JKAU: Sci., **Vol. 19,** pp: 11-22 (2007 A.D. / 1428 A.H.)

Desymmetrization of *Meso*-Diamine with Enantiopure 3-*N*,*N*-Diacylaminoquinazolin-4(3*H*)-Ones

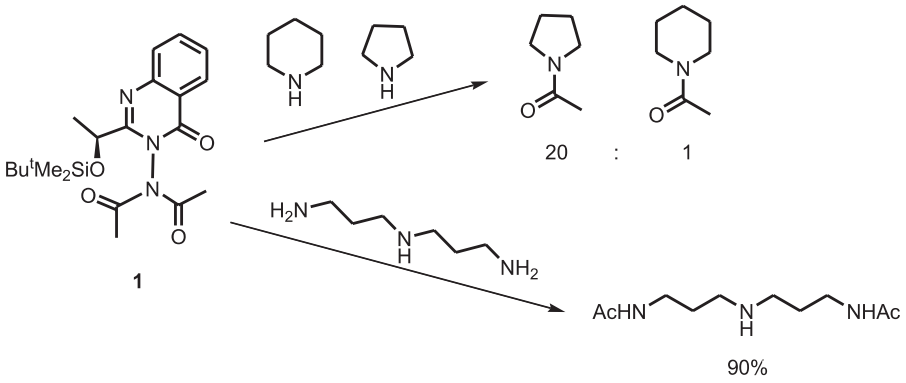
Abdullah G.M. Al-Sehemi

Department of Chemistry, Teacher's College
P.O. Box 249, Abha, Saudi Arabia

Abstract. The title compounds (DAQs) are chiral when the two *N*-acyl groups are different because of the absence of rotation around the *N*–*N* bond (a chiral axis). Enantiopure DAQs have been obtained by incorporation of a chiral centre in enantiopure form bearing a chiral substituent in the 2-position of the quinazolinone, followed by separation of diastereoisomers. One of these diastereoisomers reacts with *meso*-diamine to give *N*-(2-aminocyclohexyl)benzamide (>95%ee).

Introduction

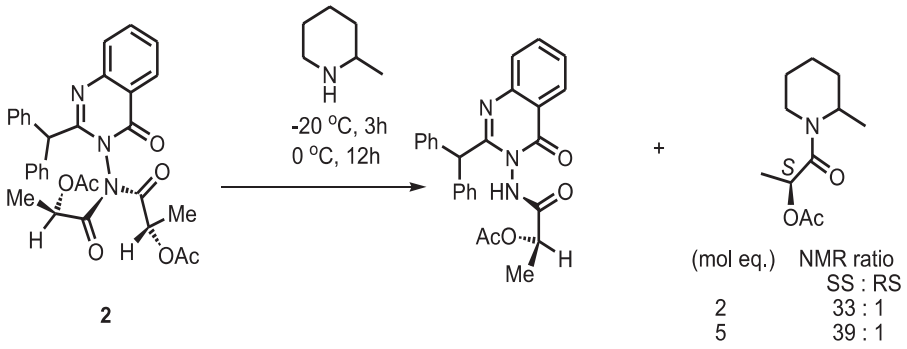
3-(Diacylamino)quinazolinones (DAQs), *e.g.* **1**, are highly chemoselective acylating agents for primary amines in the presence of secondary amines and for the less hindered of two secondary amines (Scheme 1) [1].



Scheme 1

When the two *N*-acyl groups in the DAQ are not identical, the *N–N* bond becomes a chiral axis with the two planes containing the quinazolinone and imide moieties orthogonal to one another. The barrier to *N–N* bond rotation is sufficiently high to allow separation of diastereoisomers (atropisomers) when there is a chiral centre also present in the DAQ. Thus, the stereostructures of both (racemic) diastereoisomers of DAQ **2** have been identified by X-ray crystallography determinations: interconversion between them takes place on heating in toluene ($\Delta G^{\ddagger}$ = 121 kJ mol^{-1}) by rotation around the *N–N* bond [2,3].

The *chemo*selectivity exhibited by, *e.g.* DAQ **1** towards amines (Scheme 1) has a *stereo*selective counterpart, the preferred reaction of an enantiopure DAQ **2** with one enantiomer of a racemic amine giving rise to kinetic resolution of the amine, *e.g.* 2-methylpiperidine (Scheme 2) [4,5].



