

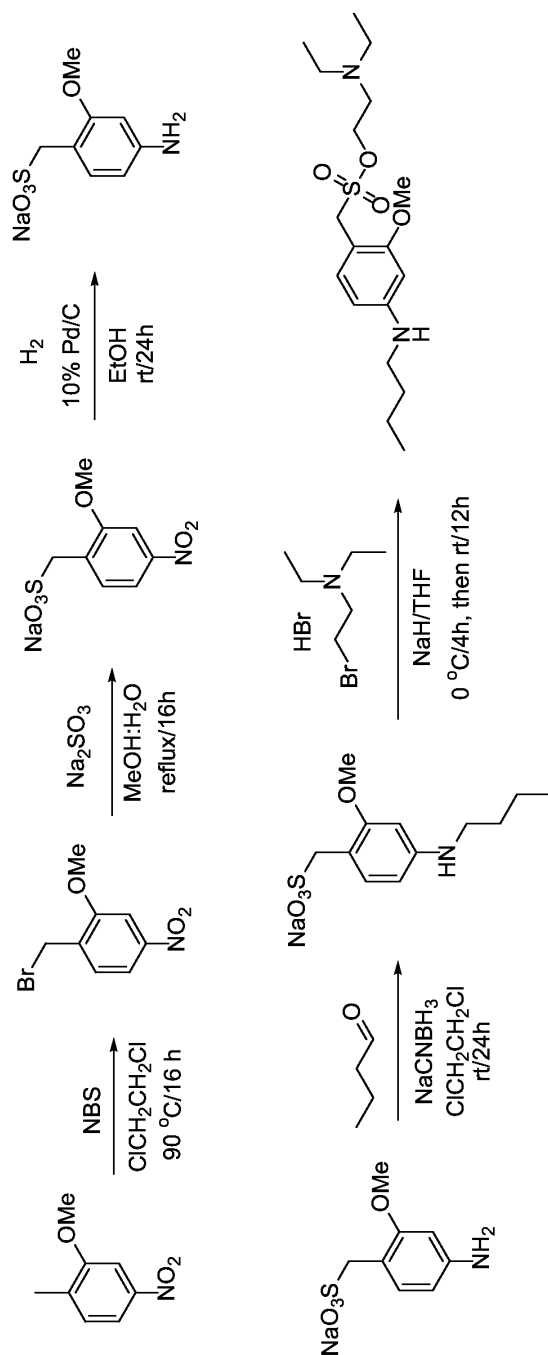
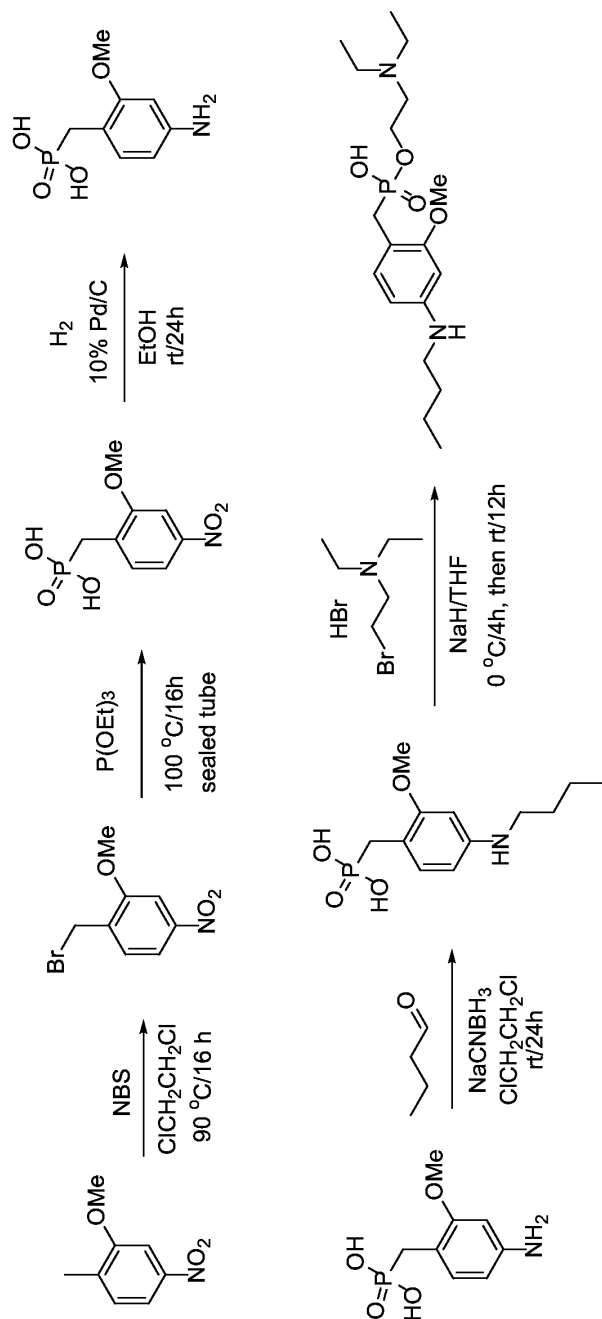


