazol-, benzthiazol- and benzimidazol-2-ylstilbenes by dimerisation of the corresponding p-chloromethylphenylbenzazoles. However, such methods suffer from the disadvantage that the preparation of the intermediates involves several reaction steps, subsequently rendering poor overall yields.

Of particular practical interest are processes in which dicarboxylic acids or their derivatives are reacted with bifunctional aromatic compounds to form the heterocyclic rings in a single reaction step.

Thus, for example, European Patent 31,296 discloses a process for the preparation of benzoxazolyl and benzimidazolyl compounds by condensation of organic carboxylic acids with o-aminophenols and o-phenylenediamines in a solvent mixture consisting of diphenyl ether and diphenyl in the presence of acidic catalysts. Furthermore, British Patent 1,201,287 describes the preparation of 2,5-bisbenzoxazol-2-yl thiophenes by condensation of thiophene-2,5-dicarboxylic acid with o-aminophenols in, for example, refluxing 1,2,4-trichlorobenzene in the presence of boric acid. Such processes are disadvantageous since they demand extremely high reaction temperatures, resulting in the formation of impurities which are difficult to remove from the final products and, as a consequence, loss of product yields. Furthermore, such high-boiling solvents are also difficult to remove from the reaction products and may further result in crust-formation inside reaction vessels, thus impeding work-up of the final products. Additionally, employment of chlorinated aromatic solvents in the present day is undesirable for ecological reasons.

Surprisingly, a new, advantageous process for the preparation of bis-benzazolyl compounds has now been found, which provides these compounds in high yields of excellent purity under reaction conditions well suited to commercial processes.

Accordingly, the current invention provides a process for the preparation of a compound of the formula


(1),

wherein

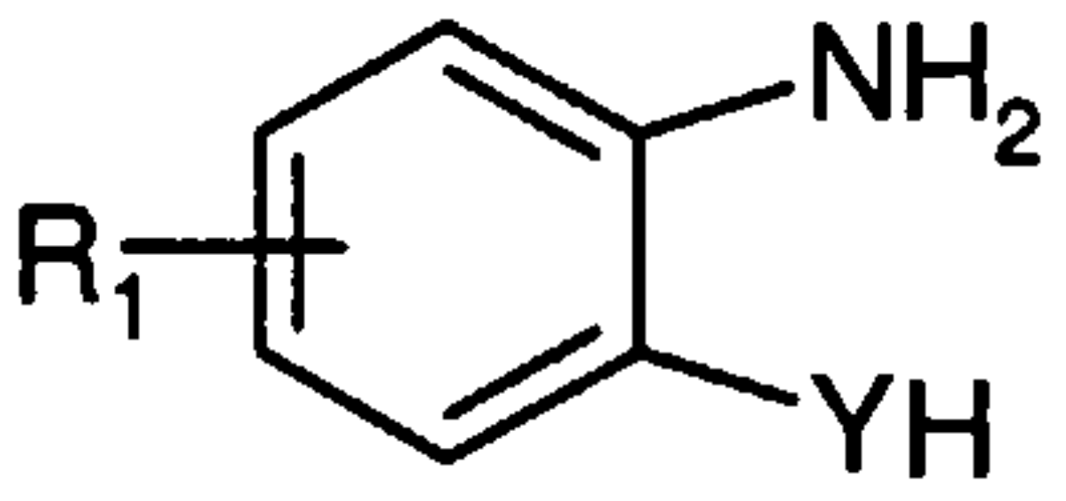
Y represents -O-, -S- or -N(R_2)-,

R_2 being hydrogen, C_1-C_{10}alkyl or aralkyl;

Z represents a 2,5-furanyl, 2,5-thiophenyl, 4,4'-stilbenyl or a 1,2-ethylenyl residue and

R_1 represents hydrogen, halogen, C_1-C_{10}alkyl, C_1-C_{10}alkoxy, cyano, COOM or SO_3M,

M being hydrogen or an alkaline or alkaline earth metal, characterized by reacting a compound of the formula


(2)

with a dicarboxylic acid of the formula

HOOC-Z-COOH (3)

or an ester thereof, Y, Z and R_1 being as previously defined, in N-methylpyrrolidone or N,N-dimethylacetamide, in the presence of an acidic catalyst and, optionally, in the presence of a secondary solvent capable of removing water from the reaction mixture.

The molar ratios of the compound of formula (2) to the compound of formula (3) may vary over wide ranges. However, it is advantageous to react at least two moles of the compound of formula (2) with at least one mole of the dicarboxylic acid of formula (3). Alternatively, a mono- or diester, preferably a diester, of the compound of formula (3) may be employed. Appropriate esters are those derived from a C_1-C_{10}-, preferably C_1-C_4alcohol, diethyl esters being most preferred.