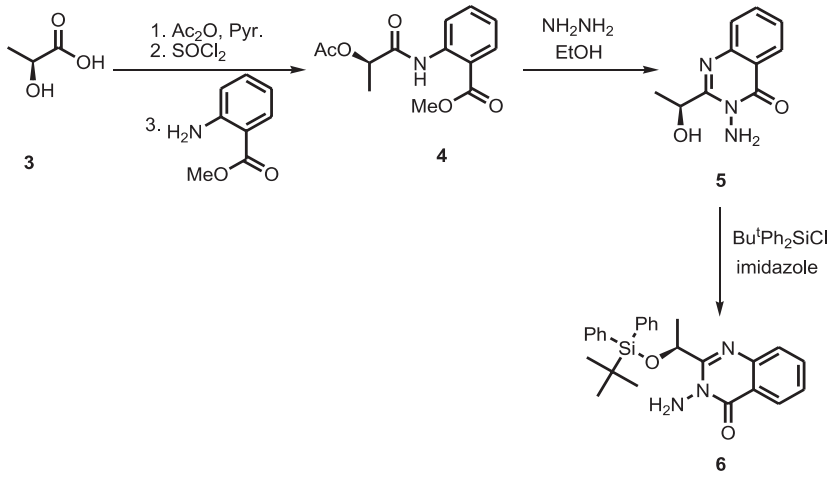
2

Scheme 2

Enantioselective desymmetrization of *meso*compounds is an attractive and challenging subject in asymmetric synthesis [6,7]. A number of enantiodifferentiation methodologies have been developed so far. *meso*-Compounds, such as *meso*-1,n-diols (*n* = 2-4), *meso*-1,2-diesters, and *meso*epoxides, have been mainly examined using enzymic [7] and chemical [8-14] methods to demonstrate the validity of this concept and its application in targeted syntheses of chiral molecules. We report herein the enantioselective desymmetrization of *meso*-diamine which have not so far been dealt with in the enantioselective desymmetrization of *meso*-compounds.

Results and discussion

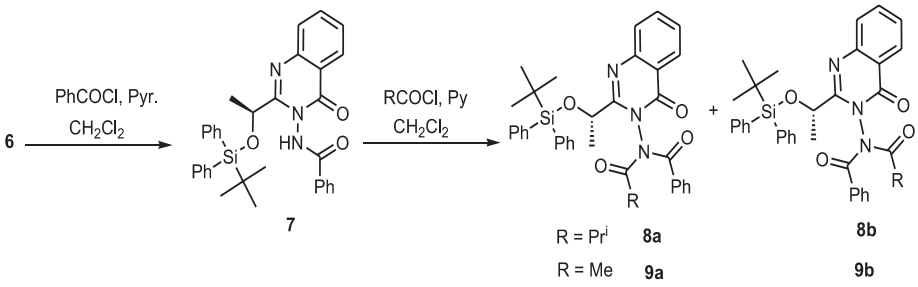
3-Aminoquinazolinone **6** was prepared in enantiopure form from (S)-lactic acid by the route shown in (Scheme 3) in good yield without the need for chromatograph.



Scheme 3

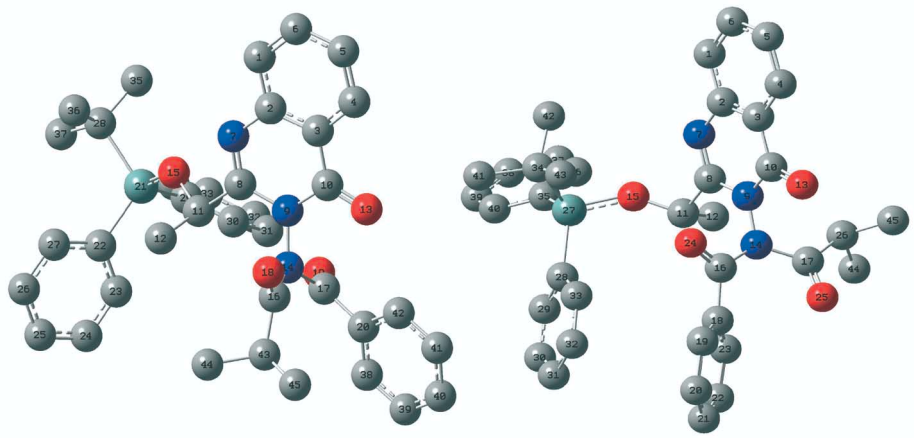
We prepared diacylaminoquinazolinone diastereoisomers **8a** and **8b (DAQ)** by sequential *N*-benzoylation and *N*-isobutanoylation of 3-aminoquinazolinone **6** (Scheme 4). Separation of the DAQ diastereoisomers **8a** and **8b**, formed in a 1.6:1 ratio, was accomplished by Kieselgel chromatography. The barrier to interconversion of DAQs **8a** and **8b** was took place completely after heating at 60ºC for 3h giving a 1:1 ratio of **8a** and **8b**. The barrier to rotation around the *N–N* bond in **7** is as expected, lower than that in DAQ **8a** and does not allow separation of distereoisomers at room temperature.

DAQ **9** was similarly prepared by acetylation of the corresponding 3-aminoquinazolinone **6** with acetyl chloride-pyridine gave a mixture of two diastereoisomeric DAQ **9a** and **9b** in 75% yield (Scheme 4). Separation of these DAQ diastereoisomers, formed in a 3:1 ratio, was accomplished by kieselgel chromatography.