FIG. 1



**FIG. 2**

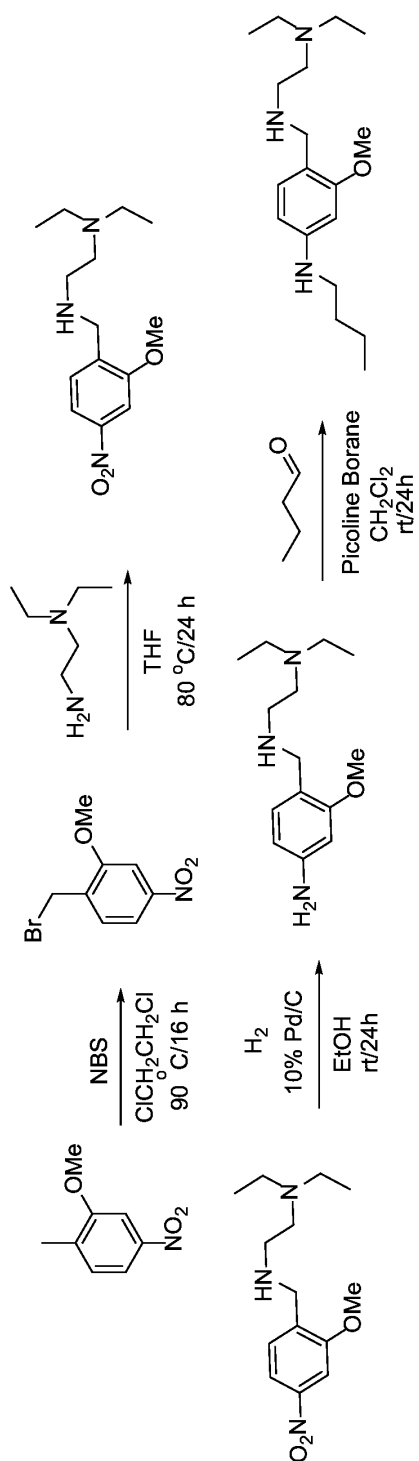


FIG. 3

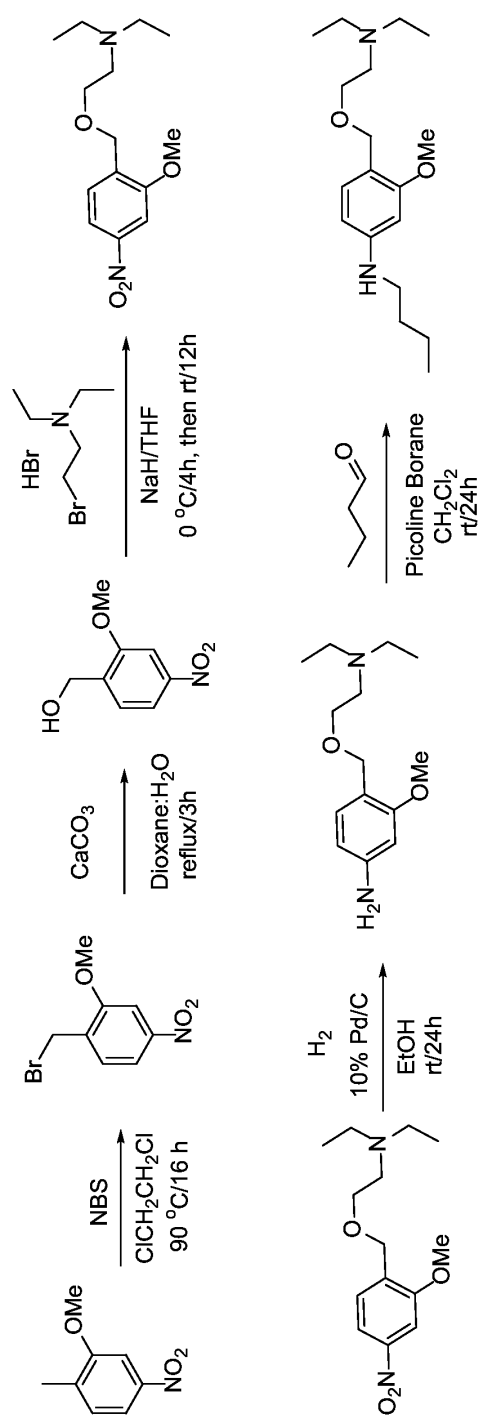


FIG. 4

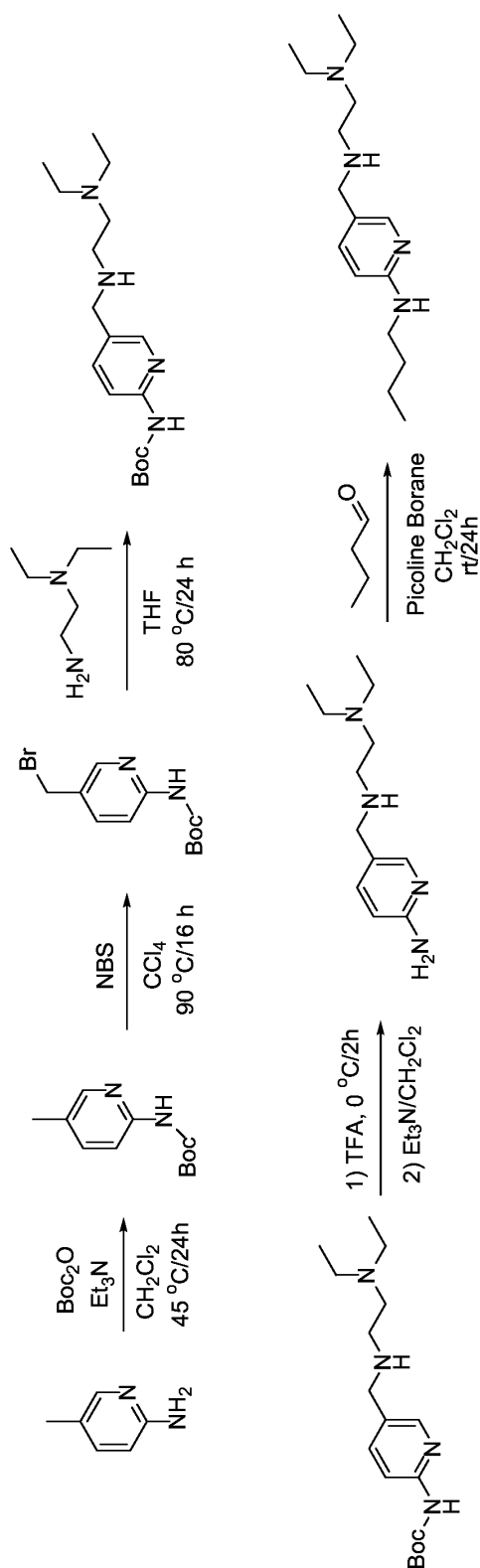