The process of the invention is particularly suitable for the preparation of a compound of formula (1) in which
Y represents -O-, -S- or -N(R_2)-,
R_2 being hydrogen or C_1-C_4alkyl;
Z is as defined previously and
R_1 represents hydrogen or C_1-C_4alkyl and, more especially for compounds of formula (1) in which
Z represents a 2,5-furanyl or a 2,5-thiophenyl residue and also for those in which
Z represents a 4,4'-stilbenyl or a 1,2-ethylenyl residue.

As reaction medium for the process of the invention N-methylpyrrolidone or N,N-dimethylacetamide or mixtures thereof are most preferred. It is also possible to use N-methylpyrrolidone or N,N-dimethylacetamide or mixtures thereof together with a further high boiling inert solvent, e. g. toluene or xylene. The use of N-methylpyrrolidone is especially preferred.

The acidic catalyst employed in the process of the invention may be selected from the group consisting of boric acid, phosphoric acid, titanium C_1-C_4orthoesters or tin derivatives, boric acid or a titanium C_1-C_4orthoester, especially tetrapropyl or tetrabutyl ester, being of preference. The amount of catalyst employed may vary over wide ranges and is dependent on the chemical entity. Thus, for example, amounts varying from 0.01 to 50mole%, based on the amount of compound (2), preferably 0.1 to 30mole% may be used.

Reaction of compounds of the formulae (2) and (3) may be carried out within a wide temperature range, but is preferably within the range of between 100 and 250°C, in particular within a temperature range of between 150 and 200°C.

The presence of a secondary solvent is of particular importance when the compound of formula (3) is in the form of a monoester or, especially, the free dicarboxylic acid. In these cases, water formed during the course of the reaction may be continuously removed from the reaction mixture. Examples of suitable solvents, without the choice being limited thereto, are selected from the group consisting of toluene, the xylenes and isomeric mixtures thereof and pyridine, toluene and xylene being especially effective.

The reaction of the invention is normally carried out under atmospheric pressure. However, under certain circumstances, it may prove advantageous to perform the reaction under higher or lower pressures.

Within the scope of the compounds of formulae (1) and (2), when R_1 represents halogen this may be fluorine, bromine , iodine or, especially, chlorine.

C_1-C_{10}alkyl groups R_1 and/or R_2 may be branched or unbranched such as methyl, ethyl, n-propyl, isopropyl, n-butyl, sec-butyl, isobutyl, t-butyl, 2-ethylbutyl, n-pentyl, isopentyl, 1-methylpentyl, 1,3-dimethylbutyl, n-hexyl, 1-methylhexyl, n-heptyl, isoheptyl, 1,1,3,3-tetramethylbutyl, 1-methylheptyl, 3-methylheptyl, n-octyl, 2-ethylhexyl, 1,1,3-trimethylhexyl, 1,1,3,3-tetramethylpentyl, n-nonyl or n-decyl. C_1-C_{10}alkyl esters of compound of formula (3) are substituted correspondingly.

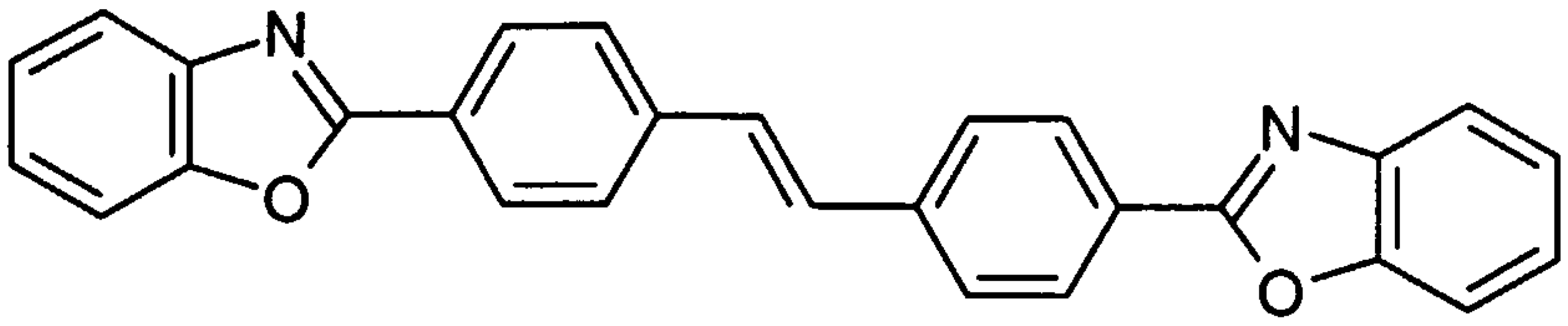
C_1-C_{10}alkoxy groups R_1 may be branched or unbranched such as methoxy, ethoxy, n-propoxy, isopropoxy, n-butoxy, sec-butoxy, isobutoxy, t-butoxy, 2-ethylbutoxy, n-pentoxy, isopentoxy, 1-methylpentoxy, 1,3-dimethylbutoxy, n-hexoxy, 1-methylhexoxy, n-heptoxy, isoheptoxy, 1,1,3,3-tetramethylbutoxy, 1-methylheptoxy, 3-methylheptoxy, n-octoxy, 2-ethylhexoxy, 1,1,3-trimethylhexoxy, 1,1,3,3-tetramethylpentoxy, n-nonoxy or n-decoxy.