Scheme 4

The geometries were optimized for both diastereoisomers **8a** and **8b** on the levels of HF/6-31G and B3LYP/6-31G. The optimized structures information was shown in Fig. 1. In the geometries structures of DAQ 8a and 8b (Fig. 1) the quinazolinone and imide planes, linked by the *N–N* bond, are as expected, approximately orthogonal to each other. In order to find whether a possible correlation could be established between the stereochemical *endo/exo* (*endo* ≡ C = O *trans* to quinazolinone group) and *exo/exo* (*exo* ≡ C = O *cis* to quinazolinone group) preference of two diastereoisomers **8a** and **8b** determined experimentally (NMR), the estimation of the total energies for the model diastereoisomers **8a** and **8b** was carried out, using several basis sets to evaluate basis set effects using the GAUSSIAN98 program [15]. For all calculations the most stable diastereoisomer corresponds to the *exo/exo* structure **8b.** The computational *endo/exo* and *exo/exo* configurations are illustrated in Fig. 1, along with their relative energies.



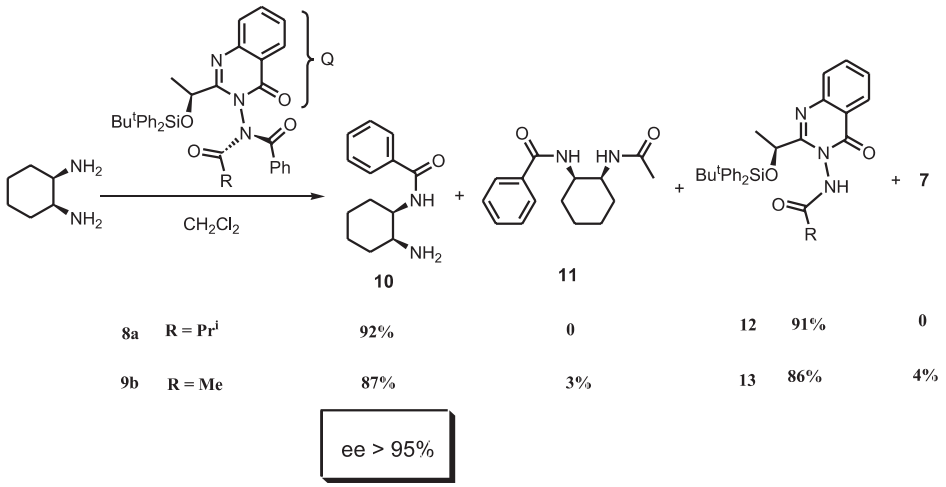
	8a	**8b**
ΔE(kcal/mol)	0	3.36
<N-N-C = O(Ph)	–55.7	–20.9
<N-N-C = O(Pri)	–6.5	30.2

Fig. 1. Optimized structures of DAQs 8a and 8b calculated at the HF/6-31G and B3LYP/6-31G level; dihedral angles (^{0}) and relative energies (k cal/mol).

We used **8a** and **9a** as chiral reagent of the asymmetric desymmetrization reaction as shown in (Scheme 5). Thus, reaction of DAQ **8a** (1 equiv.) with 1,2-diaminocyclohexane (2 equiv.) was carried out in dichloromethane at 5ºC for 12 h. The N-(2-aminocyclohexyl)benzamide **10** formed in the reaction of **8a** with 1,2-diaminocyclohexane was isolated by chromatotron chromatography of the crude reaction product obtained from the dichloromethane layer; the only other product isolated was the 3-isobutanoylaminoquinazolinone **12**. A summary of the yields, and calculated ee of products isolated from these reactions is

given in Scheme 5. The ee in Scheme 5 was based on the optical rotation of a sample of a N-(2-aminocyclohexyl)benzamide, literature results $[\alpha]_D$ = +20.0 (c 1.5, EtOH) [16].

By contrast, DAQ **9a** is formed as a 3:1 mixture of diastereoisomers in good yield (see earlier). However, its reaction, unlike those of DAQ **8a**, is not chemoselective; reaction with 1,2-diaminocyclohexane (Scheme 5) gave a mixture of *N*-benzoyl- and N-acetyl- amides **10** and **11** together with their complementary compounds **7** and **13**.



Scheme 5

Not only is the acylation in the Scheme 5 highly enantioselective but also regiospecific: Only the benzoyl group in **8a** is attacked by the amine. This regioselectivity correlates with the optimized structure of **(8a)** the carbonyl group of the benzoyl is twisted out of the plane which would allow overlap of its p-bond with the lone pair in the π-orbital on the imide nitrogen (the imide nitrogen is not planar; dihedral angle 55.7º between the two planes). The isobutanoyl group, by contrast, is oriented such that it can enjoy normal amide resonance with this imide nitrogen. In which the lone pair on the imide nitrogen overlaps with COPr^i group but not with the COPh group.