FIG. 5

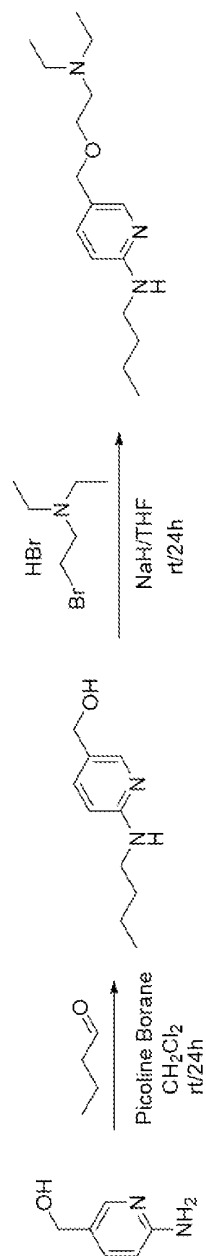


FIG. 6



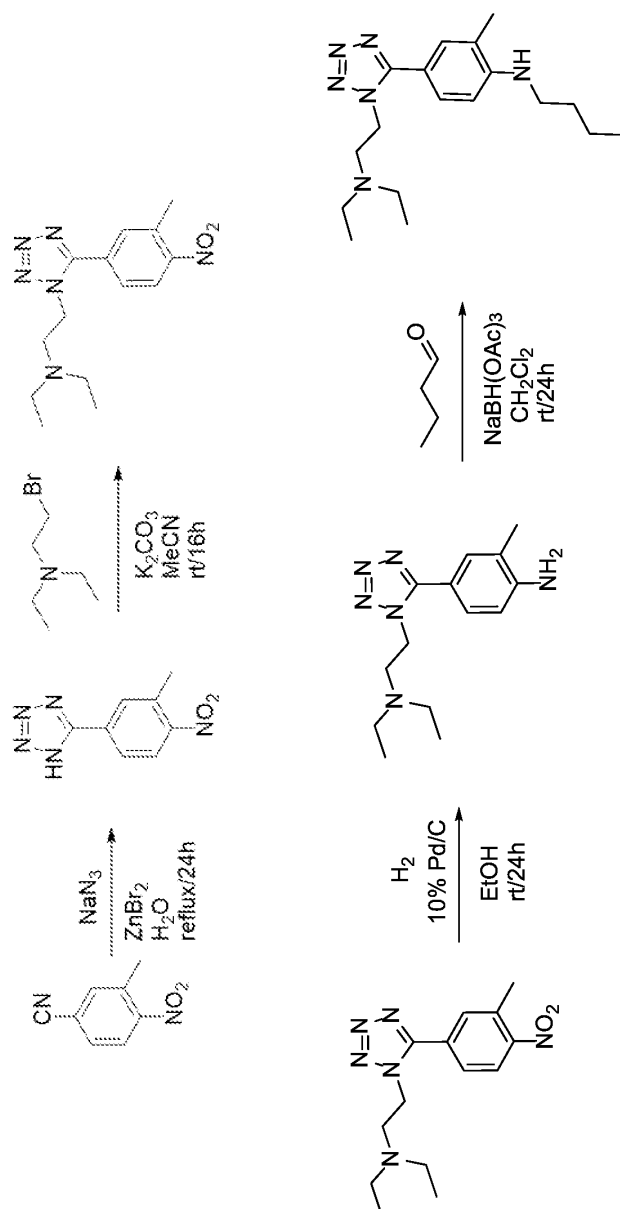


FIG. 8

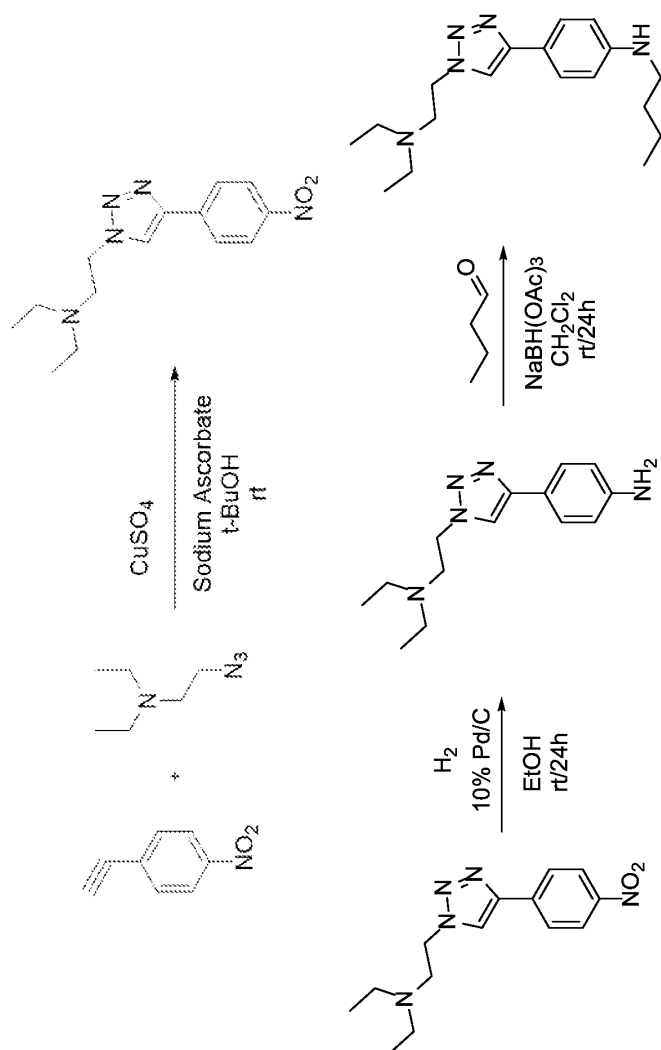


FIG. 9