Aralkyl groups R_2 may be benzyl or phenethyl which may be substituted by halogen, C_1-C_{10}alkyl or C_1-C_{10}alkoxy groups or, preferably, unsubstituted.

The alkaline or alkaline earth metal M may be selected from the group consisting of K, Na, Ca or Mg, but is preferably K or Na.

The following Examples further illustrate the present invention, without intending to be restrictive thereto:

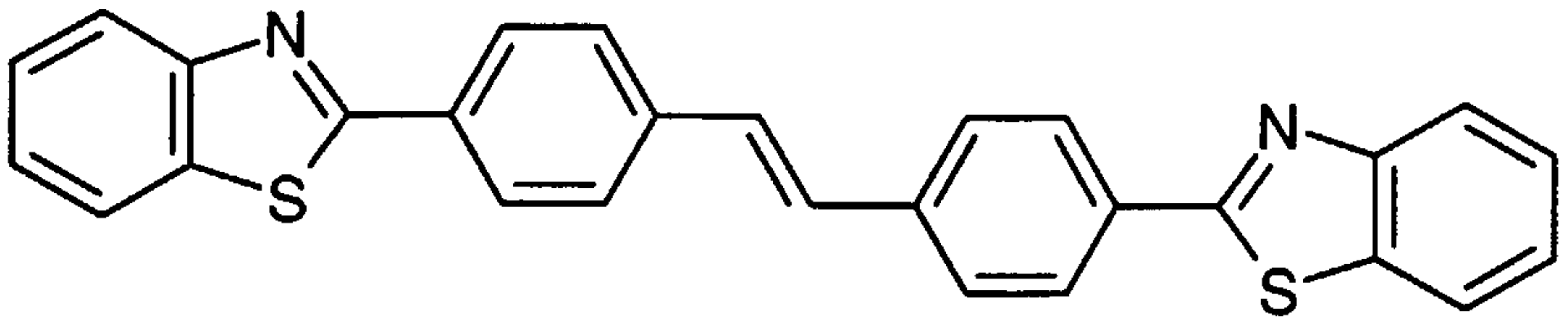
Example 1



(101)

250g of N-methylpyrrolidone are charged to a reaction vessel and 82g of 98% stilbene-4,4'-dicarboxylic acid, followed by 75g of 99% 2-aminophenol, 10g of boric acid and 30g of xylene are added with stirring. The apparatus, equipped with a Dean and Stark water trap, is evacuated and the vacuum released with nitrogen. The light yellow suspension is heated to 195°C and stirred at this temperature for 18 hours, during which time 23-25ml of water and approximately 25g of xylene are distilled off through the water trap. The reaction mixture is cooled to 20°C and stirring continued for 1 hour at this temperature. The yellow suspension is filtered, washed with 100g of N-methylpyrrolidone to give 350g of a brown solution which may be used as solvent for a further charge and then with three 80g portions of water. The resulting press-cake is dried under a vacuum of 50mbar at 100°C to yield 120g of the compound of formula (101) as a yellow solid, characterized by a UV absorption maximum λ_{max} at 368nm with an extinction coefficient ε of 71000.