Experimental

General

^{1}H NMR spectra were recorded with Bruker ARX 250 and DRX 300 NMR spectrometers respectively. ^{13}C NMR spectra were record at room temperature at 75 MHz. NMR spectra were recorded at room temperature in deuterated chlo-

roform. *J* values are given in Hz. using a Bruker DRX 400 spectrometer. IR spectra of crystalline compounds were recorded at room temperature in dichloromethane and of liquids as thin films using a Perkin-Elmer 298 spectrometer. Standard mass spectra were recorded on a Kratos Concept 1H Magnetic sector Mass Spectrometer with fast atomic bombardment (FAB). Elemental analysis was carried out by CHN analysis. Melting point was determined on a Kofler hot stage and are uncorrected. Dichloromethane was distilled from calcium hydride. Routine drying of organic solutions was carried out using magnesium sulfate. All reaction products were dried under vacuum (~1 mmHg) prior to spectroscopic analysis and further use. Removal of solvent under reduced pressure was accomplished by using a rotary evaporator (Buchi) at (~15 mmHg) water pump.

Preparation of S-(-)-3-amino-2-(1-hydroxyethyl)quinazolin-4(3H)-one 5

(S)-Lactic acid **3** (Aldrich) (22.6 g) was dissolved in dry pyridine (25 cm^3) and acetic anhydride (29 cm^3) added with strirring at 0ºC. After setting aside for 24 h, the solution was poured into ice-water (150 cm^3), stirred for 1 h and extracted with ethyl acetate (3 × 25 cm^3), the combined ethyl acetate layers washed with hydrochloric acid (1M) and then with water, drying and evaporated under reduced pressure using first a water pump and gentle warming, followed by an oil pump. The residual oil was distilled to give 2-acetoxypropanoic acid (b.p. 108-112ºC/0.8 mm Hg) (19.2g, 58%). This acid was converted to its acid chloride by dissolving in dry ether (80 cm^3) adding two drops of *N*,*N*-dimethylformamide and then thionyl chloride (56 cm^3) dropwise with stirring. After setting aside overnight, ether and unreacted thionyl chloride were removed under reduced pressure to give the acid chloride. To a briskly stirred solution of this acid chloride in dry ether (400 cm^3) was added methyl anthranilate (75 cm^3) and the thick white precipitate which formed was stirred for a further 2 h. After setting the reaction mixture aside overnight, the white solid was filtered, washed well with ether and the combined filtrates washed successively with hydrochloric acid (2 M, 5 × cm^3), saturated aqueous sodium hydrogen carbonate and saturated brine then dried and the solvent removed by evaporation under reduced pressure to give methyl-2-acetoxypropanoylanthranilate **4** (31g, 55%); δ_H 1.58 (3H, d, *J* 7, CHCH_3), 2.21 (3H, s, CH_3CO), 3.9 (3H, s, OCH_3), 5.31 (1H, q, *J* 7, C*H*OAc), 7.11 [1H, ddd, *J* 8.2, 7.0 and 1.0, 5-H(Ar)], 7.54 [1H, ddd, *J* 8.5, 7.0 and 1.6, 4-H(Ar)], 8.02 [1H, dd, *J* 8.2 and 1.6, 6-H(Ar)], 8.76 [1H, dd, *J* 8.5 and 1.0, 3-H(Ar)]. The foregoing anthranilate was dissolved in ethanol (40 cm^3) and heated with hydrazine (16.0 cm^3) in a closed steel container at 147ºC for 2 h. After cooling, the bulk of the solvent was removed under reduced pressure and the residue dissolved in dichloromethane (40 cm^3), the dichloromethane solution washed with water (3 × 30 cm^3), dried and the solvent removed under reduced pressure to give 3-amino-

quinazolinone **5** as a pale yellow oil which solidified on standing to give a colourless solid mp 119-121ºC (from ethanol) (18 g, 75%); $[\alpha]_D$ = –29.4o (*c* 1, MeOH); δ_H 1.1 (3H, br d, *J* 6.6, C*H*$_3$CH), 3.6 (1H, br, OH), 4.75 (2H, s, NH_2), 5.14 (1H, q, *J* 6.6, *C*HOH), 7.4 [1H, ddd, *J* 8.2, 7.0 and 1.3, 6-H(Q)], 7.6 [1H, ddd, *J* 8.2, 7.0 and 1.3, 7-H(Q)], 7.65 [1H, dd, *J* 8.2 and 1.3, 8-H(Q)] and 8.16 [1H, d, *J* 8.2, 5-H(Q)].

3-Amino-2-[(S)-1-tert-butyldiphenylsilyloxyethylquinazolin-4(3H)-one 6

The enantiopure 3-aminoquinazolinone **5** (6 g) was dissolved in DMF (15 cm^3), *tert*-butyldiphenylsilyl chloride (8 g,) and imidazole (5 g,) were added and the solution stirred at room temperature for two days. Light petroleum (30 cm^3) was then added, the solution washed with water, dried and evaporated under reduced pressure. Crystallisation of the resulting white solid gave the desired *3-aminoquinazolinone* **6** (11.2 g, 86%), (Found: C, 70.38; H, 6.59; N, 9.47. $C_{26}H_{29}N_3O_2Si$ requires C, 70.39; H, 6.59; N, 9.47 %); $\nu_{max.}$ /cm^{-1} 3336m, 1675m, 1559s and 1570m, δ_H 0.97 [9 H, s, (C*H*$_3$)$_3$CSi], 1.42 (3H, d, *J* 6.6, C*H*$_3$CH), 4.91 (1 H, q, *J* 6.6, C*H*OSi), 5.86 (2 H, s, NH_2), 7.6-84 [14H, structure m, 4 × H(Q) and 10 × H(Ph)]; δ_C 18.7 [(CH$_3$)$_3$*C*, 22.5 (*C*H$_3$CHOSiSi), 26.2 [(*C*H$_3$)$_3$C], 70.8 (*C*HOSi), 120.9, 122.4, 127.4, 128.4, 128.8, 130.1, 132.6, 134.0, 133.5 and 135.3 [12 × CH(Ph) and 4 × CH(Q)], 147.4 [*C*N = C(Q)], 161.4 [C = N(Q)], 166.3 [CO(Q)].