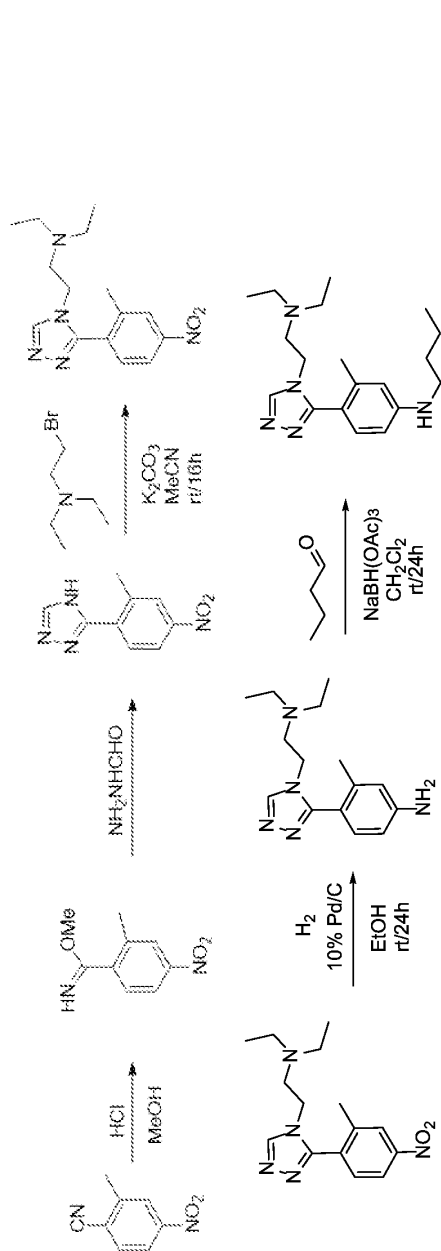


FIG. 10

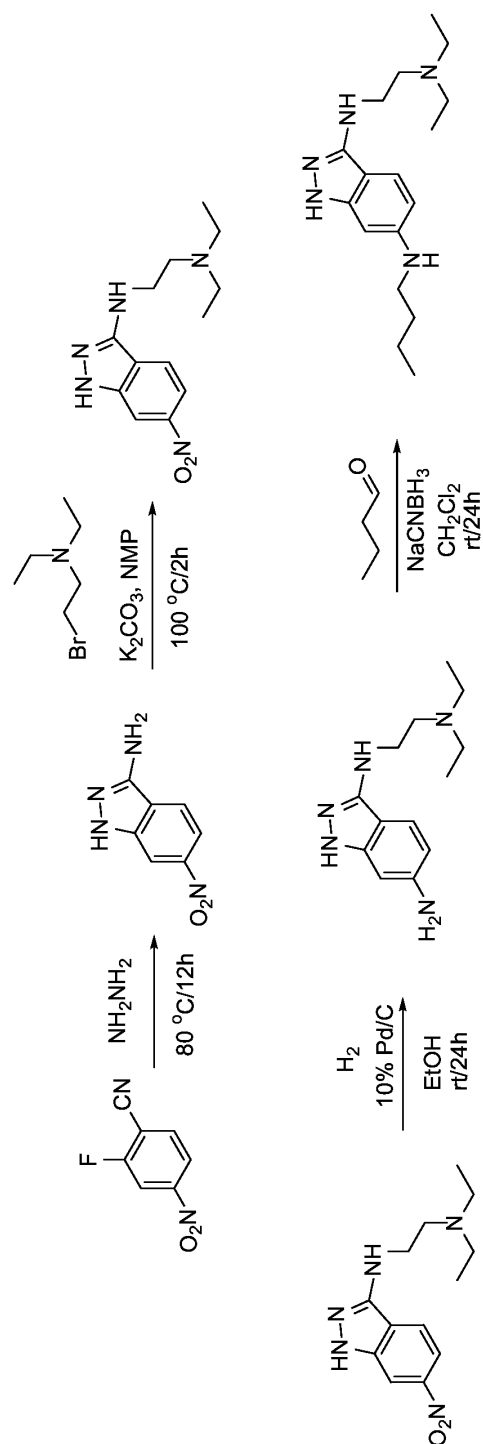
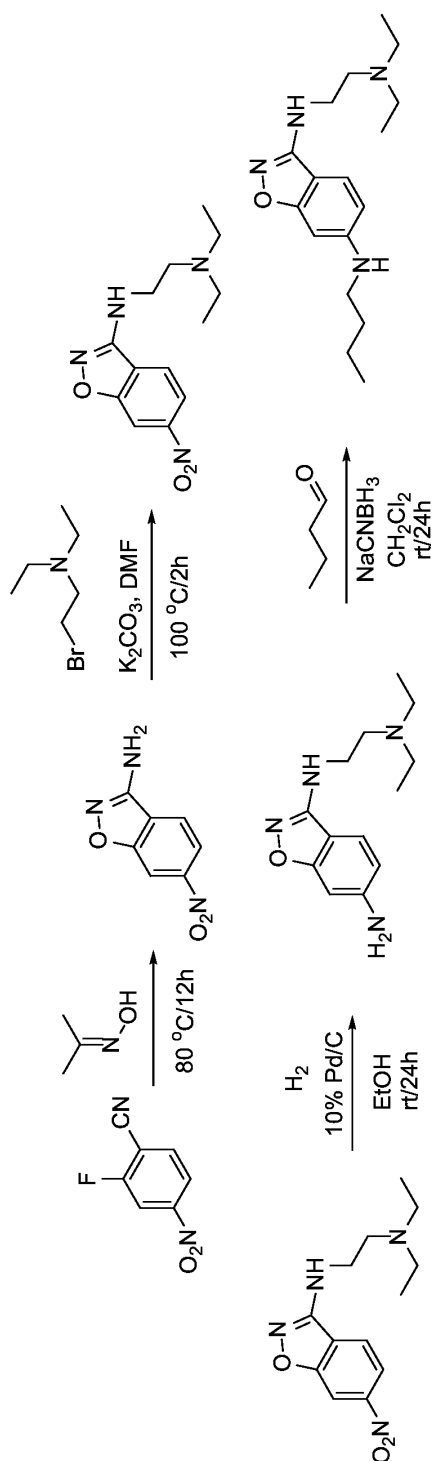
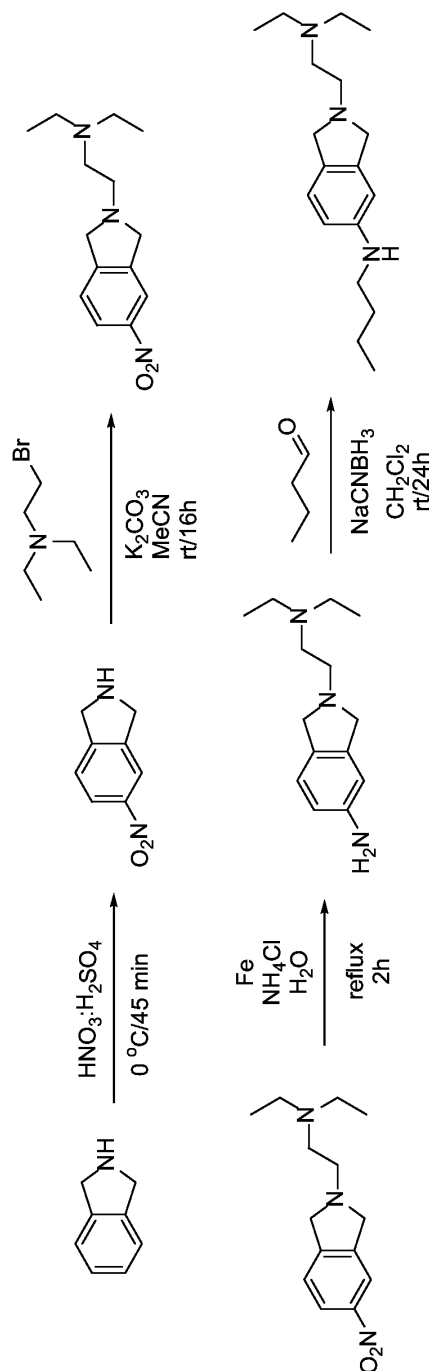