Example 2

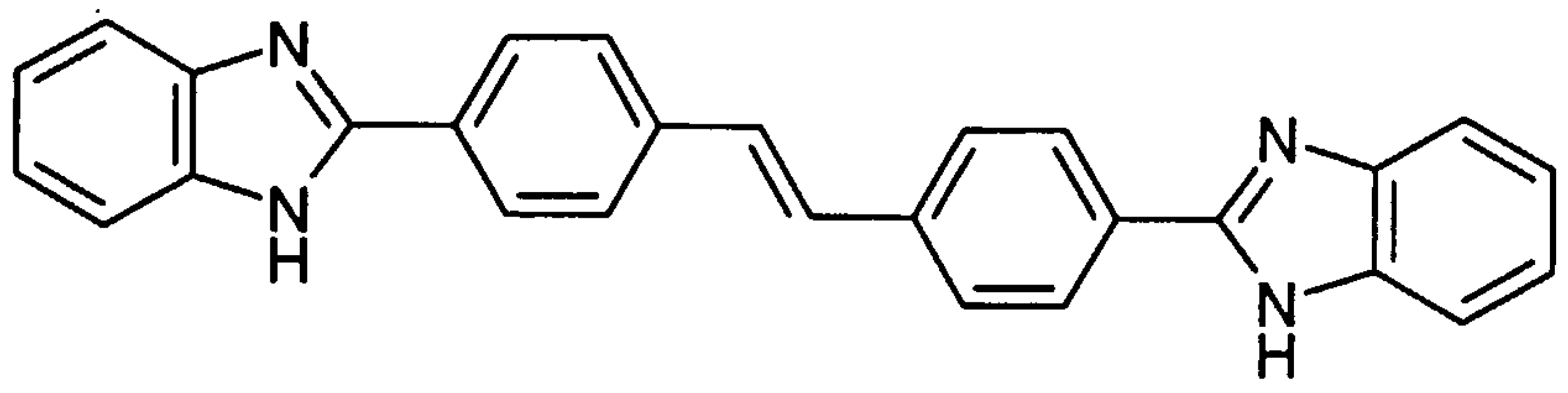


(102)

By following the procedure described in Example 1, but replacing the 2-aminophenol by 82g of 98% 2-thiophenol and the boric acid by 3g of titanic acid tetra-isopropyl ester, there are obtained 115g of the compound of formula (102) as a yellow solid, characterized by a UV absorption maximum λ_{max} at 375nm with an extinction coefficient ε of 62000 and by the following ^{1}H-NMR data in D_6-DMSO:

8.12, 4H, m; 8.00, 6H, m; 7.85, 4H, m and 7.48, 4H, m.

Example 3

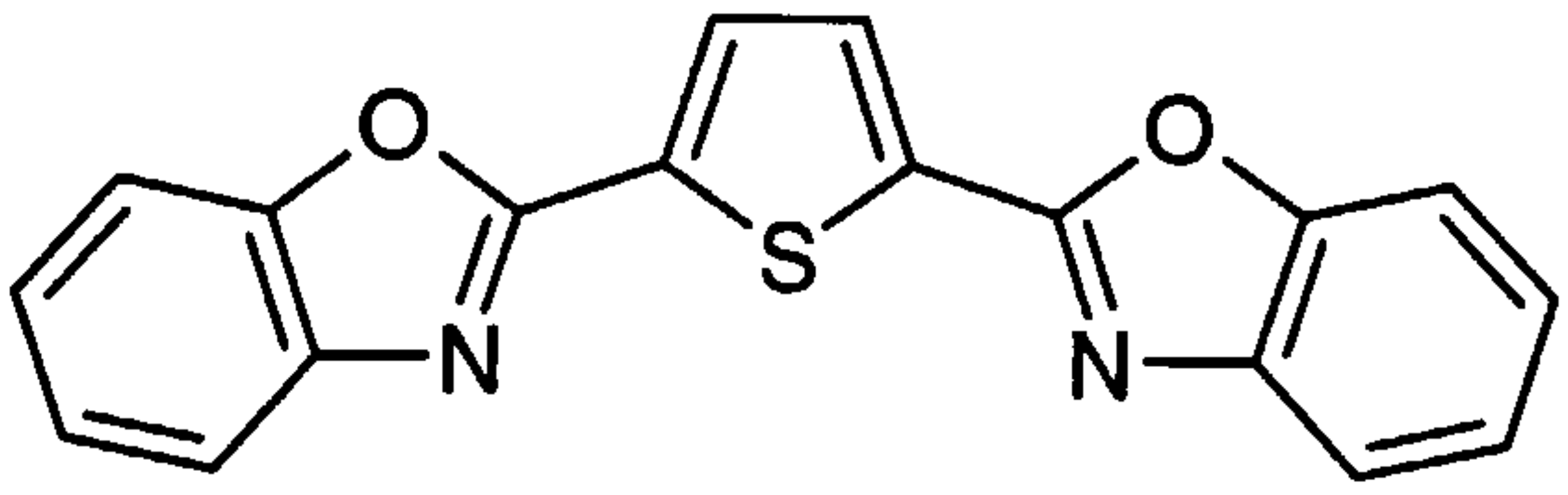


(103)

By following the procedure described in Example 1, but replacing the 2-aminophenol by 72g of 99% 1,2-phenylenediamine, there are obtained 110g of the compound of formula (103) as a yellow solid, characterized by a UV absorption maximum λ_{max} at 370nm with an extinction coefficient ε of 63000 and by the following ^{1}H-NMR data in D_6-DMSO:

13.0, 2H, s; 8.22, 4H, d, j= 7Hz; 7.80, 4H, d, j=7Hz; 7.68, 2H, d, j=7Hz; 7.54, 2H, d, j=7Hz; 7.48, 2H, s and 7.22, 4H, t, j=7Hz.