3-Benzoylamino-2-[(S)-1-tert-butyldimethylsilyloxyethy]quinazolin-4(3H)-one 7

To solution of 3-aminoquinazolinone **6** (3 g) in dichloromethane (5 cm^3) containing pyridine (1.5 cm^3) was added benzoyl chloride (1.6 g) dropwise with stirring. After stirring for 12 h at room temperature, more dichloromethane was added and the solution washed with saturated aqueous sodium hydrogen carbonate, then water, dried and the solvent removed under reduced pressure. Yellow oil obtained was triturated with ethyl acetate-light petroleum and the solid obtained crystallised to give the title *3-benzoylaminoquinazolinone* **7** as a colourless crystals (3.1 g, 84%), mp 185-187ºC (from light petroleum-ethyl acetate) (Found: C, 72.4; H, 6.1; N, 7.7. $C_{33}H_{33}N_3O_3Si$ requires C, 72.4; H, 6.1; N, 7.7%); ν_{max}/cm^{-1} 3250 w, br., 1690s and 1610s; δ_H (mixture of *N*-*N* bond rotamers), major rotamer; 1.0 (9H, s, (CH$_3$)$_3$C), 1.44 (3H, d, *J* 6.6, C*H*$_3$CHOSi), 4.91 (1H, q, *J* 6.6, C*H*OSi), 7.3-8.3 [4H, m, H(Q) and 15 × structured m, C*H* (Ph)], and 9.4 (1H, s, NH); δ_C 18.7 [(CH$_3$)$_3$*C* 22.5 (*C*H$_3$CHOSiSi), 26.2 [(*C*H$_3$)$_3$C], 70.8 (*C*HOSi), 121.4, 127.5, 128.2, 128.5, 129.2, 130.1, 131.1, 132.6 133.1, 133.5, 134.0, and 135.3 [18 × CH(Ph) and 4 × CH(Q)], 147.4 [*C*N = C (Q)], 161.4 [C = N(Q)], 166.3 and 167.7 [CO(Q) and PhCO]; minor rotamer

(observable signals), 0.79 (9 H, s, (CH_3)$_3$C), 1.2 (3 H, d, *J* 6.6, CH_3CHOSi); 5.0 (1 H, q, *J* 6.6, C*H*OSi) and 8.9 (1 H, s, NH); from comparison of the intensities of signals at δ 4.91 and 5.0 the ratio of *N-N* bond rotamers is 2:1.

3-(N-Benzoyl-N-isobutanoyl)amino-2-[(S)1-tert-butyldiphenylsilyloxyethyl] quinazolin-4(3H)-one 8a and 8b

3-benzoylaminoquinazolinone **7** (1.5g) dissolved in dry dichloromethane (4 cm^3) containing dry pyridine (0.45 g) was added isobutanoyl chloride (0.6 g) dropwise over 5 min, and the mixture stirred for 3 days with heating under reflux. More dichloromethane was added and the solution washed with saturated aqueous sodium hydrogen carbonate, then water, dried and the solvent removed under reduced pressure. The yellow oil obtained (2 g) was purified by flash chromatography over silica gel with light petroleum-ethyl acetate (4:1) as eluent to give a colourless solid (R_f 0.51). Crystallisation gave the title compound **8** as a white crystals (1.2 g, 71%) which comprised a 2:1 mixture of diastereoisomers see below. Re-chromatography using kieselgel with light petroleum-ethyl acetate (6: 1) as eluent gave the less polar *3-(N,N-diacylamino)quinazolinone diastereoisomer* **8a** (R_f 0.41) as a colourless crystal, (0.5 g, 29%); (Found: MH$^+$, 617.8088. $C_{37}H_{39}N_3O_4Si$ requires *MH*$^+$, 617.8088); δ_H 0.77 (9H, s, (CH_3)$_3$CSi), 1.12 and 1.20 [6H, 2 × d, *J* 6.6, (CH_3)$_2$CHCO], 1.47 (3H, d, *J* 6.6 CH_3CHOSi), 2.98 (1H, *h*, J 6.6 CH_3CHCH_3), 4.93 [1H, q, *J* 5.6, C*H*OSi], 7.3-8.0 [3H, m, 6, 7 and 8-H(Q) and 15 × structured m, C*H*(Ph)], and 8.12 [1H, d, *J* 8.3, 5-H(Q)]; δ_C 18.8 [(CH_3)$_3$*C*Si], 19.6, 19.8 and 20.4 (3 × *C*H$_3$), 26.3 ((*C*H$_3$)$_3$C), 39.4 [(CH_3)$_2$CH], 68.5 (*C*HOSi), 121.6, 122.4, 127.4, 127.7, 128.4, 128.8, 129.1, 129.7, 132.2, 132.6, 133.3, 133.5, 134.2 and 135.5 [(18 × *C*H(Ph) and 4 × *C*H(Q)], 147.1 [*C*N = C(Q)], 157.8 [C = N(Q)], 160.1 [CO(Q)] and 170.3 and 178.9 (2 × CO).