FIG. 11



**FIG. 12**



**FIG. 13**

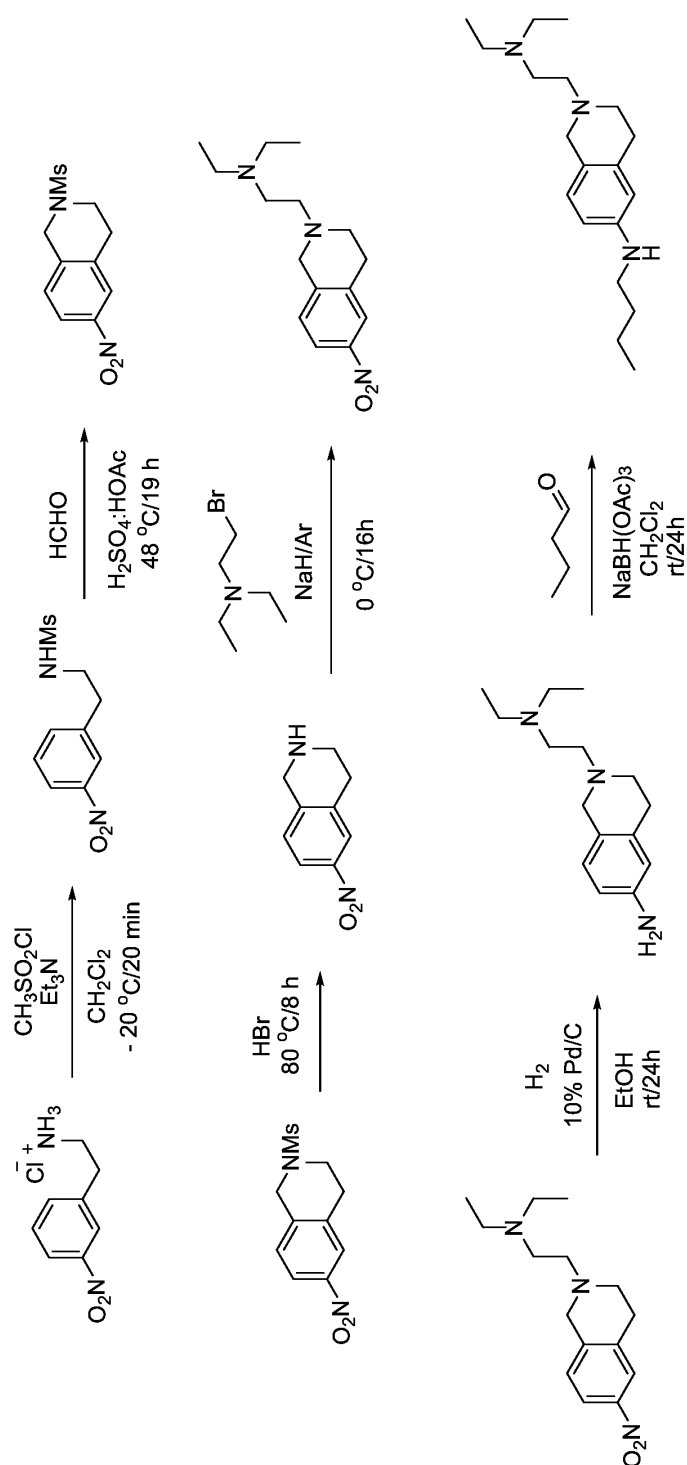


FIG. 14

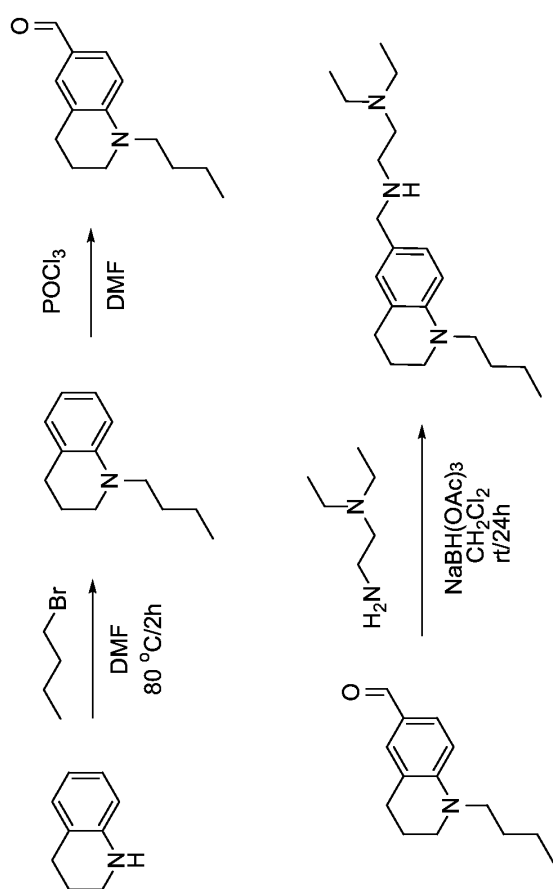


FIG. 15

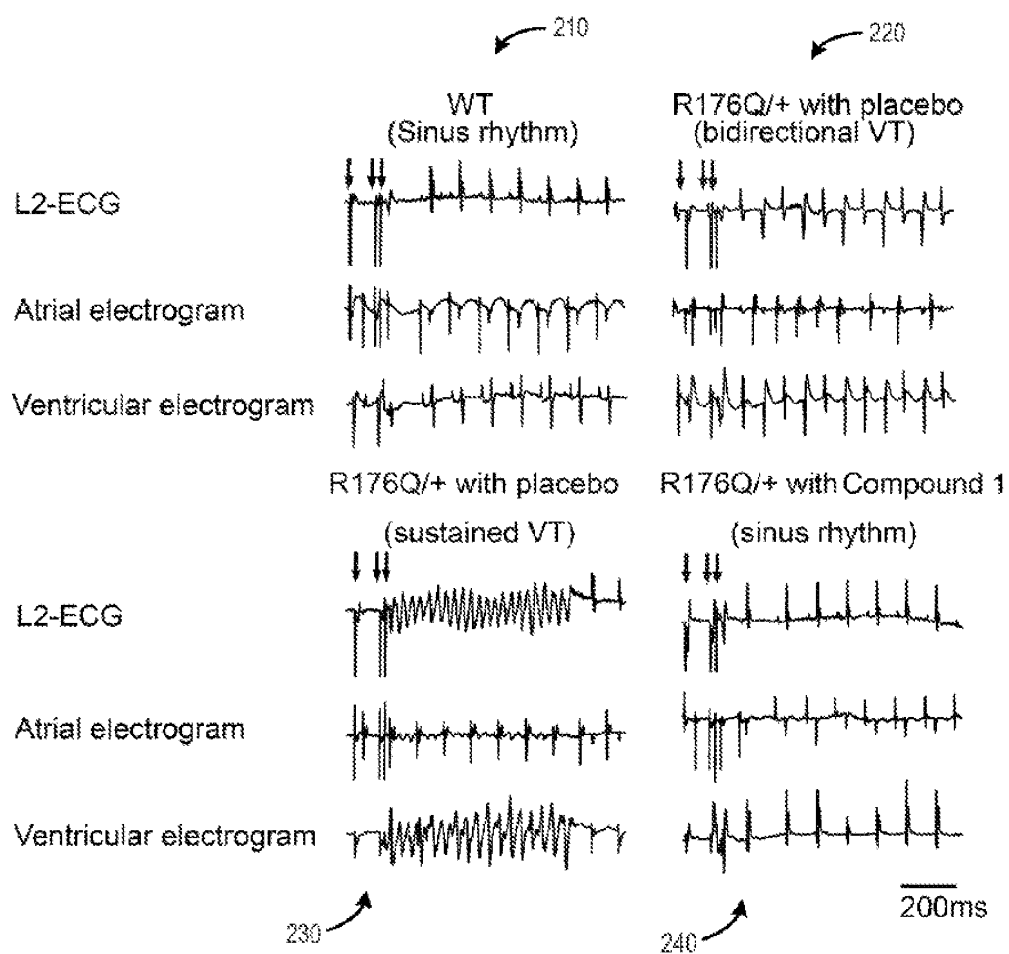


FIG. 16

| Entry | Formula | ID     | Compound Structure | Plasma Stability<br>120 min<br>(Mouse/rat/ human)<br>% | Microsomal Stability<br>60 min<br>(Mouse/Human)<br>% | Cytotoxicity<br>(HEK293/HepG2)<br>$\mu$ M |
|-------|---------|--------|--------------------|--------------------------------------------------------|------------------------------------------------------|-------------------------------------------|
| 1     | VII     | EB3001 |                    | 96.3/90.7/ 94.2                                        | 68.6/66.3                                            | >100/>100                                 |
| 2     | VII     | EB3004 |                    | ---                                                    | ---                                                  | >100/>100                                 |
| 3     | II      | EB3017 |                    | 86.6/91.6/ 91.1                                        |                                                      | >100/>100                                 |
| 4     | IIID    | 251    |                    | ---                                                    | ---                                                  | ---                                       |
| 5     | IIID    | 252    |                    | ---                                                    | ---                                                  | ---                                       |
| 6     | IIID    | 253    |                    | 100.3/97.6<br>(mouse/ human)                           | 1.0/71.4                                             | ---                                       |