Example 4

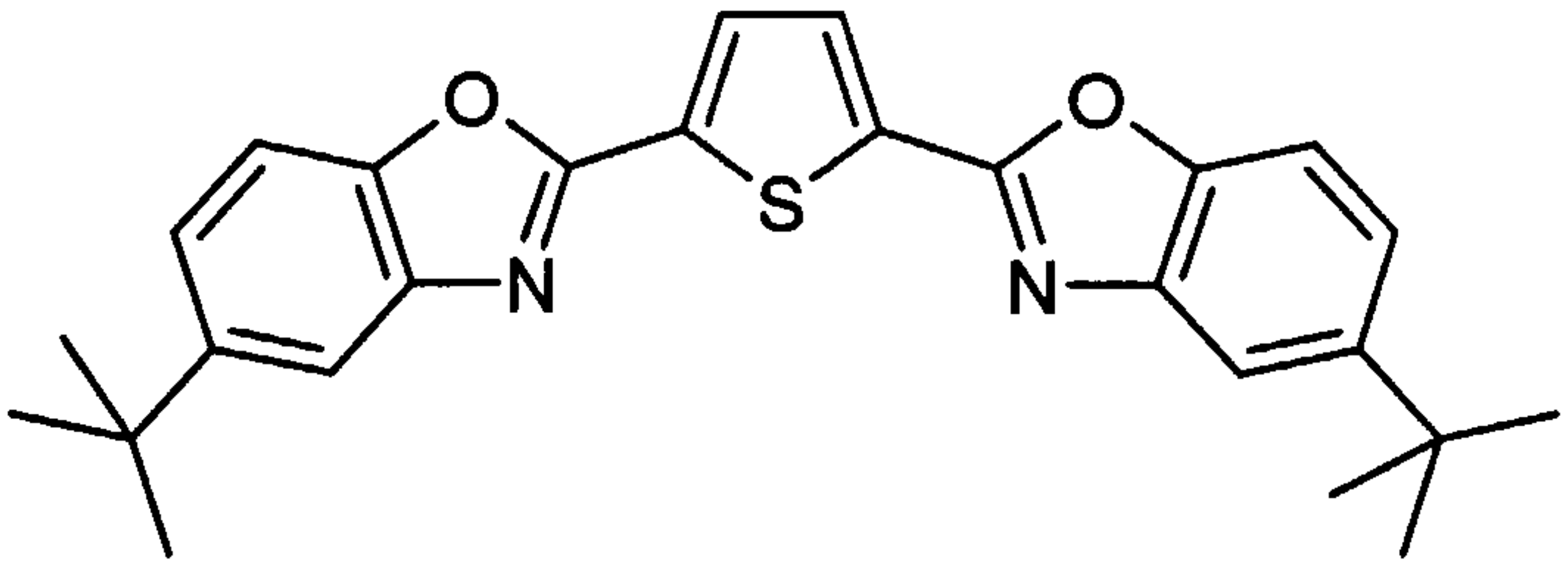


(104)

200g of N-methylpyrrolidone are charged to a reaction vessel and 52g of 98% thiophene-2,5-dicarboxylic acid, followed by 72g of 99% 2-aminophenol, 10g of boric acid and 30g of toluene are added with stirring. The apparatus, equipped with a Dean and Stark water trap, is evacuated and the vacuum released with nitrogen. The light yellow suspension is heated to 185°C and stirred at this temperature for 12 hours, during which time 23-25ml of water and approximately 25g of toluene are distilled off through the water trap. The reaction mixture is cooled to 20°C and stirring continued for 1 hour at this temperature. The yellow suspension is filtered, washed with 100g of N-methylpyrrolidone to give 300g of a brown solution which may be used as solvent for a further charge and then with three 80g portions of water. The resulting press-cake is dried under a vacuum of 50mbar at 100°C to yield 75g of the

compound of formula (104) as a yellow solid, characterized by a UV absorption maximum λ_{max} at 372nm with an extinction coefficient ε of 52000 and by the following ^{1}H-NMR data in D_6-DMSO:
8.10, 2H, s; 7.82, 4H, m and 7.50, 4H, m.