Further elution with the same solution mixture gave the more polar 3-(N,N-diacylamino)quinazolinone *diastereoisomer* **8**b (R_f 0.38) as colourless crystal (0.2 g, 15%); (Found: MH$^+$, 617.8088. $C_{37}H_{39}N_3O_4Si$ requires *MH*$^+$, 617.8088); δ_H 0.87 (9H, s, (CH_3)$_3$CSi), 1.16 and 1.31 [6H, 2 × d, *J* 6.6, (CH_3)$_2$CHCO], 1.7 (3H, d, *J* 6.6 CH_3CHOSi), 2.81 (1H, h, *J* 6.6 CH_3CHCH_3), 5.12 [1H, q, *J* 5.6, C*H*OSi], 7.1-8.1 [3H, m, 6, 7 and 8-H(Q) and 15 × structured m, C*H*(Ph)], and 8.2 [1H, d, *J* 8.3, 5-H(Q)]; δ_C 19.6, 19.9 and 22.7 (3 × *C*H$_3$), 26.3 (*C*H$_3$)$_3$C), 35.3 [(CH_3)$_2$CH], 71.6 (*C*HOSi) 121.8, 127.8, 128.2, 128.8, 129.0, 129.7, 132.0, 132.2, 132.6, 133.3, 133.5, 134 and 135.5 [(18 × *C*H(Ph) and 4 × *C*H(Q)], 147.0 [*C*N = C(Q)], 157.3 [C = N(Q)], 160.3 [CO(Q)] and 170.0 and 179.0 (2 × CO); from comparison of signals at δ_H 2.98 and 2.81 the ratio of diastereoisomers produced was 2:1.

3-(N-Benzoyl-N-ethanoyl)amino-2-[(S)-1-tert-butyldiphenylsilyloxyethyl] quinazolin-4(3H)-one 9a and 9b

3-benzoylaminoquinazolinone **7** (1.5g) dissolved in dry dichloromethane (4 cm^3) containing dry pyridine (0.45 g) was added acetyl chloride (0.45 g) dropwise over 5 min, and the mixture stirred for 2 days. More dichloromethane was added and the solution washed with saturated aqueous sodium hydrogen carbonate, then water, dried and the solvent removed under reduced pressure. The yellow oil obtained on work-up (1.9 g) was purified by flash chromatography over silica gel with light petroleum-ethyl acetate (4:1) as eluent, to give a colourless solid (R_f 0.42). Crystallisation gave the title compound **9** as a colourless crystals (1.2 g, 75%) which comprised a 3:1 mixture of diastereoisomers see below. Re-chromatography using kieselgel with light petroleum-ethyl acetate (6:1) as eluent gave deferments ratio of two diastereoisomers. (Found: MH^+ 589.7559. $C_{35}H_{35}N_3O_4Si$ requires MH^+ 589.7558); ν/cm^{-1} 1745s, 1700s and 1610s. δ_H (mixture of diastereoisomers) major diastereoisomer 0.85 (9H, s, $(CH_3)_3C$], 1.77 (3H, d, *J* 6.6, CH_3CHOSi), 2.2 (3H, s, CH_3CO), 5.14 (1H, q, *J* 6.6, CHOSi), 7.44-8.3 [19H, m, 15 × CH(Ph) and 4 × H(Q)]; δ_C 17.6 [$(CH_3)_3C$], 20.5 (CH_3CHOSi), 25.0 [$(CH_3)_3C$], 70.7 (*C*HOSi), 120.1, 122.4, 126.5, 127.4, 127.5, 127.5, 128.8, 130.1, 131.7, 131.9, 134.2, 134.4 and 134.6 [18 × *C*H(Ph) and 4 × *C*H(Q)], 145.7 [*C*N = C(Q)], 155.6 [*C* = N(Q)], 159.0 [CO(Q)] and 168.3 and 170.1 (2 × CO); δ_H minor diastereoisomer (observable signals), 0.94 [9 H, s, $(CH_3)_3C$), 1.62 (3H, d, *J* 6.6, CH_3CHOSi), 2.28 (3H, s, CH_3CO) and 8.29 [1H, dd, *J* 8.2 and 1.0, 5-H(Q)]; δ_C (observable signals): 17.4 [$(CH_3)_3C$], 20.8 (CH_3CHOSi), 24.9 [$(CH_3)_3CSi$], 70.1 (*C*HOSi), 120.3 [*C*CO(Q)], 145.6 [*C*N = C(Q)], 155.0 [C = N(Q)] 158.9 [CO(Q)] and 168.4 and 170.0 (2 × CO). From comparison of signals at δ 1.77 and δ 1.62 in the NMR spectrum above the ratio of diastereoisomers was 3:1.