FIG. 17A

| Entry | Formula | ID     | Compound Structure | Plasma Stability<br>120 min<br>(Mouse/rat/ human)<br>% | Microsomal Stability<br>60 min<br>(Mouse/Human)<br>% | Cytotoxicity<br>(HEK293/HepG2)<br>$\mu$ M |
|-------|---------|--------|--------------------|--------------------------------------------------------|------------------------------------------------------|-------------------------------------------|
| 7     | IIID    | 254    |                    | ---                                                    | ---                                                  | ---                                       |
| 8     | II      | EB3019 |                    | 94.4/78.6/ 89.0                                        | 74.8/88.6                                            | >33.3 (tox @ 100)                         |
| 9     | II      | EB3021 |                    | 84.9/93.6/ 66.3                                        | 83.1/78.2                                            | >33.3 (tox @ 100)                         |
| 10    | II      | EB3022 |                    | 82.7/93.1/96                                           | 30.76/83.44                                          | >100/>100                                 |
| 11    | VII     | EB3005 |                    | 112/38.0/ 61.2                                         | 102.6/106.8                                          | >100/>100                                 |
| 12    | IIIA    | EB3007 |                    | ---                                                    | 17.0/43.2                                            | 41.7/34.04                                |

FIG. 17B

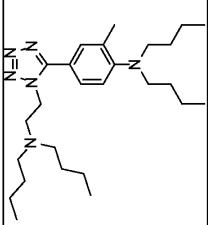
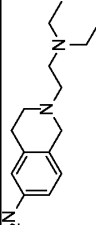
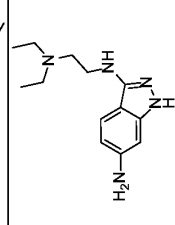
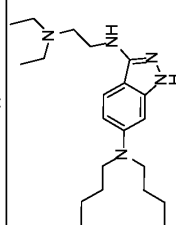
| Entry | Formula | ID     | Compound Structure                                                                   | Plasma Stability<br>120 min<br>(Mouse/rat/ human)<br>% | Microsomal Stability<br>60 min<br>(Mouse/Human)<br>% | Cytotoxicity<br>(HEK293/HepG2)<br>$\mu$ M |
|-------|---------|--------|--------------------------------------------------------------------------------------|--------------------------------------------------------|------------------------------------------------------|-------------------------------------------|
| 13    | IIIA    | EB3008 |   | 52.8/68.9/66                                           | N/A/NA                                               | >100/>100                                 |
| 14    | VIB     | EB3009 |   | 85.9/93.4/ 91.6                                        | 85.77/83.32                                          | >100/>100                                 |
| 15    | IV      | EB3010 |   | ---                                                    | 85.77/83.32                                          | >33.3/>100                                |
| 16    | IV      | EB3012 |  | ---                                                    | 2.51/23.76                                           | ---                                       |

FIG. 17C

| Entry | Formula | ID     | Compound Structure | Plasma Stability<br>120 min<br>(Mouse/rat/ human)<br>% | Microsomal Stability<br>60 min<br>(Mouse/Human)<br>% | Cytotoxicity<br>(HEK293/HepG2)<br>$\mu$ M |
|-------|---------|--------|--------------------|--------------------------------------------------------|------------------------------------------------------|-------------------------------------------|
| 17    | VA      | EB3011 |                    | --                                                     | 1.13/24.67                                           | --                                        |
| 18    | II      | EB3025 |                    | 90.4/90.3/ 93.6                                        | 108.99/71.04                                         | >100/>100                                 |
| 19    | II      | EB3053 |                    | 83.4/92.4/ 90.1                                        | ---                                                  | >100/>100                                 |
| 20    | II      | EB3056 |                    | 92.2/89.6/ 93.3                                        | ---                                                  | >100/>100                                 |
| 21    | II      | EB3057 |                    | 92.2/93.1/ 92.0                                        | ---                                                  | >100/>100                                 |
| 22    | VIA     | EB3059 |                    | 55.2/83.5/ 84.2                                        | ---                                                  | 31.49/30.55                               |

FIG. 17D

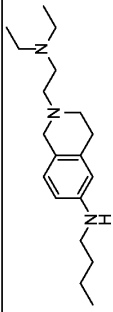
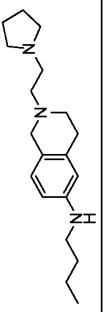
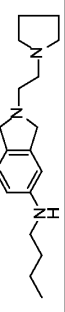
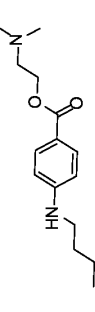
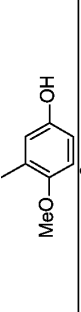
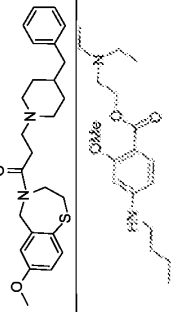
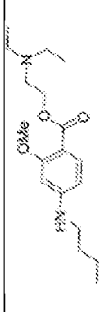
| Entry | Formula | ID                      | Compound Structure                                                                   | Plasma Stability<br>120 min<br>(Mouse/rat/ human)<br>% | Microsomal Stability<br>60 min<br>(Mouse/Human)<br>% | Cytotoxicity<br>(HEK293/HepG2)<br>$\mu$ M |
|-------|---------|-------------------------|--------------------------------------------------------------------------------------|--------------------------------------------------------|------------------------------------------------------|-------------------------------------------|
| 23    | VIB     | EB3060                  |   | 71.7/86.5/ 88.5                                        | ---                                                  | 117.27/96.12                              |
| 24    | VIB     | EB3061                  |   | ---                                                    | ---                                                  | ---                                       |
| 25    | VIA     | EB3064                  |   | ---                                                    | ---                                                  | ---                                       |
| 26    |         | tetracaine<br>(control) |   | ---                                                    | ---                                                  | >50 / >50                                 |
| 27    |         | 4-MmC<br>(control)      |   | ---                                                    | ---                                                  | >50 / >50                                 |
| 28    |         | K201<br>(control)       |  | ---                                                    | ---                                                  | 35 / 29                                   |
| 29    |         | EL20                    |  | ---                                                    | 0%/0%                                                | >50 / >50                                 |