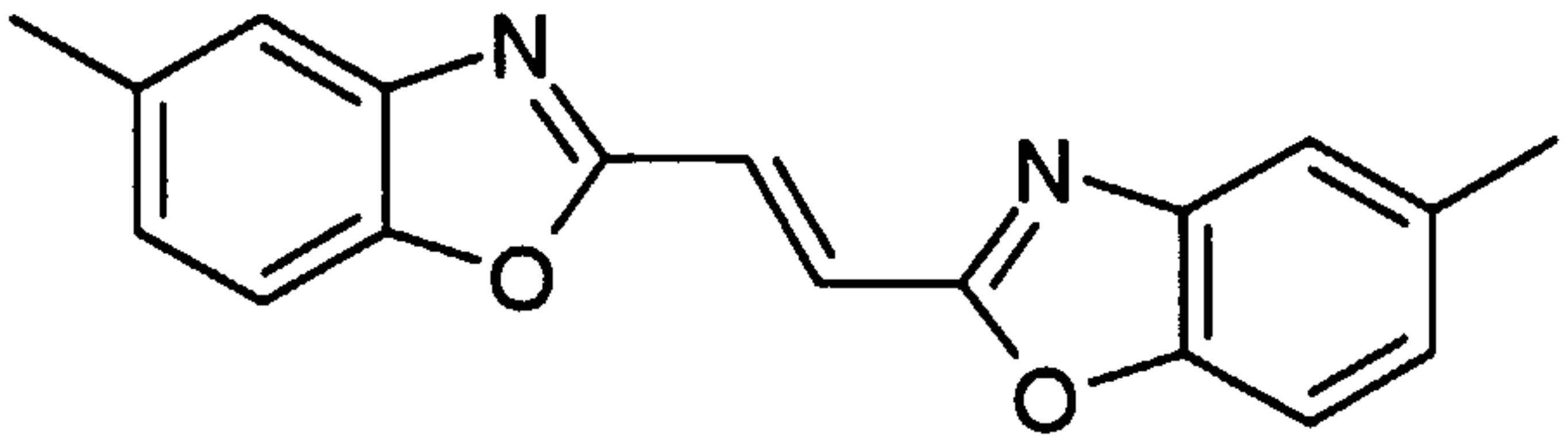
Example 5



(105)

By following the procedure described in Example 4, but replacing the 2-aminophenol by 110g of 2-amino-4-t-butylphenol, the boric acid by 2.2g of isopropyl-ortho-titanate and the toluene by 30g of xylene, there are obtained 125g of the compound of formula (105) as a yellow solid, characterized by a UV absorption maximum λ_{max} at 375nm with an extinction coefficient ε of 51000 and by a singlet at 1.30ppm in the^{1}H-NMR spectrum in D_6-DMSO.

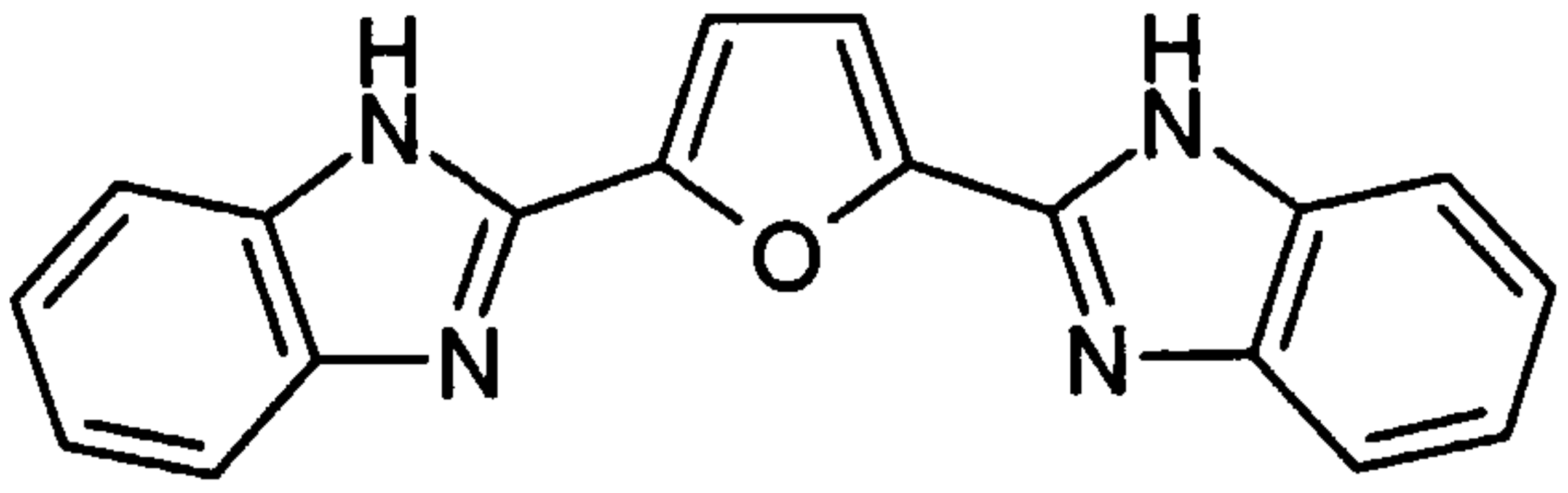
Example 6



(106)