Re-chromatography using a chromatotron with light petroleum-ethyl acetate (16:1) as eluent gave a pure sample of the major *diastereoisomer* **9a** as a colourless oil (0.2 g, 13%) (Found: MH^+ 589.7559. $C_{35}H_{35}N_3O_4Si$ requires MH^+ 589.7559); 0.85 (9H, s, $(CH_3)_3C$], 1.77 (3H, d, *J* 6.6, CH_3CHOSi), 2.2 (3H, s CH_3CO), 5.14 (1H, q, *J* 6.6, CHOSi), 7.44-8.1 [18H, m, 15 × CH(Ph) and 6, 7 and 8-H(Q)]; and 8.33 [1H, dd, J 8.2 and 1.0, 5-H(Q)].

Reaction of 3-(N,N-diacylamino)quinazolinone diastereoisomer 8a with a 1,2-diaminocyclohexane

To the 3-(N,N-diacylamino)quinazolinone diastereoisomer **8a** (0.1 g) dissolved in the dichloromethane (1 cm^3) was added 1,2-diaminocyclohexane (37 mg) and the solution stirred at –5ºC for 5h and then at 5ºC for 12 h, mon-

itoring the disappearance of the starting material by TLC. The solvent removed under reduced pressure. Separation of product was carried out using a chromatotron chromatography with light petroleum-ethyl acetate (6:1) as eluent gave compound **12** (76 mg, 91%) (R_f 0.36, 3:1 light petroleum-ethyl acetate), as colourless oil (Found: MH^+ 514.2448. $C_{22}H_{36}N_3O_3Si$ requires M^+ 513.2448), δ_H (mixture of *N-N* bond rotamers), major rotamer, 0.90 [9H s, $(CH_3)_3C$], 1.36 and 1.39 [6 H, 2 × d, *J* 6.9, $(CH_3)_2CHCO$], 1.42 (3H, d, *J* 6.6, CH_3CHOSi), 2.73 [1H, h, *J* 6.9, $(CH_3)_2CHCO$], 4.45 (1H, d, *J* 6.6, *CH*OSi), 7.3-8.0 [10H, structured m, *C*H(Ph) and 6, 7 and 8-H(Q)], 8.12 [1H, d, *J* 8.3, 5-H(Q)] and 8.21 (1H, s, NH); δ_C 18.3 [$C(CH_3)_3$], 19.4, 19.7 and 33.2 (3 × CH_3), 26.2 [$(CH_3)_3C$], (*C*HOSi) missing, 121.4, 122.4, 133.5, 127.4, 128.4, 128.8, 130.1, 132.6 and 135.3 [10 × C(Ph) and 4 × CH(Q)], 146.1 [*C*N = C(Q)], 157.6 [*C* = N(Q)] and 161.4 and 173.9 (2 × CO).

Further elution with the same solvent mixture gave N-(2-amino-cyclohexyl)-benzamide **10** as a colourless oil (65 mg, 92%); $[\alpha]_D$ = +19.6 (c 1.5, EtOH), Lit. [16] $[\alpha]_D$ = + 20.0 (c 1.5, EtOH), ee > 95% .

Reaction of 3-(N,N-diacylamino)quinazolinone diastereoisomer 9a with a 1,2-diaminocyclohexane

As in the previous experiment, a solution of 3-(N,N-diacylamino) quinazolinone major diastereoisomer **9a** (0.1 g) and 1,2-diaminocyclohexane (29 mg) in dichloromethane (1 cm^3) was stirred at 5ºC for ~16 h. After work-up, Chromatotron chromatography with light petroleum-ethyl acetate (4:1) as eluent gave **7** (4 mg, 4%) as colourless crystals (R_f 0.43; 3:1 petroleum-ethyl acetate), identical with that prepared above.

Further elution with the same solvent mixture gave N-(2-aminocyclohexyl)benzamide **10** as a colourless oil (64 mg, 87%); $[\alpha]_D$ = +19.4 (c 1.5, EtOH), Lit. [16] $[\alpha]_D$ = + 20.0 (c 1.5, EtOH) , **ee** > 95% .