FIG. 17E

| Entry | Formula | ID     | Compound Structure | <i>In vitro</i><br>Ca <sup>2+</sup><br>Spark screen | Ca <sup>2+</sup> Spark<br>IC <sub>50</sub><br>nM | <i>In vivo</i> CPVT<br>screen/ED <sub>50</sub><br>Low & High Dose<br>μg/Kg |
|-------|---------|--------|--------------------|-----------------------------------------------------|--------------------------------------------------|----------------------------------------------------------------------------|
| 1     | VII     | EB3001 |                    | Active                                              | 5.8                                              | ---                                                                        |
| 2     | VII     | EB3004 |                    | Not Active                                          | --                                               | ---                                                                        |
| 3     | II      | EB3017 |                    | Not Active                                          | --                                               | ---                                                                        |
| 4     | IIID    | 251    |                    | Active                                              | 210                                              | ---                                                                        |
| 5     | IIID    | 252    |                    | Not Active                                          | --                                               | ---                                                                        |
| 6     | IIID    | 253    |                    | Active                                              | 100                                              | ---                                                                        |

FIG. 18A

| Entry | Formula | ID     | Compound Structure | <i>In vitro</i> Ca <sup>2+</sup> Spark screen | Ca <sup>2+</sup> Spark IC <sub>50</sub> nM | <i>In vivo</i> CPVT screen/ED <sub>50</sub> Low & High Dose µg/kg |
|-------|---------|--------|--------------------|-----------------------------------------------|--------------------------------------------|-------------------------------------------------------------------|
| 7     | IIID    | 254    |                    | Active                                        | --                                         | --                                                                |
| 8     | II      | EB3019 |                    | Active                                        | 100                                        | 0.95&9.5                                                          |
| 9     | II      | EB3021 |                    | Active                                        | 21                                         | 1.36                                                              |
| 10    | II      | EB3022 |                    | Not Active                                    | --                                         | --                                                                |
| 11    | VII     | EB3005 |                    | Active                                        | 100                                        | 0.32&3.2                                                          |
| 12    | IIIA    | EB3007 |                    | Active                                        | 15                                         | --                                                                |

FIG. 18B

| Entry | Formula | ID     | Compound Structure | <i>In vitro</i><br>Ca <sup>2+</sup><br>Spark screen | Ca <sup>2+</sup> Spark<br>IC <sub>50</sub><br>nM | <i>In vivo</i> CPVT<br>screen/ED <sub>50</sub><br>Low & High Dose<br>μg/kg |
|-------|---------|--------|--------------------|-----------------------------------------------------|--------------------------------------------------|----------------------------------------------------------------------------|
| 13    | IIIA    | EB3008 |                    | Active                                              | 252                                              | --                                                                         |
| 14    | VIB     | EB3009 |                    | Not Active                                          | --                                               | --                                                                         |
| 15    | IV      | EB3010 |                    | Not Active                                          | --                                               | --                                                                         |
| 16    | IV      | EB3012 |                    | Not Active                                          | --                                               | --                                                                         |

FIG. 18C

| Entry | Formula | ID     | Compound Structure | <i>In vitro</i><br>Ca <sup>2+</sup><br>Spark screen | Ca <sup>2+</sup> Spark<br>IC <sub>50</sub><br>nM | <i>In vivo</i> CPVT<br>screen/ED <sub>50</sub><br>Low & High Dose<br>μg/Kg |
|-------|---------|--------|--------------------|-----------------------------------------------------|--------------------------------------------------|----------------------------------------------------------------------------|
| 17    | VA      | EB3011 |                    | Not Active                                          | ---                                              | ---                                                                        |
| 18    | II      | EB3025 |                    | Not Active                                          | ---                                              | ---                                                                        |
| 19    | II      | EB3053 |                    | Not Active                                          | ---                                              | ---                                                                        |
| 20    | II      | EB3056 |                    | Not Active                                          | ---                                              | ---                                                                        |
| 21    | II      | EB3057 |                    | Not Active                                          | ---                                              | ---                                                                        |
| 22    | VIA     | EB3059 |                    | Active                                              | 88                                               | ---                                                                        |

FIG. 18D

| Entry | Formula | ID                   | Compound Structure | <i>In vitro</i> Ca <sup>2+</sup> Spark screen | Ca <sup>2+</sup> Spark IC <sub>50</sub> nM | <i>In vivo</i> CPVT screen/ED <sub>50</sub> Low & High Dose µg/Kg |
|-------|---------|----------------------|--------------------|-----------------------------------------------|--------------------------------------------|-------------------------------------------------------------------|
| 23    | VIB     | EB3060               |                    | Not Active                                    | ---                                        | ---                                                               |
| 24    | VIB     | EB3061               |                    | Not Active                                    | ---                                        | ---                                                               |
| 25    | VIA     | EB3064               |                    | ---                                           | ---                                        | ---                                                               |
| 26    |         | tetracaine (control) |                    | ---                                           | 60,000–100,000                             | ---                                                               |
| 27    |         | 4-MmC (control)      |                    | ---                                           | 2,180                                      | ---                                                               |
| 28    |         | K201 (control)       |                    | ---                                           | 7,730                                      | 500                                                               |
| 29    |         | EL20                 |                    | Active                                        | 35                                         | 2.5/TBD                                                           |

FIG. 18E