200g of N,N-dimethylacetamide are charged to a reaction vessel and 35g of 98% fumaric acid, followed by 82g of 2amino-4-methylphenol, 10g of boric acid and 30g of xylene are added with stirring. The apparatus, equipped with a Dean and Stark water trap, is evacuated and the vacuum released with nitrogen. The light yellow suspension is heated to 160°C and stirred at this temperature for 10 hours, during which time 23-25ml of water and approximately 25g of xylene are distilled off through the water trap. The reaction mixture is cooled to 20°C and stirring continued for 1 hour at this temperature. The yellow suspension is filtered, washed with 100g of N,N-dimethylacetamide and then with three 80g portions of water. The resulting press-cake is dried under a vacuum of 50mbar at 100°C to yield 85g of the compound of formula (106) as a yellow solid, characterized by a UV absorption maximum λ_{max} at 365nm with an extinction coefficient ε of 42000.

Example 7

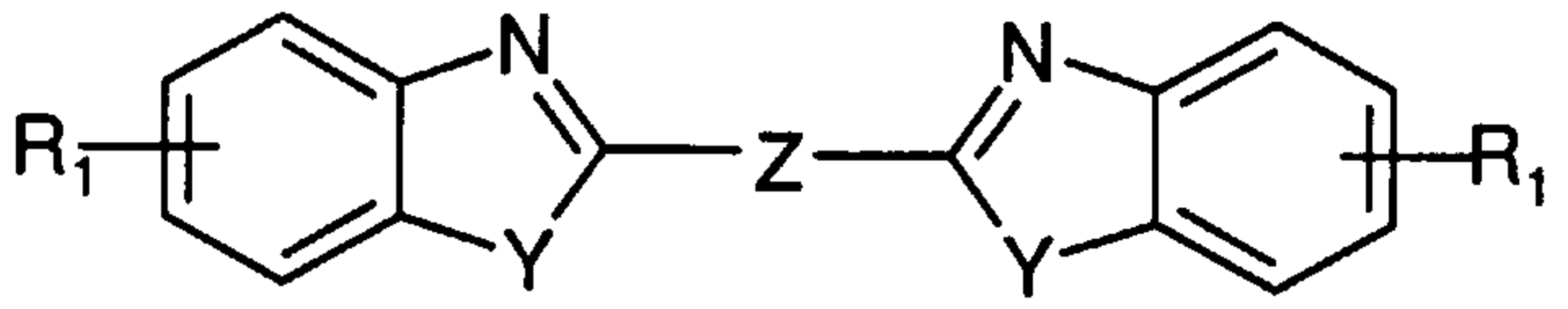


(107)

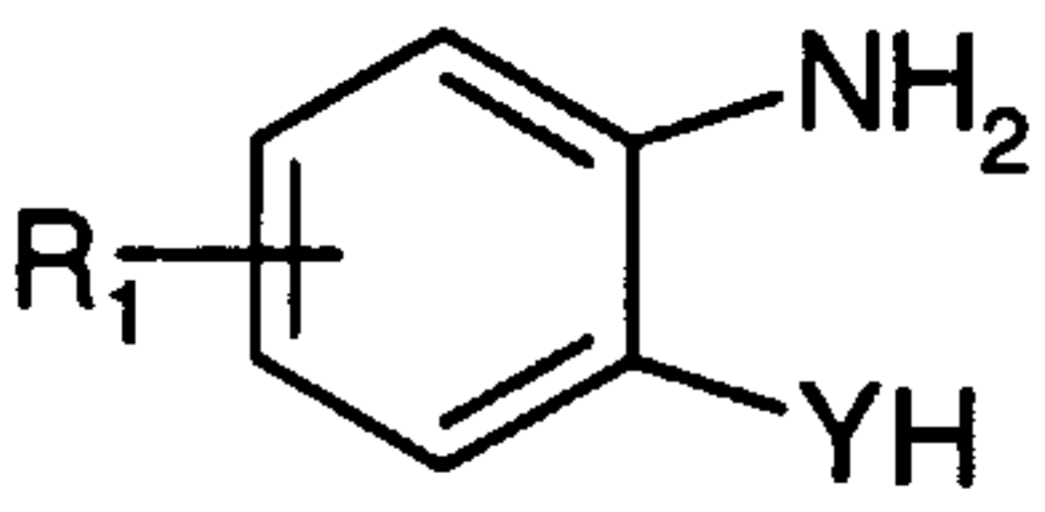
200g of N-methylpyrrolidone are charged to a reaction vessel and 65g of furan-2,5-dicarboxylic acid, followed by 72g of 99% 1,2-phenylenediamine and 10g of boric acid are added with stirring. The apparatus, equipped with a Dean and Stark water trap, is evacuated and the vacuum released with nitrogen. The light yellow suspension is heated to 175°C and stirred at this temperature for 12 hours, during which time 28g of ethanol are distilled off under a weak vacuum. The resulting solution is cooled to 20°C and stirring continued for 1 hour at this temperature. The yellow suspension is filtered, washed with 100g of N-methylpyrrolidone to give 300g of a brown solution which may be used as solvent for a further charge and then with three 80g portions of water. The resulting press-cake is dried under a vacuum of 50mbar at 100°C to yield 95g of the compound of formula (107) as a yellow solid, characterized by a UV absorption maximum λ_{max} at 375nm with an extinction coefficient ε of 42000.