Further elution with same solvent gave 12 as a colourless solid (70 mg, 86%) (R_f 0.18) (Found: MH^+ 485.6459. $C_{28}H_{31}N_3O_3Si$, requires MH^+ 485.6458); ν_{max}/cm^{-1} 3470 w br., 1692s, 1610s and 1470s; δ_H (mixture of *N-N* bond rotamers), major rotamer; 0.83 [9H s, $(CH_3)_3C$], 1.42 (3H, d, *J* 6.6, CH_3CHOSi), 2.15 (3H, s, CH_3CO), 4.89 (1H, q, *J* 6.6, C*H*OSi), 7.3-8.0 [10H, structured m, *C*H(Ph) and 6, 7 and 8-H(Q)], 8.12 [1H, d, *J* 8.3, 5-H(Q)] and 8.45 (1H, s, NH); δ_C 18.6 [$(CH_3)_3C$], 21.4 and 22.4 (CH_3CO and CH_3CHOSi), 26.2 [$(CH_3)_3C$], 71.2 (*C*HOSi), 121.4, 122.4, 133.5, 127.4, 128.4, 128.8, 130.1, 132.6 and 135.3 [10 × C(Ph) and 4 × CH(Q)], 147.1 [*C*N = C(Q)], 157.8 [*C* = N(Q)] and 169.4 and 170.9 (2 × CO); minor rotamer (observable

signals), 0.79 (9H, s, (CH_3)$_3$C), 1.49 (3H, d, *J* 6.6, CH_3CHOSi) and 8.27 (1H, s, NH); from comparison of the intensities of signals at δ 1.42 and δ 1.49 the ratio of *N*-*N* bond rotamers is 2:1.

References

[1] **Al-Sehemi, A.G., Atkinson, R.S, Fawcett, J.** and **Russell, D.R.,** *J. Chem. Soc., Perkin Trans*., **1:** 4413 (2000).

[2] **Al-Sehemi, A.G., Atkinson, R.S., Fawcett, J.** and **Russell, D.R.,** *Tetrahedron Lett.*, **41:** 2239 (2000).

[3] **Al-Sehemi, A.G., Atkinson, R.S., Fawcett, J.** and **Russell, D.R.,** *Tetrahedron Lett.*, **41:** 2243 (2000).

[4] **Al-Sehemi, A.G., Atkinson, R.S.** and **Fawcett, J.,** *J. Chem. Soc.*, *Perkin Trans.*, **1:** 257 (2002).

[5] **Al-Sehemi, A.G.,** *J. Saudi Chem. Soc*., **8:** 461 (2004).

[6] **Matsumura, S., Kawai,Y., Takahashi, Y.** and **Toshima, K.,** *Biotechnol. Lett.*, **16:** 485 (1994).

[7] **McKenzie, M.J.,** *Synlett*, 774 (1998).

[8] **Willis, M.C.,** *J. Chem. Soc.*, *Perkin Trans.*, **1:** 1765 (1999).

[9] **Hodgson, D.M., Gibbs, A.R.** and **Lee, G.P.,** *Tetrahedron.*, **52:** 14361 (1996).

[10] **Vedejs, E., Daugulis, O.** and **Diver, S.T.,** *J. Org. Chem*., **61:** 430 (1996).

[11] **Maezaki, N., Soejima, M., Sakamoto, A., Sakamoto, I., Matsumori,Y., Tanaka, T., Ishida, T., In, Y.** and **Iwata, C.,** *Tetrahedron: Asymmetry*, **7:** 29 (1996).

[12] **Yamad, S.A.** and **Katsumata, H.,** *Chem. Lett*., 995 (1998).

[13] **Tierney, J.P., Alexakis, A.** and **Mangeney, P.,** *Tetrahedron: Asymmetry*, **8:** 1019 (1997).

[14] **Nugent, W.A.,** *J. Am. Chem. Soc.*, **120:** 7139 (1998).

[15] **Frisch, M.J., Trucks, G.W., Schlegel, Scuseria, H.B., G.E., Robb, M.A., Cheeseman, J.R., Zakrzewski, V.G., Montgomery, J.A.** and **Stratmann, Jr. R.E.,** *Gaussian, Inc*., Pittsburgh PA (1998).

[16] **Schlichter, W.H.** and **Frahm, A.W.,** *Arch. Pharm. (weinheim)*, **326:** 429 (1993).

إعادة اكتساب التماثل لمركب ميزو ثنائي أمين بمركب ن، ن–ثنائي أسيتيل أمينوكينوأُكزالين–٤–(٣–هـ)–أون

عبدالله غدران السهيمي

قسم الكيمياء ، كلية المعلمين ، أبها – الرمز البريدي ٢٤٩

المملكة العربية السعودية

المستخلص . المركبات المذكورة في العنوان أعلاه تعتبر مركبات كيرالية عندما تكون مجموعتي الأسيل مختلفة، وذلك بسبب غياب الدوران حول الرابطة N-N، وهذا ما يسمى بالمحور التماثلي Chiral axis. حصلنا على متمارئ نقي من DAQs ، وذلك بفصل الدايستريوأزومر المتكون، والذي خطط لعملية الفصل بجعل المجموعة التي في الموضع ٢ لحلقة الكوينازولينون تحتوي على ذرة كربون كيرالية، مما سهل عملية الفصل باستخدام الكروماتوجرافي ، كما تم مفاعلة واحد من الدايستريوأزومر المفصول سابقاً مع مركب ميزو– ثنائي الأمين وأعطى N–(٢–أمينوسيكلو هكسايل) بنزا إمايد بكفائة فصل عالية (٩٥٪).