Claims

1. A process for the preparation of a compound of the formula


(1),

wherein
Y represents -O-, -S- or -N(R_2)-,
R_2 being hydrogen, C_1-C_{10}alkyl or aralkyl;
Z represents a 2,5-furanyl, 2,5-thiophenyl, 4,4'-stilbenyl or a 1,2-ethylenyl residue and
R_1 represents hydrogen, halogen, C_1-C_{10}alkyl, C_1-C_{10}alkoxyl, cyano, COOM or SO_3M,
M being hydrogen or an alkaline or alkaline earth metal, characterized by reacting a compound of the formula


(2)

with a dicarboxylic acid of the formula

HOOC-Z-COOH (3)

or an ester thereof, Y, Z and R_1 being as previously defined, in N-methylpyrrolidone or N,N-dimethylacetamide, in the presence of an acidic catalyst and, optionally, in the presence of a secondary solvent capable of removing water from the reaction mixture.

2. A process according to claim 1, in which at least two moles of the compound of formula (2) are reacted with at least one mole of the dicarboxylic acid of formula (3) or an ester thereof.

3. A process according to claims 1 or 2 for the preparation of a compound of formula (1) in which
Y represents -O-, -S- or -N(R_2)-,

R_2 being hydrogen or C_1-C_4alkyl;
Z is as defined in claim 1 and
R_1 represents hydrogen or C_1-C_4alkyl.

4. A process according to claim 3 in which
Z represents a 2,5-furanyl or a 2,5-thiophenyl residue.

5. A process according to claim 3 in which
Z represents a 4,4'-stilbenyl or a 1,2-ethylenyl residue.

6. A process according to any one of claims 1 to 5 in which reaction of compounds of formulae (2) and (3) is carried out in N-methylpyrrolidone.

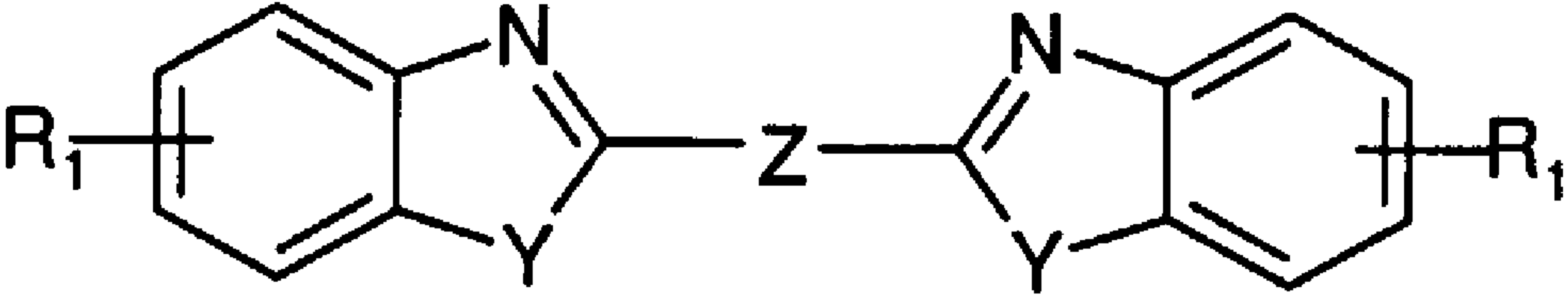
7. A process according to any one of claims 1 to 6 in which the acidic catalyst is boric acid, phosphoric acid, a titanium C_1-C_4orthoester or a tin derivative.

8. A process according to claim 7 in which the acidic catalyst is boric acid or a titanium C_1-C_4orthoester.

9. A process according to any one of claims 1 to 8 in which reaction of compounds of the formulae (2) and (3) is carried out within a temperature range of between 100 and 250°C.

10. A process according to claim 6 in which reaction of compounds of the formulae (2) and (3) is carried out within a temperature range of between 150 and 200°C.

11. A process according to any one of claims 1 to 10 in which the secondary solvent capable of removing water from the reaction mixture is selected from the group consisting of toluene, the xylenes and isomeric mixtures thereof and pyridine.



(1)